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SONS OF GENIUS: CHEMICAL MANIPULATION AND ITS SHIFTING NORMS FROM JOSEPH BLACK TO MICHAEL FARADAY*

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Chemistry, for all the growth in theoretical chemistry, is *the* laboratory science. Some laboratory chemists have the chemical equivalent of the gardener's green thumb; some have raised practice to an art; while others have demonstrated less skill, or have arrived at their results in such a way that their experiments were unreproducible by others. I want to look at some prominent chemists from around the 1750s to 1830, to see how far their writings and published results give us an indication of what made for good practice. Good practice changed a lot in the decades around the Chemical Revolution: acceptable margins of error, accuracy and precision, replicable experiments leading to reliable results—much that we take for granted had to be invented. I shall begin with Joseph Black and end with Michael Faraday. Both were brilliant lecturers and masters of demonstration experiments. Black's public experiments always succeeded, and his publications show a very clear grasp of experimental error. Before Faraday began his electrochemi-
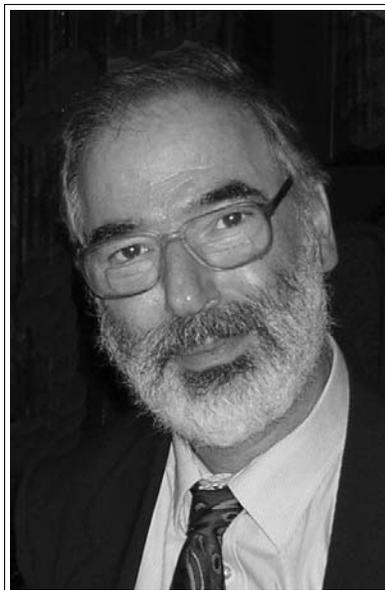
Trevor Levere

cal researches, he worked mainly in analytical chemistry and wrote a book on *Chemical Manipulation*. Faraday explained that he wrote it (1):

>…as a book of instruction, no attempts were made to render it pleasing, otherwise than by rendering it effectual; for … if the work taught clearly what it was intended to inculcate, the high interest always belonging to a well made or successful experiment, would be abundantly sufficient to give it all the requisite charms ….

Joseph Black, like Faraday, inspired his audiences with the charms of chemistry. In the 1750s he had carried out researches on magnesia alba, basic magnesium carbonate. He obtained his results by weighing solid magnesia before heating it and the residue after heating; he concluded that the loss in weight was equal to the weight of gas evolved, and he determined the latter's chemical properties. He described and justified each step of the process, the consequences of omitting any operations, the proportions of reactants, and the need for repeated washing and decanting—as many as twelve washes where perfectly pure substances were required.

Black was wise to obtain the weight of the gas by weighing solids; the process of weighing and measuring gases was a very chancy business in the 1750s. Judging by the crudeness of his surviving glassware supplied by a local bottle factory, he would have had a hard time measuring gases directly. He gave his results to one part in 250, which is very close to what John Stock's modern examination of Black's balance has shown was possible: the balance is accurate to one part in 200 (2).

Joseph Priestley discovered more gases than any other eighteenth-century chemist. He measured gas volumes to two or sometimes three figures. He was aware of the problem of impure substances and of the loss of gas through leakage. His quantitative results were sometimes as good as Black's, sometimes a little (but never a lot) worse. And although some of his apparatus was made for him at the Wedgwood factory, much of it was what one could find in a kitchen or shed.

Priestley, like Black, obtained respectable and acceptable results with simple instruments. Thirty years later than Black, and a decade after most of Priestley's pneumatic experiments, the wealthy and reclusive Henry Cavendish, surely one of the most meticulous experimenters ever, obtained impressive results with simple apparatus, and astonishing results with sophisticated apparatus. The results of his researches on gases were more accurate than those of his contemporaries by an order of magnitude. In 1783 he published an account of a new eudiometer for measuring what we would call the oxygen content of a sample of air. By Cavendish's time, what began as a marginal experiment in chemistry applied to medicine had developed into a key experiment in chemistry. Cavendish worked with nitric oxide, which combined with oxygen to produce the dioxide, which was then absorbed in water; the diminution in volume gave an indication of the goodness of the air, its oxygen content. Previous chemists had measured this volumetrically; it was easier to measure the volume of a gas than its weight, because gases were so much lighter than the vessels that contained them. Cavendish bucked the trend by weighing gases under water, thereby avoiding the problem of moisture adhering to the sides of the reaction vessels. He had a balance vastly superior to Black's, made for him by John Harrison, inventor of the marine chronometer. Cavendish was soon carrying out observations to 1/10 grain, a ten-fold increase in accuracy and sensitivity over Black's—we are up to one part in 2,500.(3) Jesse Ramsden, arguably the finest instrument maker of the eighteenth century, made a balance that was used by Cavendish and others in the Royal Society

of London in the 1780s, and that was sensitive to a hundredth of a grain, a further ten-fold increase in accuracy (4). Although he provided more details of experimental procedure than anyone before him (the best ratio of gases, the shape and size of the vessels used, the rate of mixing the gases, the purity of the airs involved, the importance of using distilled water, and much besides), he observed that (5):

> There are several contrivances which I use, in order to diminish the trouble of weighing the vessels; but I omit them, as the description would take up too much room.

He did, however, assert that his gravimetric method required less dexterity than the volumetric methods used by others. He checked to see if atmospheric air varied from day to day; he tested samples collected on sixty different days and found differences of less than 0.013 (5):

> Though this difference is but small, yet as each of these means is the mean of seven or eight trials, it is greater than can be expected to proceed from the usual errors of experiment.

Consistent results, obtained by repeating experiments, were nothing new; but Cavendish's standards were higher than those of his predecessors and most of his contemporaries, who would have been very happy with such small discrepancies.

Cavendish also determined the oxygen and nitrogen content of the atmosphere, after removing carbon dioxide. There was a small bubble of air left unabsorbed, not more than 1/120 part of the whole. Anyone who used Cavendish's apparatus and who looked carefully would have detected a very small residual bubble; but no one else in the eighteenth century recorded such an observation (6). In 1894 William Ramsay and Lord Rayleigh announced their discovery of argon, the first inert gas (7). No one, to my knowledge, detected the inert residue in the ninety years between Cavendish and Ramsay (8).

It was, as Black and Cavendish knew, essential to work with pure substances, but the way to obtain them was often obscure. In the mid-1790s, Thomas Beddoes, a former pupil of Joseph Black, was the leading English figure in the development of medicine using various gases for therapeutic purposes. He advocated the use of oxygen for respiratory disorders and recommended manganese treated by mineral acids to prepare the oxygen. The purity of the manganese used was crucial. Beddoes sought a pure mineral source, rather than purifying impure ores himself. Erasmus Darwin, Charles Darwin's grandfather, perhaps the bulkiest and

the foremost physician in England, was a close friend of the engineer James Watt (9); he followed pneumatic treatments closely and used manganese supplied by Watt. It was not uniformly reliable. Darwin informed him that one of his patients (10):

> has breathed …pure oxygene [daily] for … 2 or 3 weeks, till he tried the last parcel of manganese, which was sent from your people; the air from which gave him a burning feel[ing in] his lungs with something like suffocation, which obliged him to desist...

Darwin blamed impure manganese. Watt was a good but not great laboratory chemist, who also practiced pneumatic medicine on his employees. The same could be said about Beddoes. While lecturing at Oxford, Beddoes experienced difficulties in performing demonstration experiments. He wrote to Black (11):

> What I find most difficult is to repeat some of those apparently simple exp^s. which in your hands are so striking and so instructive. I have not yet learned how to show the gradual approach towards saturation by throwing slowly a powdered salt into water. What salt do you use? & how do you perform the exp^t? How do you contrive to make that capital exp^t which shews the burning of iron in deph^d air? I mean to attempt it, but am told that the vessel has been frequently in other hands burst with great violence?

Joseph Black

Beddoes was no Black; one account of his lectures complains that he was (12):

> …so singularly awkward in the mechanical part of his experiments that they generally failed, and he was then compelled to proceed in his discourse on the hypothesis that the result had been the reverse of that which the eyes of his audience would have led them to believe.

Beddoes's demonstration experiments sometimes failed; those carried out by Lavoisier in the 1780s were successful. Lavoisier, the presiding genius of the Chemical Revolution, had encouraged his instrument makers to construct what was the most dramatic and, in the case of his best balance, the most sensitive chemical apparatus of the eighteenth century. Modern estimates put the accuracy of his great balance made by Fortin, formerly engineer to the King, at 1/400,000, an accuracy that cannot be beaten by the best mechanical balances today (13). His gasometers were masterpieces. He used them to demonstrate the composition of atmospheric air and of water. His demonstration experiments were on the grand scale. In using his gasometers, Lavoisier worked volumetrically. When working with gases by volume and solids by weight, for example in the oxidation of mercury, he measured the volumes of gases, corrected these for temperature and pressure, and then converted these to weights, via densities. That sounds straightforward; but he noted that gases were sometimes lost through leakage from the apparatus and sometimes contaminated by the accidental entry of atmospheric air. He often dismissed such leakage and contamination as trivial. Predictably, this could lead him astray. He reported in his *Traité* of 1789 that atmospheric air was composed of 27% of oxygen and 73% nitrogen by volume (14)—a poor result, so poor that chemists elsewhere had a hard time replicating it. Water was 16% hydrogen by weight, a pretty poor result again, since water is about 11% hydrogen. Lavoisier was working in the certainty (shared by all chemists) that the weight of reactants was equal to the weight of products, and once he had obtained a result manifesting this equality, he *knew* that this was the right result, superior to one obtained by taking the average of a large number of experiments; at most, he would rely on a small number of experiments. He sometimes published his results to six, seven, or even eight figures. These figures were the result of computation, converting from one system of measurement to another, and Lavoisier explained this—but his explanation was and is easily overlooked.

William Nicholson, editor of *A Journal of Natural Philosophy, Chemistry and the Arts* and author of textbooks and a dictionary of chemistry, was scathing about publishing long strings of numbers (15). In his dictionary, Nicholson gave an account of balances, from which (16):

> …the student may form a proper estimate of the value…of the theoretical deductions in chemistry that depend upon a supposed accuracy in weighing, which practice does not authorize. In general, where weights are given to five places of figures, the last figure is an estimate, or guess figure; and where they
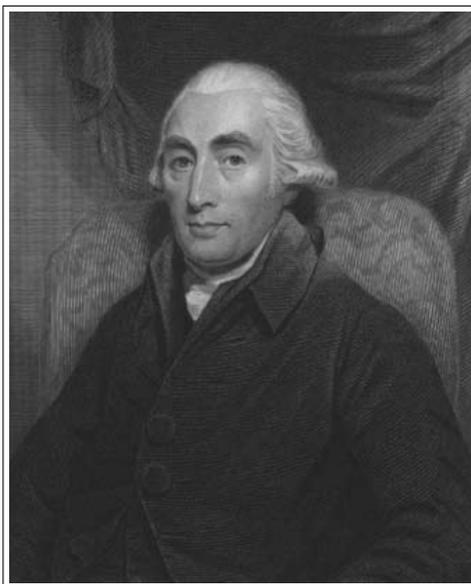
are carried farther, it may be taken for granted that the author deceives either intentionally, or from want of skill in reducing his weights to fractional expressions, or otherwise.

He examined the stages involved in Lavoisier's experiment of the synthesis of water by the continuous combustion of hydrogen and oxygen and concluded that the estimation of hydrogen was at best good to three figures, and of oxygen to four (17).

Lavoisier was, in spite of these strictures, a skilled experimenter and brilliant theoretician; and his published and unpublished results were mostly good and repeatable by others. But there were other chemists who knew what the results *should* be, and whose results were not repeatable. Usselman has charitably called them careless chemists. Thomas Thomson was one such (18). His weakness was his conviction that Prout's hypothesis was true: all atomic weights had to be integral multiples of the atomic weight of hydrogen. Thomson was convinced that the very numerous investigations he described fully confirmed Prout's hypothesis (19).

He had taken great pains to obtain the right results, sometimes repeating an experiment eight or ten times before he was satisfied. In the case of nitrogen, he started with nitrates and nitric acid. One set of results gave him the atomic weight of nitrogen as exactly 14 times that of hydrogen. Another set of experiments gave him a slightly different figure. It was clear to him that the latter set of experiments was in error (20):

Had I obtained from 8.65 grains of nitre 4.004 cubic inches of azotic gas, instead of 4 cubic inches, this error would not have existed. But my apparatus was not delicate enough to measure the gas evolved 80 exactly—I may, in reality, have obtained 4.004, cubic inches, without perceiving the slight difference in volume.

And so he was able to explain away the small discrepancy in the results of one set of experiments. When he came to hydrochloric acid, containing one atom of hydrogen and one atom of chlorine, he showed that the atomic weight of chlorine was exactly 36 times the atomic weight of hydrogen. He cited Gay-Lussac's measurement

of the vapor density of chlorine, which differed slightly from his own (21):

If the temperature (as is most likely) was a few degrees above 60, his experiments would coincide exactly with my own.

Such reasoning enabled him to accept Prout's hypothesis as absolute (22). Contemporary chemists, including Berzelius, were far from convinced.
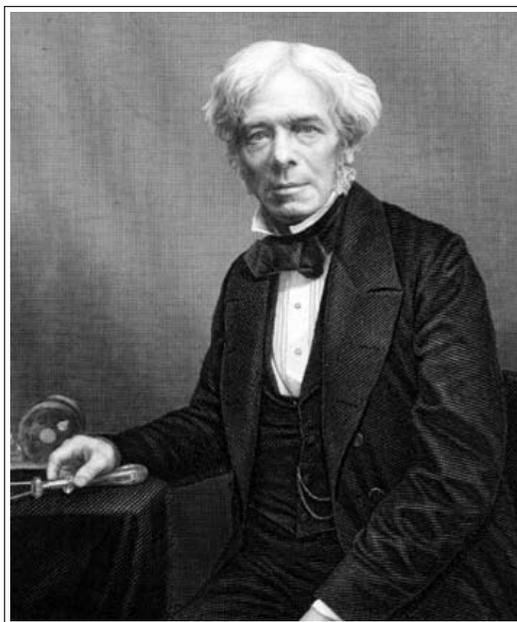
Berzelius, Davy, Faraday, and, as Rocke and Usselman have shown, Liebig (23) were among Thomson's near contemporaries who were meticulous in obtaining reproducible results that others could verify by repeating their experiments. Liebig and Thomson both had a teaching-research laboratory, although Liebig's was successful and Thomson's failed. Davy and Faraday each gave brilliant public lectures on chemistry. Faraday uniquely wrote a manual on the practice of experimental chemistry. Reading that manual gives us the opportunity to be guided by a great chemist through the full range of operations and apparatus in the early nineteenth century.

Michael Faraday

Up until the late eighteenth century, chemistry had been predominantly a science of qualities, although noting quantities; after the chemical revolution, chemical quantities were as important as qualities. The central instrument for quantifying chemistry was the balance. Faraday devoted 44 pages to its use. The precision balance was the most complex instrument that he discussed, and he explained that active chemists would need one, as well as two common balances, one for large and one for small weights (24):

…for the weights with which it is necessary to work are almost without limit, and cannot be estimated by the same instrument.

The precision balance should be able to ascertain differences of the 1/50,000 or 1/60,000 part of the weight in the scale

Faraday devoted 116 pages to "pneumatic manipulation, or management of gases", a field where, as we have

seen, experimental skills and therefore experimental results had varied widely. But Faraday was not concerned merely with sensitive apparatus and complex operations. At the other extreme were brief accounts of the uses of such simple items as corks and filter paper. Glass blowing was a crucial skill for chemists, at a time when there were few suppliers of chemical apparatus, and when most chemists were their own glass blowers; he gave a detailed account of "bending, blowing, and cutting of Glass." All his descriptions and prescriptions are clear, concise, and elegant. But Faraday insisted that one could not become a chemist by merely reading his book (25):

> No valuable experimental knowledge can be obtained at so cheap a rate. Practice is essential to that facility, without which nothing dependant upon the hands can be done well.

And so he provided a course of "inductive and instructive practices." Faraday was a virtuoso in performing experiments, and a superb teacher of chemical practice.

By the time Faraday wrote, the canons of good laboratory practice had shifted significantly from those of a quarter century before. Volumetric analysis had become precise, and getting results as good as Cavendish's was a reasonable goal for competent chemists. Weighing gases directly and accurately had replaced Black's indirect method. Gone was Lavoisier's insistence that single experiments sufficed if reactants and products could be shown to have exactly the same weight; Lavoisier's method unwittingly showed that weights could balance and yet, given compensating errors, could be seriously awry. Reasonable limits of error were defined and refined; Nicholson's criticisms of Lavoisier showed this process at work, as did Cavendish's insistence that it was necessary to be able to repeat an experiment several times to demonstrate consistency and to arrive at an acceptable result. Cavendish had provided a model for identifying causes of error and modifying experimental procedures to minimize them. Black had been scrupulous about the need to obtain pure substances by repeated washing, distillation, solvent extraction, and more. Davy's first Bakerian lecture, on some chemical agencies of electricity, was a model for eliminating contamination from the atmosphere, from reagents, and from reaction vessels. Chemists increasingly described their experiments and their apparatus in sufficient detail for others to repeat them, and sought to avoid unnecessary complexity in the design of experiments. By Faraday's time, chemical methods had been transformed from those in normal use at the start of the chemical revolution.

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25.   Ref. 1, p 620-621.

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Teaching History of Chemistry

The report on "TEACHING HISTORY OF CHEMISTRY IN EUROPE," based on the information sent by many teachers of history of chemistry in Europe, has been a project of the Working Party on the History of Chemistry EuCheMs *http://www. euchems.org/Divisions/History/*

It has been coordinated by José Ramón Bertomeu-Sánchez, with the help of Ernst Homburg and Evangelia Varella, and is now available for download at:

http://www.euchems.org/binaries/Nov07TeachingHistReport_tcm23-108306.pdf

In order to update the information, please send your comments, additions and amendments to José R. Bertomeu, Departament d'Història de la Ciència i Documentació Facultat de Medicina Blasco Ibañez, 17 46010-València, SPAIN. bertomeu@uv.es .

'AFFINITY': HISTORICAL DEVELOPMENT IN CHEMISTRY AND PHARMACOLOGY

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'Affinity' is a word familiar to chemists and pharmacologists. It is used to indicate the qualitative concept of 'attraction' between a drug molecule and its receptor molecule without specification of the mechanism (as in, drug A has affinity for receptor R) and to indicate a relative measure of the concept (as in, drug **A** by the following measure has greater affinity than does drug B for receptor R). It also is used to quantify the concept (as in, the affinity of drug A for receptor R is some nM value). Unfortunately, the meaning and use of affinity have diverged historically such that a pharmacologist would likely be puzzled by the recent statement in Khoruzhii *et al*. (1) "… the binding affinity, *or equivalently binding free energy* [emphasis added]…", whereas a chemist would not (2).

That different disciplines use the same term in different ways is not unusual, nor generally of much concern if the fields do not overlap. But the recent ability to measure thermodynamic parameters of drug-receptor interactions by means of isothermal titration microcalorimetry devices and other techniques (see Ref. 3), increasing use of thermodynamics in computational molecular modeling and other aspects of the study of drug-receptor interactions (see Ref. 4) and practical application to drug discovery efforts (see *e.g*., 5 and example below) portends an inevitable intersection of the different 'affinities' and likely confusion. We review the history of the use of the word affinity leading to the different contemporary definitions in chemistry and pharmacology.

Affinity as Proximity

From the derivation of the word from the Latin, it can be seen that affinity originally referred to the proximity of two things (6):

> **Affinity** [L. *affinitas*, from *affinis*, adjacent, related by marriage (as opposed to related by blood, consanguinity); *ad*, to, and *finis*, end]

This use is purely descriptive in that it refers to a situation that already exists, *i.e*., the marriage has taken place already. No predisposing or mechanistic explanation was explicit—that is, although the state of being 'related by marriage' is recognized as being attributable to emotional or social driving forces, the final state (the marriage) is not the same as what led to the marriage (the emotional and/or social driving forces). More modern use of the word denotes a *mutual attraction*, as, there is an affinity between them, or, they have affinity for each other. This is an important distinction that also underlies the divergence of definitions in the scientific use of the word. Note the subtle transition from the adjacency itself (the marriage) to the explanation of why they *remain* adjacent (*viz*., the affinity between them) and a second subtle transition towards why they *became* adjacent (*viz*., the affinity drew them together, as if it were a force).

~ Esprits acides.
Acide du sel marin.
Acide nitreux.
Acide vitriolique.
Sel alcali fixe.
Sel alcali volatil.
Terre absorbante.
SM Substances metalliques.
Mercure.
Regule d'Antimoine.
Or.
Argent.
Cuivre.
Fer.
Plomb.
Etain.
Zinc
PC Pierre Calaminaire.
Soufre mineral.   [Principe.
Principe huileux ou Soufre
Esprit de vinaigre.
Eau.
Sel   [denta
Esprit de vin et Esprits ar

Fig 1.   *The first of several affinity tables (tables des rapports) prepared by Geoffroy based on displacement reactions and presented to the French Academy (Ref. 8).*

Affinity as (Mutual) Attraction

The use of the term affinity in chemistry appears to have followed a similar transition. From the Oxford English Dictionary (7):

An attraction drawing to anything

1616   [Surflet & Markh] "For this dung, by a certaine affinitie, is grateful and well liked of Bees".

Chemical attraction; the tendency which certain elementary substances or their compounds have to unite with other elements and form new compounds

1753   [Chambers] "M. Geoffroy has given [in 1718] a table of the different degrees of affinity between most of the bodies employed in chemistry." (**Fig. 1**) (8).

1782   [Kirwan] "Chemical affinity or attraction is that power by which the invisible particles of different bodies intermix and unite with each other so intimately as to be inseparable by mere mechanical means."

In light of subsequent developments, it is instructive to see how Lavoisier (**Table 1**) used affinity in his influential 1790 book *Elements of Chemistry* (9). Noting the reversible nature of the separation and recombination of substances, he remarked (p 3):

It is supposed, that, since the particles of bodies are thus continually impelled by heat to separate from each other, they would have no connection between themselves; and, of consequence, that there could be no solidity in nature, unless they were held together by some other power which tends to unite them, and, so to speak, to chain them together; which power, whatever be its cause, or manner of operation, we name Attraction. Thus the particles of all bodies may be considered as subjected to the action of two opposite powers, the one repulsive [which he terms caloric (10)], the other attractive, between which they remain in equilibrium.

In discussing water, Lavoisier stated that the particles of water are held together because of "reciprocal attraction" (p 4) and in the first occurrence of the word affinity in the book, used it in a remarkably modern-sounding way (p 18):

…the proportional quantities of water imbibed by the pieces [of wood] will depend upon the nature of the

constituent particles of the wood, and upon the greater
or lesser affinity subsisting between them and water.

In a book in which such attention is given to the definitions and the derivations of the meanings of words, it
is notable that affinity is used without such attention.
This must indicate that most chemists of the time were
familiar with and comfortable with the way Lavoisier
used it. Lavoisier also makes it clear that the affinity
between substances is not identical for all of them by use
of terms such as "strong affinity" or "stronger affinity"
(pp 74, 95, 159), inclusion of several Tables in which
combinations of substances are "… arranged according
to the affinities [to/with] (11) …", and explicitly in the
following (p 185):

> Several conditions are requisite to enable a body to
> become oxygenated, or to permit oxygen to enter into
> combination with it. In the first place, it is necessary
> that the particles of the body to be oxygenated shall
> have less reciprocal attraction with each other than
> they have for the oxygen, which otherwise cannot
> possibly combine with them.

Interestingly, at one point (p 171), Lavoisier seems to
equate, without comment, affinity and force: "… the degree of *force or affinity* [emphasis added] with which the
acid adheres to the base." That this is still a new concept
in 1790 is indicated by the statement on the same page
that: "… even the principles upon which [this] is founded
are not perhaps sufficiently accurate." However, in 1860
the connection is made explicit by Faraday (7):

> This new attraction we call chemical affinity, or the
> *force* [emphasis added] of chemical action between
> different bodies.

This date is important in relation to the work of Guldberg
and Waage, of the Law of Mass Action fame, as described
in the following sections.

Affinity as Driving Force

Between 1864 and 1879 affinity as used in chemistry
attained a dramatically new level of quantitative and
conceptual rigor in light of the advancement of the atomic
theory earlier in the century by Dalton, Avogadro, and
others and because of improvements in the accuracy and
precision of experimental data. It might be surprising that
two people who played a major role in this development
were Guldberg and Waage, better known for developing
the Law of Mass Action. In fact, none of the titles of
their five presentations and publications in which the
Law of Mass Action is developed contains the descriptor 'Law of Mass Action.' Instead, all of them contain

the word affinity: "Studies concerning Affinity" (1864),
"Experiments for Determining the Affinity Law" (1864),
"Concerning the Laws of Chemical Affinity" (1864),
"Studies in Chemical Affinity" (1867), and "Concerning
Chemical Affinity" (1879).

Guldberg and Waage were schoolmates, brothers-in-law (twice), and academic colleagues (professors of
applied mathematics and chemistry, respectively) at the
University of Christiana (now Oslo) (for biographies, see
Ref. 12). They made clear in the very first sentence of
their first presentation that they were interested in studying the forces that drive chemical reactions (13):

> The theories which previously prevailed in chemistry
> regarding the mode of action of the chemical forces are
> recognized by all chemists to be unsatisfactory.

They briefly discussed the strengths and shortcomings of
some previous theories of chemical affinity. For example:
Bergman in 1780 (prior to modern atomic theory) proposed that each substance has its own particular affinity,
but the magnitude is *independent* [emphasis added] of the
mass of the substance, and Berthollet during 1801–1803
correctly proposed that the affinities of substances are
dependent on their specific nature and on the original
amount of the substances, but incorrectly proposed that
they are also dependent on their physical character (*e.g.*,
solubility or volatility).

Further historical background is given by Lund
and Hassel (14). Around 1850 Williamson formulated the concept of dynamic chemical equilibrium; in
1850 Wilhelmy, called by some the father of chemical
kinetics, wrote a differential equation to describe the
acid-catalyzed conversion of a sucrose solution into a
1:1 mixture of glucose and fructose and found experimentally that the reaction's rate was proportional to the
concentration of sucrose and acid present (15); In 1862
Berthelot and Péan de Saint-Gilles proposed a kinetic
formulation for the reaction of an alcohol and an acid in
which the rate is set proportional to the product of the
'active masses' (16):

> le quantité d'éther produite à chaque instant est
> proportionelle au produit des masses active qui sont
> en presence.

This is almost the Law of Mass Action, but it falls short
in that it did not include the reverse reaction and it was
not generalized. The work of Bergman, Berthollet, and
Berthelot and Péan de Saint-Gilles was known to Guldberg and Waage, as evidenced by their reference to it
in their presentation of 1864. According to Lund and
Hassel (14), it appears certain that Guldberg and Waage

were not aware of the work of Wilhelmy. They clearly set out their goal (13):

> We have therefore sought to find a more direct method for determining the mode of action of these forces, and we believe that, by a quantitative investigation of the mutual interaction of different substances, we have hit upon a way which will most surely and naturally lead to the goal.

In this publication (13), they specifically considered only those chemical processes that involve 'perfect' chemical compounds (17). Of direct relevance to drug-receptor interactions are those processes defined as 'simple' (18):

> For each of two simple chemical processes, two forces assert themselves, either a composing or a decomposing, or acting and a reacting, and we view it as unavoidably necessary to regard these forces together if one is to find any quantitative expression for these forces. … we very often see in chemistry that these two opposing forces simultaneously assert themselves in one and the same chemical process.. If one modifies the conditions under which the forces operate in one way or the other, then one will either cause the opposing force to become about as strongly effective as the first—and in such a case both directions of the process will be apparent simultaneously… In order to determine the size of the chemical forces, we regard it as always necessary to study the chemical processes under such conditions that both its opposite directions are apparent simultaneously … If we maintain that for a given chemical process two opposing forces are in effect, one which strives to form new substances and one which strives to restore the original compounds from the new, it is enlightening that, when in the chemical process these forces become equally large, the system is in equilibrium. That the same equilibrium state occurs under the same conditions, whether one goes one way or the other in the process, lies in the nature of the matter.

Based on a large number of their own and others' experiments, they set forth two initially separate laws: *the law of mass action* and *the law of volume action* from which the *equilibrium condition* for the forces acting on the system is derived [italics in original]. The two laws, based on concentrations, would later be combined into one. The major concepts were numbered as follows (13):

> The Action of Mass (*Massernes Virkning*)
>
> The substitution force (19), other conditions being equal, is directly proportional to the product of the masses provided each is raised to a particular exponent. If the two substances which act on each other are designated *M* and *N*, then the substitution force for these are ['substitution force', later called 'action force'] $= \alpha (M^a N^b)$ The coefficients α, a, and b are

constants which, other conditions being equal, depend only on the nature of the substances.

In this initial presentation, no claim is made that *a* and *b* are the stoichiometric coefficients of the reaction. It is stated explicitly that α, *a*, and *b* are to be determined experimentally (and did not need to be whole numbers). Guldberg and Waage were justifiably circumspect about not equating the powers to the stoichiometric coefficients because they are the same only if the reaction is an *elementary* one (20). Further, it is noteworthy that Guldberg and Waage's initial formulation related force to mass, which they called the Law of Mass Action. Their rate equation, derived in later publications (see below), was based on the assumption that rate is proportional to force.

> The action of Volume (*Volumets Virkning*)
>
> If the same masses of the interacting substances occur in different volumes, then the action of these masses is inversely proportional to the volume.
>
> The Equilibrium Equation (*Ligevægtsligningen*)
>
> If one begins with the general system which contains the four active substances in a variable relationship and designates the amounts of these substances, reduced to the same volume, according to the first law by *p*, *q*, *p'*, and *q'*, then when the equilibrium state has occurred, a certain amount *x* of the two first substances will be transformed. The amounts which keep each other in equilibrium are the action force for the first two substances is
>
> $\alpha(p-x)^a(q-x)^b$ and the reaction force for the last two is $\alpha'(p'+x)^{a'}(q'+x)^{b'}$. Since there is equilibrium, $\alpha(p-x)^a(q-x)^b = \alpha'(p'+x)^{a'}(q'+x)^{b'}$ [where primed symbols represent the 'reverse' reaction].

This equation is credited with being the first generalized mathematical formulation of the condition of dynamic chemical equilibrium (21).

Later in the same year (1864) Guldberg and Waage took up the question of the relationship between time and a chemical reaction (*i.e.*, the reaction rate) and considered it reasonable to assume that the rate of a 'simple' chemical reaction is proportional to the driving force of the reaction. They stated (21):

> Let *p* and *q* be the number of molecules of A and B, *v* the velocity, *t* the time, and x the quantity which has transformed during this time. Then one has, regarding the total volume to be constant
>
> $$v = \frac{dx}{dt} = k(p-x)^a(q-x)^b$$

where k is a constant depending on the nature of the bodies, the volume, the temperature, and the solvent.

There are two points worth noting about this equation. First, it is the one that is often cited as the Law of Mass Action, whereas the originators explicitly gave that name not to this equation relating reaction rate to mass, but to the equation relating driving force to mass. Thus, the equation for rate was an extension of the equation for force, not the other way around. Second, the rate equation is much less general than the force equation, subject to many more restrictions.

The clear association of affinity with force was emphasized a few years later in 1867 and finally in 1879 (22) when Guldberg and Waage presented a more elaborate and refined version of their ideas. There was a critical new feature (14, 21): The exponents in their equations were presented as integral powers of the concentration. Deviations from integer values were to be viewed as due to experimental error or to secondary forces, just the opposite of their original view about the exponents. For a reaction of the type $\alpha A + \beta B + \gamma C$, the rate is expressed as being equal to $kp^{\alpha}q^{\beta}r^{\gamma}$. This is the first time their exponents were definitely stated to be equal to the number of like molecules that take part in the reaction (23), and k was given the name <u>affinity coefficient</u> [underline ours].

This publication essentially marks the end of the first stage in the history of the development of affinity. In short, the meaning of affinity transitioned from an attribute (substances *have* affinity) to a force (the driving force of a chemical reaction *is* the affinity).

Of significance for subsequent use of the term in pharmacology, it should be noted that for a bimolecular drug-receptor interaction at equilibrium (in the notation of Guldberg and Waage), the forward (nonprimed) and reverse (primed) forces are equal: $kpq = k'p'q'$, so

$$\frac{k'}{k} = \frac{pq}{p'q'}.$$

The right-hand side of this equation is familiar as the 'dissociation constant' (reciprocal of the equilibrium constant). The left-hand side is the ratio of what we would today call the 'rate constants' (k and k'), but Guldberg and Waage called 'affinity coefficients.' It is easy to see—in the absence of further developments—why the

dissociation constant might be erroneously thought to be the same as affinity.

Affinity as Reaction Free Energy Change

During the time Guldberg and Waage were publishing their accomplishments, others were beginning to quantify the rate of reactions in terms of the numbers, or mass, or concentration of the reactants. van 't Hoff, for example, proposed a rate law for the same data of Berthelot and Péan de Saint-Gilles used by Guldberg and Waage (**24**). More importantly, it was around this time that new ideas about heat, energy, and thermodynamics were being developed by Count Rumford (Benjamin Thompson), Carnot, Clapeyron, Mayer, Joule, Rankine, Helmholtz, Clausius, Lord Kelvin (William Thomson), Maxwell, Boltzmann, and others (25). Pfaundler von Hadermur and Horstmann were among the first to apply emerging thermodynamic principles to chemical equilibrium (21); Gibbs provided the most comprehensive treatment (26).

As a consequence of these developments, earlier concepts such as 'driving force' were considered to be too vague. Instead, chemical reactions were viewed as occurring with a change in internal energy, equal to the difference between energy content of the reactants and products. Formulated in terms of more easily measured quantities, chemical reactions proceed with a net change in enthalpy (ΔH), entropy (ΔS), or most commonly, both (29, 30). Two factors are involved in determining the occurrence and direction of a chemical reaction: the system seeks to minimize its energy and maximize its entropy. Since both usually occur during a chemical reaction (drug-receptor interaction), and often in opposition, some approach must be devised to represent the optimization process. The most convenient way was by introduction of the concept of free energy (energy available to do useful work). Chemical reactions occur in the direction in which free energy decreases (*i.e.*, the change in free energy is negative) and continues until the free energy is a minimum. In the case of a reversible reaction such as a drug-receptor interaction, the minimum is reached (and defines) the equilibrium state, a point at which the system cannot perform useful external work.

Several formulations have been proposed for representing free energy. The most useful for the type of reactions typical of drug-receptor interactions, *i.e.*, isothermal and isobaric, is the Gibbs free energy. The free energy change is usually given in the form $\Delta G = \Delta H - T\Delta S$. This leads to the simple and extremely useful rules: $\Delta G < 0$, the

reaction proceeds spontaneously (31) in the direction as written; $\Delta G = 0$, equilibrium (steady-state); $\Delta G > 0$, the reaction proceeds spontaneously in the opposite direction as written. For drug-receptor interactions, which occur as a 'closed system' (no other matter enters or leaves) and under dilute conditions, we can simplify by using concentration rather than chemical potential (partial molar free energy) and instead of activity (a measure of non-ideal behavior). Given all of the caveats, the change in Gibbs free energy for a chemical reaction (or for a drug-receptor interaction, where drug molecule A combines with receptor molecule R to form a drug-receptor complex according to: A + R $\rightleftharpoons$ AR) is

$$\Delta_r G = \Delta_r G^\circ + \Re T \ln \frac{[AR]}{[A][R]}$$

where $\Delta_r G^\circ$ is the change in reaction (subscript r) standard free-energy ($\Delta_r G$) (32) compared to standard state (superscript $^\circ$), an arbitrary set of conditions of temperature, pressure, *etc.*, that is usually defined for convenience, and $\Re$ is the universal constant = 8.314 JK^{-1}mol^{-1}. At equilibrium, $\Delta_r G = 0$ and [AR]/[A][R] is the familiar equilibrium constant (K_{eq}), so at equilibrium

$$\Delta_r G^\circ = -\Re T \ln K_{eq}$$

An example of the application of thermodynamics to drug design is provided by Lafont *et al.* (33). In drug discovery, once a lead compound is identified, it is often desirable to find (design, synthesize) an analog that has greater binding affinity. From a thermodynamic point of view, this means a search for interactions that have more favorable $\Delta_r G$, which in turn means favorable enthalpy and entropy contributions. Lafont *et al.* (33) found that for the system they examined (HIV-1 protease inhibitors) the enthalpy gain associated with introduction of a hydrogen-bonding functionality was offset by an entropy loss, resulting in no gain in affinity. Close analysis of the thermodynamic parameters provided guidance for a strategy for optimizing affinity in this system.

There are two very useful equations relating chemical reactions to energy. One is general ($\Delta_r G$) and the other applies to equilibrium ($\Delta_r G^\circ$). But what about reactions not yet at equilibrium? Isn't that what was sought by the concept of a 'driving force'? Isn't that what was meant by affinity? This question was answered by de Donder in a series of presentations and publications during the 1920s (summarized in 34). De Donder introduced a simple way to represent the degree of progress of a reaction, designated ξ. This is easy to represent by a straight line, where the origin, ξ = 0, represents the reaction before it begins (all reactants and no products) and ξ = 1 represents the reaction at its completion (all products and no reactants) (35). In drug-receptor terminology (5), ξ = 0 represents dissociated drug and receptor and ξ = 1 represents complete association as drug-receptor complex. Thus the free energy (G) is a function of ξ and can be graphed relative to ξ (progress of reaction) as displayed in **Fig 2**. For reversible reactions, the free energy is a minimum at the point where the forward and reverse reactions balance ($\Delta_r G = 0$) and is larger on either side of equilibrium, indicating that the reaction can proceed in both directions, depending on the concentrations of reactants and products. Rather than the static information, it would be preferable to have a way of indicating the change in free energy as a function of extent of reaction—in other words, the equivalent of the long-sought *driving force.*
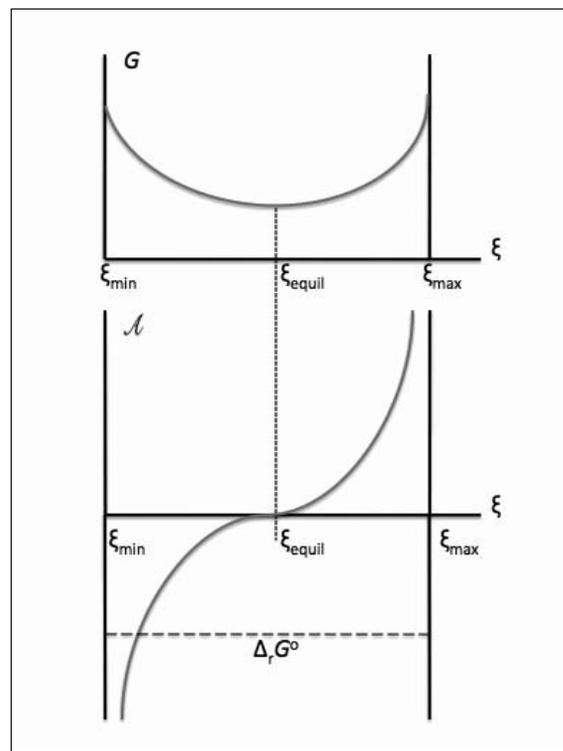
Fig 2.   *The free energy (G) and affinity (**A**) graphed as functions of the extent of a chemical reaction (ξ) as the reaction proceeds—either from the left (in the direction reaction written: e.g., binding of drug with receptor to form drug-receptor complex) or from the right (opposite the direction reaction is written: e.g., dissociation from the drug-receptor complex)—towards equilibrium (at which G is minimum and **A** = 0).*

De Donder provided the answer when he defined affinity (**A**) such that, in the usual case of constant pressure and temperature,

$$\mathbf{A} = -\left(\frac{\partial G}{\partial \xi}\right)_{pT} = -\Delta_r G$$

This function is shown in **Fig. 2** 36, 37). Unlike *G*, the affinity indicates the direction of the reaction: when **A** < 0, the drug-receptor interaction proceeds in the forward direction (association); when **A** > 0, it proceeds in the reverse direction (dissociation); and **A** = 0 when both are equal (equilibrium). The magnitude of affinity also represents the thermodynamic 'distance' from equilibrium. The larger the magnitude of **A** (either positive or negative), the further the interaction is from equilibrium and the interaction will proceed spontaneously toward equilibrium until **A** = 0. Thus, we see the utility of affinity defined this way.

Affinity in Pharmacology

The history of the use of affinity in pharmacology is much less extensive than that of its use in chemistry. Langley, who is considered a father of receptor ('receptive substance') pharmacology, used the term affinity (38) in a manner that at first might seem qualitative, but careful reading implies that he was aware of the work of Guldberg and Waage and was using the term in the same manner (38):

> Until some definite conclusion as to the point of action … is arrived at it is not worth while to theorise much on their mode of action; but we may, I think, without much rashness, assume that there is some substance or substances … with which both [drugs] are capable of forming [drug-receptor complexes]. On this assumption then the … [complexes] are formed according to *some law of which their relative mass and chemical affinity* [emphasis added] for the substance are factors.

This was not an accidental use of terms as demonstrated two sentences later in a general example and reiteration of the terms, including specific repetition of the use of 'chemical affinity' rather than merely affinity. Chemists continue to describe affinity in such terms (39):

> …firstly, there is the *affinity* of the small molecule for the receptor binding site. Affinity is a measure of the binding free energy between the partners.

So where did the common contemporary use of affinity

in pharmacology, as the reciprocal of the dissociation constant, originate? Erhlich, who coined the word 'receptor' in 1900, used the term 'specific affinity,' but not in a chemical or mechanistic way (40). Of the more quantitative early pharmacologists, Clark did not discuss affinity in his 1937 text (41), and neither did Gaddum in his extensive 1953 review (42). So one must look elsewhere for the different uses of this term by pharmacologists and chemists. There seem to be two reasons. First, the formal equivalence of affinity and the Gibbs reaction free energy change led some chemistry and thermodynamics authors to use the latter instead of the former term; second, the extensive pioneering and influential work of Ariëns and colleagues as presented in a series of articles published starting in the 1950s.

It is impossible to overestimate the importance of Ariëns in the development of drug-receptor theory and its widespread dissemination and application. He and his colleagues systematized the thinking about drug-receptor interactions and they promoted approaching the subject in a quantitative way. An example of this was the distinction between two properties of the drug-receptor interaction. One was the binding process itself and the other was the ability to induce a biological effect. This distinction helped explain competitive antagonism: an agonist possesses both properties; an antagonist possesses the first, but not the second (intrinsic activity = 0). For the first property, Ariëns used the term affinity; for the second, he used the term 'intrinsic activity.'

From the beginning, Ariëns referred to the law of mass action as the basis for his treatment of the drug-receptor interaction (43). Given his training in chemistry, it is a bit surprising that he cites Michaelis-Menten, but does not discuss the use of affinity as used by Guldberg and Waage, but writes (43):

> This means that the numbers of receptors that will be occupied at a definite concentration of A [drug] depends on the affinity between R [receptor] and A depends on the affinity between R and A thus on the reciproke [sic.] of what is mostly called the dissociation constant (K_A) of complex RA. *Affinity thus is a substance constant determining for given conditions of concentration etc. how much of the drug-receptor complex will be formed* [emphasis in original].

This view is reinforced a few pages later by "… with different *affinities* for the receptor (dissociation constants …)." This meaning of affinity is maintained throughout subsequent studies (44).

Thus we have come almost full circle. But Ariëns also writes (44):

Table Names and Dates of Prominent Scientists in the History of 'Affinity'

Name	Birth – Death
Everhardus Jacobus Ariëns	1918 – 2002
Torbern Olof Bergman	1735 – 1785
Pierre Eugène Marcellin Berthelot	1827 – 1907
Claude-Louis Berthollet	1748 – 1822
Ludwig Eduard Boltzmann	1844 – 1906
Nicolas Léonard Sadi Carnot	1796 – 1832
Benoît Paul Émile Clapeyron	1799 – 1864
Alfred Joseph Clark	1885 – 1941
Rudolf Julius Emanuel Clausius	1822 - 1888
Theophile Ernest de Donder	1872 – 1957
Paul Erhlich	1854 – 1915
Sir John Henry Gaddum	1900 – 1965
Étienne François Geoffroy	1672 – 1731
Josiah Willard Gibbs	1839 – 1903
Cato Maximilian Guldberg	1836 – 1902
Léopold Pfaundler von Hadermur	1839 – 1920
Hermann Ludwig Ferdinand von Helmholtz	1821 – 1894
James Prescott Joule	1818 – 1889
John Newport Langley	1852 – 1925
Antoine-Laurent Lavoisier	1743 – 1794
James Clerk Maxwell	1831 – 1879
Julius Robert von Mayer	1814 – 1878
William John Macquorn Rankine	1820 – 1872
Léon Péan de Saint-Gilles	1832 – 1863
Sir Benjamin Thompson (Count Rumford)	1753 – 1814
William Thomson (Lord Kelvin)	1824 – 1907
Jacobus Henricus van 't Hoff	1852 – 1911
Peter W. Waage	1833 – 1900
Ludwig Ferdinand Wilhelmy	1812 – 1864
Alexander William Williamson	1824 – 1904

It is worth while to realize that what is defined here as affinity [emphasis in original] is what is generally called the activity of a drug: a drug is "active" if it shows an effect in low concentration i.e. when it has high affinity.

The circle is now completed. Affinity has been restored to its qualitative vernacular use, and it also has a precise definition: reciprocal of the dissociation constant. But the definition seems to have been formulated in a way that was independent of the developments of affinity in chemistry. It is not clear why a new term was created for the reciprocal of the dissociation constant (K_d), since $1/K_d$ already had a well-known name—the equilibrium constant. Furthermore, by defining affinity in terms of an equilibrium constant, its meaning reverts to a completed event (proximity, marriage) rather than to the

driving force. Nevertheless, this use has persisted in pharmacology.

Summary and Perspective

Colloquial use of the term affinity evolved historically from meaning 'proximity' to meaning 'attraction.' Scientific use of affinity underwent a similar evolution and as traced in this review further evolved in chemistry and thermodynamics to quantify the driving force of chemical reactions. Pharmacology developed a related, but different definition for affinity. The different fields could continue to define and use affinity in different ways, but confusion might arise as thermodynamics is increasingly used in practical applications in drug-discovery (5, 45). Recognition of the differences and some type of unification would seem worthwhile.

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6. http://www.merriam-webster.com/dictionary/affinity (accessed February 21, 2009).

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11. The assignment of relative affinity was cleverly based, for example, on relative ability to form precipitates (p 127): "If … any sulphuric acid is suspected in the nitric acid, it is easily separated by dropping in a little nitrate of barites, so long as any precipitation takes place; the sulphuric acid, from its greater affinity, attracts the barites, and forms with it an insoluble neutral salt, which falls to the bottom."

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17. "… any phenomenon in which the chemical forces bring about a chemical change in the material; … always occur according to particular atomic relationships."

18. "… direct combination of two molecules to a new molecule [in drug-receptor interactions, the drug-receptor complex] (addition) and, in reverse, splitting of the molecule into two others [dissociation]."

19. This statement was restricted to "simple" processes in which "a mutual exchange or substitution of the constituent parts of two molecules and, in reverse, regeneration of the original molecule by a backwards substitution. One could call the one action and the other reaction.

20. An elementary reaction is one that occurs exactly as written in a single step, with no intermediate steps, *i.e.*, the reaction as written represents the actual physical combination of atoms and does not represent a net reaction consisting of several steps.

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22. It is said that the final publication was stimulated by the impression that their previous work had not been sufficiently known, possibly because it was in periodicals not readily available to chemists outside Norway (Ref. 14, 15).

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REVISITING PHARMACY MORIANEN: REVEALING FIRST TRACES OF ELEMENTAL SILICON IN A LABORATORY ENVIRONMENT

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Introduction

In a previous work in collaboration with National Museum of Art, the present author performed Raman analysis of pigments used by the 17th-century painter, Elias Brenner (1647-1717). Brenner published a book in 1680 in which he gave samples and names in three languages (Swedish, Latin, and French) of 30 different pigments he used in his work as a miniature painter. Three copies of this book could be found and were analyzed with Raman spectroscopy and other techniques (work still in progress). A first report was published in 2006 (1).

Since it is believed that artists of those days mainly bought their pigment material in pharmacies, alternatively producing many themselves, it is tempting to investigate findings of vessels from pharmacies of that time. Such an opportunity exists in this case, since the cellars of an old pharmacy were discovered during the construction of a garage for the Houses of Parliament in Stockholm in 1977. Written sources (2) clearly state that the Pharmacy Morianen was in operation at this site during the time 1670-1674. Then it was demolished to make space for a new stable for the king's horses. The idea emerged that it might be possible to find at least some of the sources of pigments by going through the traces of contents in the jars and vessels found. The operational period coincides well with Brenner's first years in Stockholm, where he arrived in 1673, so he could very well have been a customer at Morianen.

The owner and founder of Morianen is well known. His name was Christian Heræus (1643-1691), originally from Güstrow in Mecklenburg, Germany. He operated the pharmacy from its inauguration in 1670, during the time it was moved to another site, and up to 1678, when he left Stockholm for Leyden, where he took his doctorate degree in 1679. From 1671 to 1678 he was the court pharmacist for Queen Hedvig Eleonora.

Interesting for this investigation is also his employment by "Bergskollegium" as "chemicus." This organization had a neighboring house to the pharmacy, and Heræus's task was to find new uses for metals and minerals that were known and found during this time. He probably had a diversified chemical laboratory, to produce pharmaceutical products as well as to experiment with virtually anything. So the chemical activity in the pharmacy was not only related to medicine.

The findings from the pharmacy are relatively scarce. The cellars contain four rooms, which were almost empty since they were evacuated before the house was demolished. It was abandoned to give space for other buildings and moved to a new place (the pharmacy Morianen was in operation in different locations in Stockholm until 1971). Everything of value was of course taken away. The most interesting findings constitute a selection of some 50 more or less intact jars and vessels of glass and ceramic and some laboratory equipment like retorts, found in a latrine well at one side of the house. When or why they were deposited in the shaft is

impossible to know, but most likely it had been used as a waste bin. By means of modern techniques it may be possible to unravel what kind of activity was going on during that period.

In Ref. 2 a detailed description of shape and origin of some of these findings is given. Some analyses of contents were also made directly after excavation, mainly by means of X-ray diffraction and thermal analysis and reported by Wadsten (3). Some vessels contain insects, obviously collected for some medical reason; others remainders of syrup and raspberries, which were very often used as bases for drugs at that time. Subsequently, the findings have been stored at the premises of Stockholm Stadsmuseum for about 30 years.

This investigation was from the outset focused on finding traces of pigments that could have been sold to the artists, but some very interesting results were obtained that cannot have anything to do with making of pigments or producing pharmaceuticals. The fact that Heræus was also employed by "Bergskollegium" provides the opportunity for wide speculation as to what he might have been doing.

Techniques Used

Since the previously mentioned investigation of Brenner's pigments was performed with Raman spectroscopy, a nondestructive vibrational spectroscopy technique most commonly used with lasers in the visible spectral range, the same technique was used here. In addition some samples were analyzed with Fourier transform infrared (FTIR) spectroscopy, another well known technique.

The Raman instrument is a Renishaw InVia Reflex microspectrometer equipped with two lasers (514 nm and 785 nm), a deep depletion enhanced CCD detector, microscope objectives with different magnifications (x5 – x100), and also a white light video camera to observe the sample on the stage in the microscope. The laser spot can be monitored in the image and the point of analysis well defined. Photographs can also be taken of the samples.

The FTIR is an IlluminatIR from Smiths Detection, mounted on a Leica microscope with a white light video camera for sample observation and photography. The instrument is equipped with both all reflective (ARO) and an attenuated total reflection (ATR) objective, but here only ATR was used.

Results on Fibers and Insects

Many objects contain fibers. It is difficult to say whether these are original fibers or whether they have come into the vessels during the centuries or even after excavation. The most common fiber is actually a typical cellulose fiber; one example of an FTIR spectrum is shown in Figure 1. This spectrum compares very well with one of fibers from modern pine wood. Another common fiber is that from an animal, and in Fig. 2, one example is compared with a modern fiber from a horse and also with a spectrum from an old fur hair taken from the battle horse Streiff, belonging to King Gustav II Adolf (who died with him at the battle of Lützen, November 6, 1632). This horse was returned to Sweden and is now conserved and displayed at Livrustkammaren, Stockholm Castle. It is easy to imagine that these fibers have been embedded in the King's stable during the centuries following the demolition of the pharmacy. Horses' walking on the floor of pine plank is the probable source.
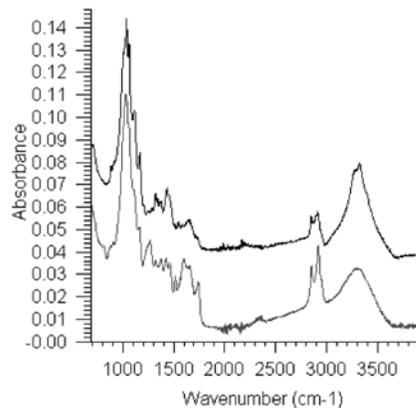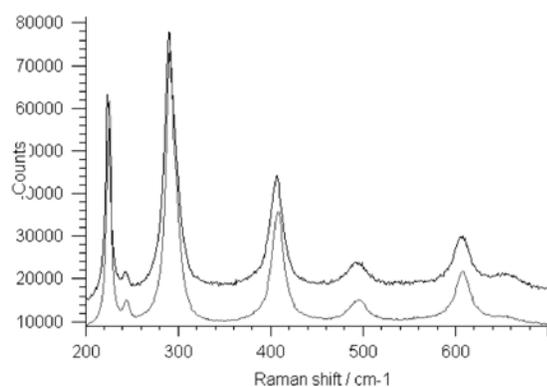

Figure 1. *Fiber 1 commonly found in the vessels (upper), and as reference, a fiber from a modern pine tree (lower)*
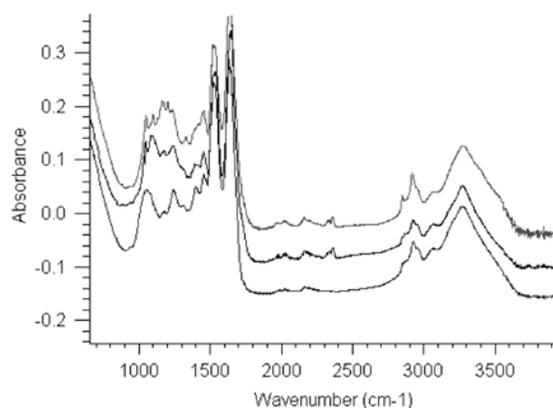
Figure 2. *Fiber 2 commonly found in the vessels (middle), and as references, a fiber from a modern horse's fur (lower) and a spectrum from an old horse Streiff (upper).*
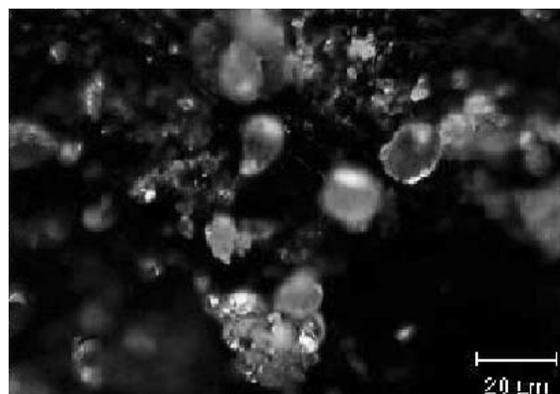
Other common findings analyzed with FTIR are parts and fragments of insects. These can of course have been collected for pharmaceutical usage. This is certainly the case for one closed jar with dry, intact beetles, which was discovered in 1977; and since this particular insect did not have a name, it was dubbed "Kyrkogårdsbagge" by Wadsten (3). Other more commonly occurring findings in this investigation are much more fragmentized and more probably remains of dead insects that have accumulated in the cellars during the centuries, rather than collected for pharmaceutical usage. In general, all artifacts are covered by a layer of dust, and spectra of common minerals like feldspars stem from this dirt layer. No examples are shown. The only finding that possibly could have been the remains of a pigment container is a fragmented ceramic jar, with a lump consisting of hematite mixed with charcoal (carbon). Fig. 3 shows the spectra of the sample and reference.
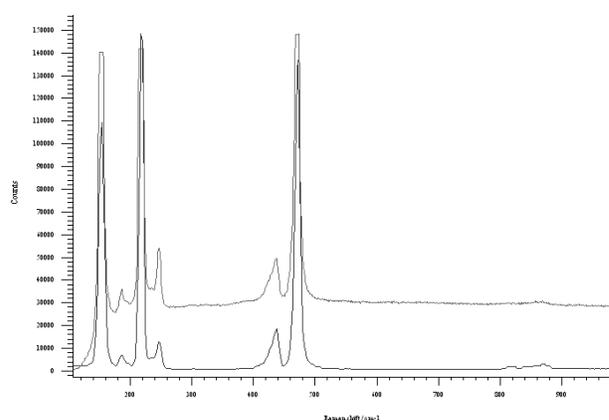

Figure 4. *White light picture of crystals in vessel 19907.*

Figure 5. *Spectra of crystals in vessel 19907 (upper) and reference Sulfur (lower).*

Figure 3. *Sample from ceramic vessel 533 (lower) and reference Hematite, Fe_2O_3 (upper).*

S, Si, Hg, As, and C: Elements and Compounds

Another wide and open ceramic jar has fine small crystals of pure sulfur scattered over the surface. Fig. 4 and 5 show a white light picture of the crystals and the Raman spectrum, together with a modern reference spectrum. Sulfur has been used in both medicine and chemistry – and alchemistry !– for very long time.

The most interesting and puzzling finding is part of a retort—a vessel with an Erlenmeyer-like design and a narrow tube that projects almost horizontally. (A picture of this artifact, named 457 in this investigation, is given on page 353 in Ref. 2.) This vessel was typically used as early distillation equipment. Heating the content in the vessel and then condensing the reaction products in the cooling tube allowed for some separation. This particular finding of glass is a part of the cooling tube. It has a very narrow hole, about 2-3 mm in diameter, and thick walls. The length is approximately 180 mm. First discovered in the tube were droplets of metallic mercury, easily recognized by their luster and shape (see Fig. 6). Some compounds of Hg have also formed (see Fig. 7a and 7b). The spectrum in Fig. 7a is from HgCl, commonly named calomel. The spectrum in Fig. 7b is similar to imiterite, a compound of Ag_2HgS, with just a single peak at 281 cm^{-1} (rruff id R080014).
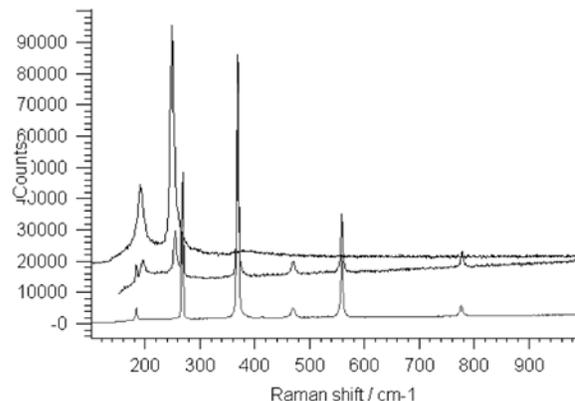
Figure 6. White light picture of a droplet of Hg in 457.
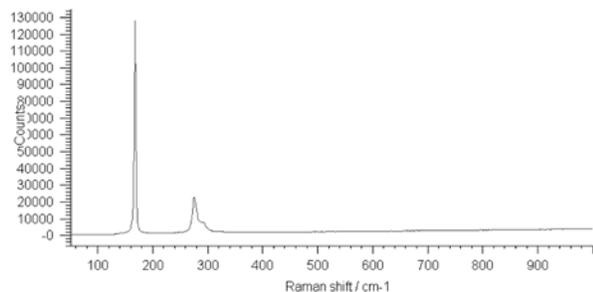
Figure 7a. *Peaks at 166 cm^{-1} and a double peak at 274 and 286 cm^{-1}, identified as calomel.*
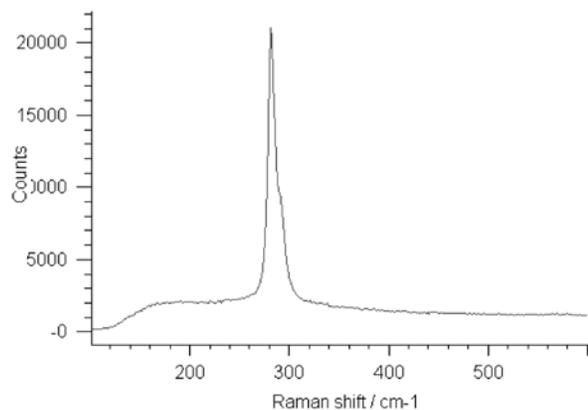
***Figure 7b****. Double peaks at 282 and 291 cm^{-1}.*

The Raman analysis revealed many more interesting things. There are pure crystals of arsenic inside the tube. In Fig. 8, a spectrum of As is compared to that of a modern reference material.

Figure 8*. Newly cut surface of As reference (upper), oxidized outer surface of reference sample (middle) and spectrum from the finding, vessel 457 (lower).*

The upper spectrum is from a clean, newly cut surface of elemental As. The spectrum in the middle is from the oxidized surface of this modern sample. The lower spectrum is from the finding in the retort. One can see that the oxidation peaks have grown higher than those in the other spectra, indicating that this is indeed an old sample. It seems as if elemental As has sublimed at a position along the tube, where the temperature allowed this to happen, and then later was oxidized.

In the tube there are also two bones from a fish's spinal cord. These are most certainly from herring (4), a common fish that was a very basic food at that time.
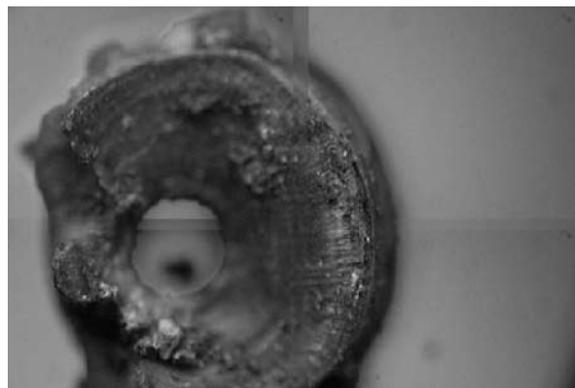

Figure 9. *White light picture of a fish bone, spinal cord of herring. Magnification x5.*

On these bones there are small crystals of elemental silicon! Fig. 9 shows a white light image of one of the bones; Fig. 10 displays the shiny crystals, whose spectrum is shown in Fig. 11. It was also found that some silicon is strained: the main peak at 520 cm^{-1} has

shifted 3-5 wave numbers. The occurrence is really an unexpected finding; although silicon is a very common element in nature, it never exists in the pure elemental form, always as compounds such as silicates or quartz (5). There are, however, some examples of Si in solid solutions, for instance copper in ancient arrow heads of bronze, manufactured about 525 BC. It is probable that silica was unintentionally reduced in the smelting process and Si contaminated the alloy, where it hardened the product (6). Elemental silicon was produced and described as an element for the first time by Berzelius in 1823—more then 150 years later than the findings in Morianen (7)!
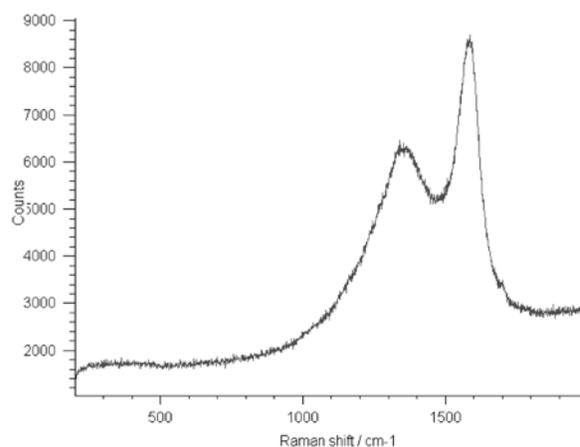

**Figure 10.** *White light picture of metal inclusion in fish bone 457. Magnification x50.*
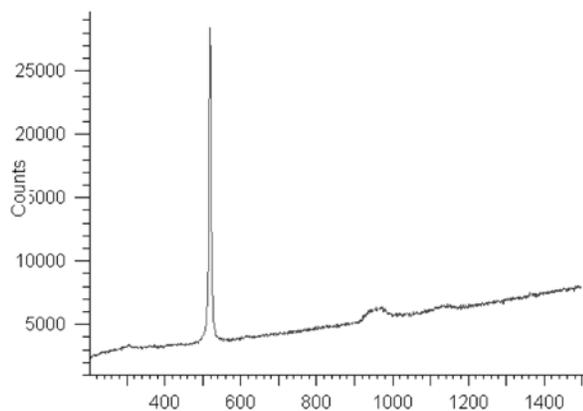
Figure 11. *Spectrum of Si on the fish bone. Main peak at 515 cm^{-1}.*

On the fish bones there are also small particles of pure carbon; one spectrum is shown in Fig. 12.


Figure 12. *Carbon spectrum from particulates on the fish bones*.

There are also small white crystals on the fish bone that have not been clearly identified (see spectra in Fig. 13). These are taken on different occasions and from different spots, but the relative intensities among the peaks are almost the same. If the spectrum comes from a mixed compound, these relations would most probably not have been reproduced. The best fit from reference libraries is therefore mullit ($3Al_2O_3x2SiO_2$) common in glass. The peaks below 700 cm^{-1} are similar to rutile, TiO_2, but the peaks at higher wave numbers do not fit. (Rutile was not known in 17th-century Sweden).
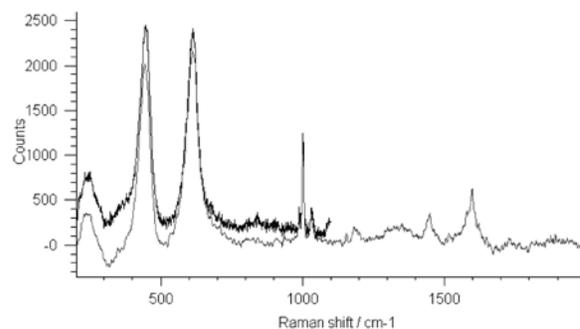
Figure 13. *Two examples of spectra of the white crystals on the fish bone in vessel 457.*

Finally, in this sample there are also traces of quartz, again being present on the fish bone pieces and on the surface of charcoal particles (see Fig. 14).
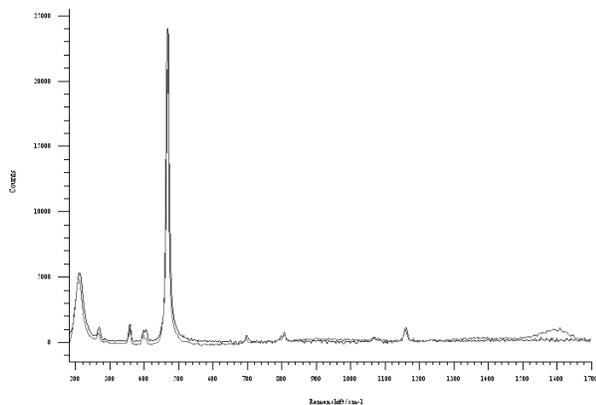
Figure 14. *Spectra from particles on the fish bone (lower at low wave numbers), similar to reference spectrum of quartz (upper at low wave numbers).*

What was Heræus Doing?!

As mentioned, the first successful synthesis and description of elemental silicon were done by Berzelius and published first in a letter to the French Academy of Science, where it was read by M. Dulong, and later printed in Ref. 7. The element Si was not known before 1823.

The pharmacist, chemist—alchemist—Heræus was obviously experimenting wildly. In the glass vessel, (source of quartz, mullite?) item 457, he must have mixed mercury, arsenic, salt (NaCl?), fish bones, and other organic materials like charcoal. Then he must have raised the temperature relatively high. (It has been reported by Wadsten (3) that traces of "probing" analysis, i.e. analysis at high temperatures to decide purity of noble metals, were found in the pharmacy). What reactions occurred, and how could they lead to formation of elemental silicon? In the early attempts to reduce silica by Berzelius and others, many routes were tried. Even electrolytic methods were used (8), and later on during the 19th century also high temperature reactions between silica and carbon in electric arc furnaces. Berzelius, however, mentions processes applying "ordinary chemical agents," as he expressed it in an even earlier article (9). In a work by Davy as early as 1808, silica (in his glass vessel) reacted by chance with potassium to form a brown powder (10). Davy did not realize that this probably was silicon. The full understanding of the reaction was given by Berzelius in the referenced paper (7). In his work Berzelius used SiF_4 gas, which was treated with potassium. This did not require very high temperatures (in

Berzelius words "heated by a spirit lamp"). In the retort from pharmacy Morianen there are large amounts of Hg and also calomel. Is it possible that salt, NaCl (commonly used to preserve fish), had reacted with the mercury, and then in addition to calomel an amalgam between sodium and mercury might have formed? Amalgams do not have Raman spectra, so remainders of this would not show up in these analyses. On the assumption that this could happen, elemental sodium could perhaps have the same reducing effect on silica as potassium, described in the referenced old papers. In fact, Oersted published as early as 1825 a paper in which he described reduction of silicon chloride by sodium amalgam (11). Both the amalgam and metallic mercury in the retort of course evaporate at low temperatures and sublime along the cooling tube. This could have provided a transportation reaction and brought the sodium in contact with silica.

Arsenic also evaporates and sublimes (sublimation temperature 616° C (12)); and since it probably did not react during the process, it indicates that the environment should have been reducing. (It was oxidized later in air over the course of 300 years). The presence of large amounts of elemental carbon also indicates a reducing atmosphere.

Christian Heræus was obviously aiming at something completely different, and he would not have had the capability to find or analyze the small pieces of Si in this reaction vessel, even if it had not been broken and thrown away in the latrine well. Once formed, the Si is very stable; and it is no wonder that it has survived for 350 years in a protective environment. But this property of Si is well known to all current chemists, as a result of the intense research on Si since the 1960s.

literature. Matthew Bloomfield at Renishaw for help to interpret some Raman spectra. Anne-Marie Dahlberg at Livrustkammaren for providing the samples of Streiffs fur, Marianne Johansson for providing samples of a modern horse fur. Christian Helldahl, Jenny Hälldahl and Lena Karlsson for reading the text and suggesting improvements. Jakob Thyr for keeping the instruments in good order.

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BÖTTGER'S EUREKA! : NEW INSIGHTS INTO THE EUROPEAN REINVENTION OF PORCELAIN*

Nicholas Zumbulyadis, Independent Scholar (Retired, Eastman Kodak Research Laboratories, Rochester, NY)

Introduction

The opening of Europe's first porcelain manufactory in Dresden, in January, 1710 represented the successful culmination of efforts to unlock the secret of Chinese porcelain, a quest that had gone on for at least 800 years. By royal decree, on the 6th of June 1710 the manufactory was moved from Dresden to the Albrechtsburg in the city of Meißen. Developed initially as a medium of artistic expression, porcelain quickly became one of the most widely used composite materials ever invented (1). The objective of the present paper is to fill in new details about the invention of European porcelain by examining the plausibility of an early 19th-century account in the light of recent analytical data together with archival material.

Porcelain was first discovered in China, with the earliest recorded pieces dating to the T'ang Dynasty (618-907 AD). While it is generally believed that this discovery was accidental, Chinese porcelain does have compositional similarities to earlier, dense, high-temperature stoneware from 200 BC to 200 AD. These wares are known as protoporcelain, a term used more frequently in China than in the West (2).

According to tradition, the earliest examples of porcelain arrived in Europe from China towards the end of the thirteenth century with the return of Marco Polo from his legendary voyage. One cannot be certain that this was the first encounter of Europeans with porcelain since Chinese porcelain objects dating to 900 AD were excavated in Samarra, Iraq. The porcelain specimens Marco Polo brought back must have displayed properties puzzling to the people of the Middle Ages. They were probably white, definitely vitreous, (and hence, unlike European pottery, nonporous) and translucent. By the middle of the 15th century porcelain objects from the Far East had found their way into Italian collections by way of the Middle East, mostly through the exchange of diplomatic gifts. Later, during the 16th and 17th centuries, when Portuguese and Dutch traders brought back large quantities of porcelain from China, Europeans became widely appreciative of porcelain's unique resistance to thermal shock.

The problem of producing true porcelain perplexed potters and alchemists for several centuries. Islamic potters, trying to imitate the white appearance of porcelain, introduced tin oxide into the transparent glaze as an opacifier. They were thus able to produce a ceramic surface that was an ideal canvas for further decoration. This approach ultimately led to materials known in Europe as Italian maiolica, French faience, or Delftware. Alchemists, both in 13th-century Persia and later in Southern Europe, attempted to introduce the property of translucency into the clay by mixing it with ground glass (3). In 1575 Grand Duke Francesco Maria de' Medici of Florence, himself an alchemist, produced a translucent material by co-melting kaolin-containing clay from Vicenza and glass. Known as Medici-porcelain, this material (one of many variants of what is now called soft-paste porcelain or fritware) was produced until 1586 (until 1620 in Pisa), with very few pieces surviving today. While used to produce objects of great beauty and elegance, none of these materials possessed porcelain's resistance to thermal shock.

One of the earliest attempts to break away from these purely phenomenological approaches was made by the English potter John Dwight (founder of the Fulham pottery), who sought to improve German salt-glazed ware by firing it at higher temperatures to bring about vitrification of the clay body (4). It was, however, Johann Friedrich Böttger (1682-1719), an alchemist in pursuit of the philosopher's stone, together with Ehrenfried Walther von Tschirnhaus (1651-1708) and their circle of laboratory assistants and kiln builders, who finally succeeded in reinventing porcelain in Europe. Böttger was both a prisoner and in the employ of Prince-Elector Augustus the Strong (5) and charged with making gold to finance the profligacy of his master. In 1706 Tschirnhaus gradually nudged Böttger towards working on porcelain.

While the story of the European reinvention of porcelain has been told countless times, the exact circumstances of this invention are still shrouded in mystery. Popular histories focus mostly on the colorful characters and salacious details. Only two scholarly Böttger biographies exist, the first by Carl August Engelhardt dating to 1837 (6). The second was published recently by Klaus Hoffmann in 1985 (7). Hoffmann explicitly makes the point that there is no body of work that specifically examines Böttger's chemical activities (8). The purpose of this paper is to take a first small step in the direction of filling in this gap. It is definitely not the author's intention to rekindle the centuries-old debate on the relative merits of the contributions of Böttger vs. Tschirnhaus to the reinvention of porcelain (see, however, the references cited in the concluding remarks for a synopsis of this debate, particularly those of Pietsch and Ufer).

Figure 1. Engraving of Johann Friedrich Böttger

The Basics of Porcelain Chemistry

In this section a brief review of the chemistry of porcelain will be presented. The chemical composition and heat treatment protocol followed during the manufacturing process give porcelain its unique properties and set it apart from all other ceramic materials. Certain aspects of the manufacturing process are of key significance to the reconstruction of the circumstances that led to the reinvention of porcelain.

The starting material for porcelain is a mixture of approximately 50% kaolinite, 25% quartz, and 25% feldspar. Kaolinite $[Al_2Si_2O_5 (OH)_4]$, a white-burning clay, is structurally a phyllosilicate which can intercalate water molecules between its layers, thus acquiring its unique plasticity. Kaolin (from Chinese, *kao-ling*, meaning mountain ridge) and quartz constitute the basic body, what the Chinese poetically described as the bones, of porcelain. Feldspar $[KAlSi_3O_8]$ (*petuntse* and also called the flesh of porcelain by the Chinese) plays a very special role during the final thermal processing step. The components are finely ground, thoroughly mixed, and after an elaborate hydration step acquire the necessary plasticity to create shapes of almost arbitrary complexity. The objects are subjected to an initial firing at 850-1000°C which renders them dimensionally stable yet absorbent. They are glazed by being dipped into aqueous slurry of the starting materials containing a higher proportion of feldspar.

The formation of porcelain occurs during the second heating to 1450°C. At this temperature feldspar softens and acts as flux, forming a eutectic with kaolin and quartz. Upon cooling, porcelain forms as a composite. It consists of a vitreous silica-rich continuous phase with needle like crystals of mullite (9) embedded in it. The continuous phase gives porcelain its translucency; the mullite crystals, because of their exceedingly small thermal expansion coefficient, provide the resistance to thermal shock. Feldspar is not the only substance that can act as a flux. Calcium sulfate in the form of gypsum was actually the flux material used by Böttger in his experiments, as well as commercially by the Meissen Manufactory during Böttger's lifetime. Calcium carbonate and calcium phosphate behave similarly.

How could anybody come up with these starting materials and conditions in order to duplicate the manufacturing process of porcelain during the first decade of the 18th century, when analytical chemistry was virtually unknown? The contemporaneous primary sources are silent on this matter. The official biographers speak only in generalities about Böttger's diligence, inventiveness, and methodical approach. There is, however, a remarkably detailed but little known early 19th-century account that comes from a totally unexpected source.

Simeon Shaw's Account of the Porcelain Invention

Simeon Ackroyd Shaw (1785-1859), an author and schoolmaster, was born in Lancashire, England. He came to Staffordshire, the center of English pottery manufacturing, to work as a printer for the "Potteries Gazette and Newcastle under Lyme Advertiser." In the 1820s and 1830s Shaw ran a number of academies for young gentlemen and was the author of several books, among them "The History of the Staffordshire Potteries," published in 1829, and "The Chemistry of Pottery," published in 1837. "The History of the Staffordshire Potteries" is one of the earliest chronologically based surveys of the area's development from the late medieval period to the state of the industry in Shaw's own times. Buried in the "History" and without any reference to a source or document lies a surprisingly detailed description of Böttger's invention (10):

> …While Reaumur was thus employed in France, Baron De Botticher was equally busily engaged in Saxony, and first produced the white kind of real porcelain in Europe. The Baron professed Alchemy, or the secret of the Philosopher's Stone, for transmuting metals into Gold; and having exhibited to his dupes several specimens, by some means they were shewed to the King of Poland. To gratify the cupidity of this monarch, by compulsory divulgement of this secret, an order was issued for his incarceration in the castle of Koningstein, where he unremittingly continued making experiments. While pursuing this useless research without opportunity to destroy or mal-appropriate whatever was produced, he found in one of his crucibles, what completely answered his purposes; the intense heat he employed to fuse some of his materials, rendered the crucibles themselves of similar appearance to the white Chinese porcelain;(very probably because of accidentally employing some materials in quality like those used in China;) he carefully repeated the process, and produced white porcelain; which caused Dresden to become the seat of the art..

Shaw is just as specific about the location as he is about the experimental details, Königstein, an impregnable fortress at the eastern corner of Saxony, about 20 miles from Dresden (curiously, Shaw uses a quasi-Dutch spelling, Koningstein). The specification of this location establishes the time frame, which must coincide with Böttger's second incarceration there from September 5, 1706 until September 22, 1707 to prevent his falling into the hands of the invading Swedish army.

To assess the plausibility of Shaw's account we must answer three questions: First, is the transformation described by Shaw chemically possible? Second, could it have actually taken place? and Third, is Shaw's account consistent with the known timeline of other, well documented events associated with the reinvention of porcelain? What follows is an examination of all three questions, albeit in reverse order. A fatal objection could be raised immediately. It is known that no kilns or ovens were allowed at Königstein because of the danger of fire. This well documented fact may have led scholars to dismiss Shaw's statement right from the outset, ending all further discussion. We shall see that this is actually a spurious objection.

Milestones in the Invention of Porcelain

Europe's first porcelain manufactory began its operations in 1710 in the castle of Albrechtsburg in the city of Meissen. Its founding followed Böttger's famous Memorandum to the King, dated March 28, 1709, where he announced that he can produce "good white porcelain **with the appropriate glaze and decoration;"** in other words, a finished, commercializable product. Based on this document the influential art historian Ernst Zimmermann in 1909 declared March 28, 1709 as the official date of Böttger's invention. Careful reading of the memorandum actually shows that it is a defensive document, intended to mollify a Saxon government growing impatient with Böttger's failure to deliver on his promises of transmutation, rather than a triumphant announcement of success in making porcelain. Nevertheless, Zimmermann's view prevailed until 1962, when a page of a laboratory notebook dated January 15, 1708 was discovered in the Meissen archives (11). The document is shown in Fig. 2. A transcript and commentary were published by Mields in 1967 (12).

The text describes a set of experiments involving the firing of mixtures of clay from Colditz with alabaster (calcium sulfate) as the flux. The quality of the ensuing porcelain for different clay to alabaster ratios is indicated

in notes on the margin written in Medieval Latin. The document appears to be describing a matrix of optimization experiments. Mields attributes the authorship of the notebook page directly to Böttger because of a comparison of the handwriting to letters in the Dresden archives known to be by Böttger's hand (13). The contents of this document suggest that the basic formulation for porcelain must have already been known to Böttger and his circle of collaborators prior to January, 1708. This is confirmed by Paul Wildenstein (1682-1744), one of Böttger's assistants. Wildenstein describes how, during the last days of December 1707, Böttger showed a small unglazed porcelain teapot to Augustus the Strong and demonstrated its resistance to thermal shock by pulling it out of the white-hot oven and throwing it into a pail of cold water (14). More significantly, on November 20, 1707 Augustus had already issued a decree assigning Böttger the task of creating several factories that made use of Saxony's mineral resources (15). If one rejects Shaw's account, one must conclude that the invention of porcelain took place in Dresden, after Böt-

Figure 2. Laboratory notebook page dated January 15, 1708 recording the results from a series of experiments with different clay/flux ratios (image courtesy of Staatliche Porzellan-Manufaktur Meissen Historical Collections, reproduced with permission).

tger's return from Königstein, sometime during October/November, 1707. Böttger's main preoccupation during those two months was, however, the construction with the assistance of Balthasar Görbig (1672-1739) of more efficient ovens for the high-temperature firing of large porcelain objects. Actual work in ceramic chemistry was left to two of his assistants, Wildenstein and David Köhler (1683-1723). It is unlikely that Böttger and Tschirnhaus would have left any work more challenging than the refinement of known experimental conditions to their assistants. To this end Wildenstein and Köhler used a most unusual apparatus, an extraordinary invention of Tschirnhaus. As we shall see, this apparatus resolves the conundrum of being able to carry out high temperature experiments at Königstein without access to kilns.

Experimentation at Königstein?

Tschirnhaus, a mathematician, physicist, and mineralogist, was born in Kieslingswalde (today Sawnikowice in Poland) and died in Dresden. During 1675 he worked with Robert Boyle (1627-1691), Isaac Newton (1643-1727), Christiaan Huygens (1629-1695), and was introduced to Gottfried Wilhelm Leibniz (1646-1716), with whom he maintained a lifelong scientific correspondence. Besides his contributions to mathematics (theory of polynomials), Tschirnhaus is perhaps best known for his invention of large parabolic mirrors (1686) and burning lenses (1687) to create very high temperatures. In 1687 he was able to melt asbestos for the first time, a substance regarded since antiquity as infusible. Tschirnhaus was also the first to observe the phenomenon of eutectic formation. In 1699 he reported to the French Academy of Sciences (16) that, while chalk and quartz cannot be fused at the temperatures available to his burning mirrors, a finely ground mixture of the two ingredients could be made to flow. Based on a written record by Leibniz, Tschirnhaus became interested in porcelain as early as 1675. In 1694 he used a burning lens to melt a shard of Chinese porcelain and showed that metal oxides can be made to adhere to porcelain at high temperatures. Specifically, he found that gold under such conditions gives porcelain a purple color, an observation he communicated to Leibniz.

A two-stage burning lens built by Tschirnhaus is shown in Fig. 3. It can be seen today at the Physikalisch-Mathematischer Salon as part of the Staatliche Kunstsammlungen, Dresden. The instrument is 2.5 m in height, and the two lenses are 50 cm and 26 cm in diameter. On the basis of Tschirnhaus' accounts of the substances he could bring to a molten state, the highest documented temperature is about 1600 °C. The solar energy could be
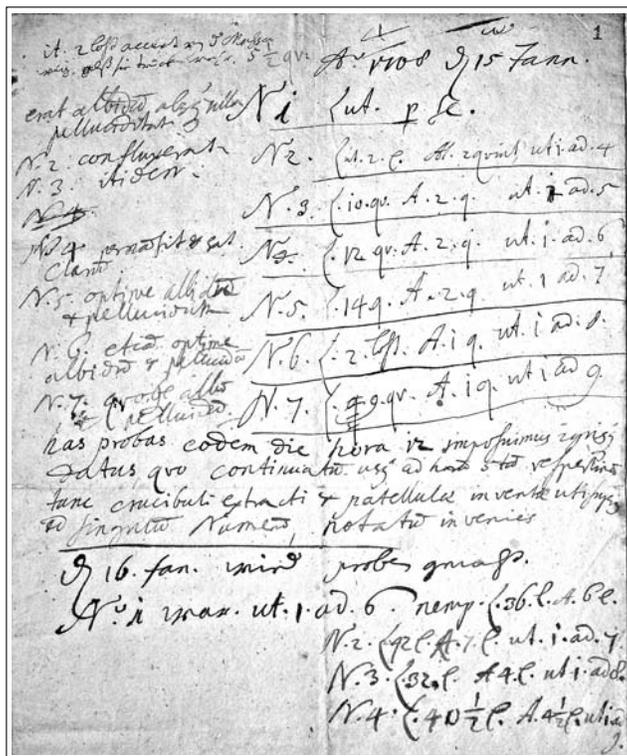
Figure 3. *Two-stage burning lens apparatus built by Ehrenfried W. v. Tschirnhaus, in Kieslingwalde around 1690; reproduction (image courtesy of Staatliche Kunstsammlungen Dresden, Mathematisch-Physikalischer Salon, Photographer: Michael Lange, Dresden, reproduced with permission).*

focused down to an area of about 10-15 cm^2. There is little doubt that burning lens equipment played a major role in Böttger's work. This is hardly surprising, since Tschirnhaus, the leading Saxon scientist of his time, was assigned by Augustus in 1704 to supervise Böttger's experiments closely. The earliest evidence comes from Johann Melchior Steinbrück (1673-1723), who was initially at Böttger's private service, and later was charged with the day-to-day administration (*Inspektor*) of the Meissen Porcelain Manufactory. In 1717 he submitted a lengthy report to Augustus summarizing the events leading to the founding of the Manufactory in 1710 and its development in the following seven years under his supervision. In his report Steinbrück recounts that Tschirnhaus was a proponent of the use of burning lenses in ceramics experiments. Böttger, in response, raised the curious objection that the lenses caused melting of the substances that altered their "essence" (a puzzling concern coming from somebody attempting transmutation). Nevertheless, Steinbrück writes, at the end Böttger did make use of such a device for his invention (17). It is conceivable that the absence of ovens at Königstein encouraged Böttger to change his mind. Similarly, Wildenstein complains in his Petition (18) about how his own eyesight was damaged from the use of burning lenses when he and Köhler were testing

mixtures of clays and fluxes for porcelain. A less well known document in the Meissen manufactory archives and dated to 1743 (19) also refers to experiments with burning lenses both for the development of red stoneware (a project that was being run in parallel) and for porcelain. A passage from the document states that "Tschirnhaus' burning lenses were used to test not only the red clays, some of the white clays tested would soften and become porcelain-like."

But it is Karl Berling who gives us the most direct evidence. In the Introduction to the History of the Meissen Manufactory published in 1911 on the occasion of the 200th anniversary of the Manufactory, Berling states almost in passing that Böttger used this equipment for ceramics experiments while in Königstein. He writes (20):

> …and Böttger seems to have been more fortunate than his master [i.e. Tschirnhaus] in working with the burning glass of the latter. On the Königstein he succeeded in making Dutch ware, a sort of Delft fayence, and in the last months of the year 1707 he brought forth in Dresden red stoneware.

We have so far established that Shaw's account is consistent with the known timeline of events leading to the manufacture of commercially viable porcelain, and that high-temperature experiments on the Königstein even without the use of ovens were feasible and had in fact taken place. We shall now turn to the pivotal question of whether the transformation described by Shaw is chemically possible.

Crucible Chemistry and Porcelain

The one passage in Shaw's account that is most important to the chemical history of porcelain states (10):

> …the intense heat he employed to fuse some of his materials, rendered the crucibles themselves of similar appearance to the white Chinese porcelain…

The passage describes the observation of an unexpected event, thus vividly capturing a moment of discovery. To what extent is this description realistic?

In January, 1702, as Böttger prepared to start his transmutation experiments for Augustus the Strong, he gave councilor of mines Gottfried Pabst von Ohain (1656-1729) a list of chemicals and equipment he would need for his experiments (21). Included in this list were Hessian crucibles, a most remarkable type of stoneware, first invented during the late Middle Ages in the village of Grossalmerode near Kassel in Hessen. These

Figure 4. *Hessian crucibles from ca. 1607-1610 excavated at Jamestown with evidence of copper smelting, which may have been used in attempts to produce brass (image courtesy zof the APVA Image Bank, reproduced with permission).*

thin-walled crucibles are 2-20 cm in height and have an astonishing resistance to thermal shock. They were the favorite tools of metallurgists, goldsmiths, assayers, and of course alchemists the world over. Their characteristic triangular shape allows for convenient pouring in all directions. Hessian crucibles have been found across continental Europe, from Portugal to Norway, and also in Great Britain and the British colonies of the New World. The examples of Hessian crucibles shown in Fig. 4 were indeed excavated in the Settlement of Jamestown, Virginia, the first English speaking settlement in North America. According to Hudgins (22) they were used by early settlers for cementation experiments (a step in the production of brass) around 1607-1610.

The factors behind the heat resistance of Hessian crucibles became clear only very recently through the work of M. Martinón-Torres, Th. Rehren of the University College London, and I. Freestone of Cardiff University (23, 24, 25). They used scanning electron microscopy and X-ray powder diffraction to detect both mullite (see Fig. 5) and quartz in Hessian crucibles, together with iron oxide. Just as with porcelain, the resistance of Hessian crucibles to thermal shock can thus be attributed to the presence of mullite. By examining the crystal morphology Martinón-Torres et al. (24) conclude that most, but not all of the
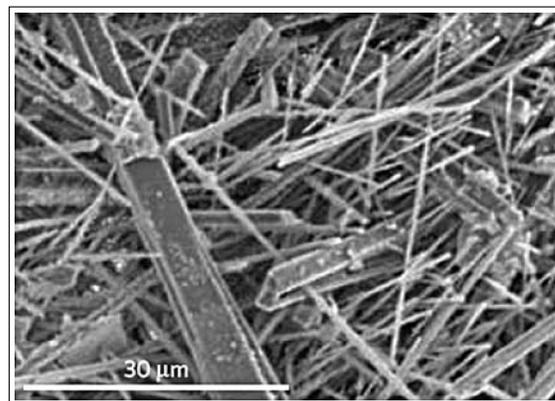
Figure 5. *Electron micrograph of mullite needles from a flux-rich region within a Hessian crucible (image courtesy of M. Martinón-Torres reproduced with permission).*

mullite (26) comes directly from the decomposition of kaolin during processing at an estimated temperature of 1200-1400°C, rather than through the action of a flux. All the ingredients for porcelain with the exception of a sufficient quantity of a flux are therefore present within the crucible body. Böttger could have indeed transformed all or part of a crucible into a porcelaineous body in the manner Shaw describes. He would only need to add a calcium salt like calcium carbonate or calcium sulfate (27) under the higher temperatures afforded by a burning lens apparatus as part of some transmutation experiment. Calcium salts were commonly found in the alchemist's tool kit for purifying and assaying silver or gold by a process known as cuppelation.

Concluding Remarks

In the light of the evidence presented here, Shaw's account appears plausible and indeed likely. Böttger could have gained several key insights from this observation that later guided his work and that of Tschirnhaus and their laboratory assistants upon Böttger's return to Dresden. Shaw's account is also consistent with the archival evidence presented in Ref. 14 and 20, that the basic formulation of porcelain was known to the team of Böttger and Tschirnhaus as early as the latter months of 1707, in contradistinction to opposing claims first voiced by Bussius in 1719 (28). The observation would have pointed to the need for higher temperatures. Neither the small laboratory ovens described by Johann Rudolf Glauber (1604-1668) nor the larger more efficient ones by Johann von Löwenstern Kunckel (1630-1703) could reach the temperatures needed for porcelain production (29). The observation would have also established

the flux material. Pabst von Ohain, in notes written on May 29, 1706 was already speculating that the secret of Chinese porcelain possibly lay in the use of a calcareous flux (30).

Most significantly, the observation would have led Böttger and Tschirnhaus to consider clays with properties similar to those of clay used in the production of Hessian crucibles. The use of clay from nearby Colditz for making heat resistant containers and bricks for ovens that could withstand high temperatures was already well established. In fact, upon his return from Königstein, Böttger contended that he knew how to make crucibles that would surpass the Hessian ones in performance. A crucible manufactory was one of the several enterprises he proposed to Augustus. Böttger did bring in Meister Johann Just Gundeloch, one of the last surviving Hessian crucible manufacturers from Grossalmerode, to verify his contention. It was ultimately decided not to build such a factory—based purely on economic considerations (31).

In conclusion, Simeon Shaw's little noticed passage is proven plausible and significant in understanding the process leading to the reinvention of porcelain in 18th century Europe. An important challenge for future research would be to identify the source for Shaw's insight.

ACKNOWLEDGMENTS

REFERENCES AND NOTES

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1. To appreciate how multifaceted the role of porcelain in our society is, the reader need only consider that as heat resistant high voltage insulators, porcelain components are found on virtually every utility pole. At the same time, a Vienna teapot from ca 1720, made essentially of the same material, was sold at a recent Sotheby's auction well in excess of its pre-auction estimate of $215,000.

2. For a discussion of protoporcelain ware from the Han Dynasty see N. Wood, *Chinese Glazes: Their Origins, Chemistry, and Recreation*, University of Pennsylvania Press, Philadelphia, PA, 1999, 21-23.

3. This attempt to introduce the "essence" or "form" of porcelain into the clay is entirely within the alchemistic tradition. For a discussion of the ideas of the alchemists see F. S. Taylor, *The Alchemists: Founders of Modern Chemistry*, Collier Books, New York, 1962, 12-21.

4. During the 1650s John Dwight (1635-1703) worked for Robert Boyle, which might explain why he embraced a chemical rather than alchemistic approach. He was granted a patent on April 17, 1672 for making "transparent Earthen Ware" which, nevertheless did not rise to the level of true hard paste porcelain. Dwight's move away from the use of glass frit is pointed out by Honey; see: W. B. Honey, *Dresden China*, Tudor Publishing Company, New York, 1946, 7.

5. Augustus the Strong (1670-1733), Prince Elector of Saxony (r. 1694-1733) and King of Poland (r. 1697-1704 and again 1709-1733).

6. C. A. Engelhardt, *J. F. Böttger, Erfinder des Sächsischen Porzellans,* Verlag von Johann Ambrosius Barth, Leipzig, 1837, (reprinted by the Zentralantiquariat der Deutschen Demokratischen Republik, Leipzig, 1981).

7. K. Hoffmann, *Johann Friedrich Böttger: Vom Alchemistengold zum weißen Porzellan,* Verlag Neues Leben, Berlin, 1985.

8. Eine detaillierte Darstellung der chemischen Experimentiertätigkeit Böttgers muß jedoch einer Spezialstudie vorbehalten bleiben." (A detailed presentation of Böttger's experimental work must be left to [a future] specialized research on the subject); Ref. 7, p 187

9. Mullite has the nominal composition $3Al_2O_3.2SiO_2$ and is the only chemically stable intermediate phase in the $SiO_2\text{-}Al_2O_3$ system. Its high temperature strength and resistance to thermal shock and chemical attack make mullite one of the most versatile engineering ceramics.

10. S. Shaw, *History of the Staffordshire Potteries*, Praeger Publishers, (reprint of the1829 ed.), New York, 1970, 196.

11. Staatliche Porzellan-Manufaktur Meissen, Historische Sammlungen P 44 Blatt 1.

12. M. Mields, "Eine Versuchsaufzeichnung von Johann Friedrich Böttger zur Porzellanerfindung aus dem Jahr 1708," *Ber. Dtsch. Keram. Ges.,* **1967**, *44*, 513-517. A transcript and English translation of the document in pdf-format are available from the present author upon request.

13. An alternate view holds that the document is by the hand of Dr. med. Johann Jakob Bartholomaei (1670-1742), Böttger's personal physician, who on January 6, 1708 was also assigned to help him with his ceramics work.

Regardless of who wrote the document, it pushes the date of the actual invention to the previous year.

14. Wildenstein gives a colorful account of this demonstration 29 years after the fact in his lengthy 1736 petition for payment of salary owed to him by the Meissen Manufactory. A transcript of the text with commentary has been published by Walcha: O. Walcha, "Paul Wildensteins Eingabe," *Mitteilungsblatt Keramik-Freunde d. Schweiz*, **1958**, *42*, 17-22. The author would like to thank Dr. Pierre Beller, treasurer of the Keramik-Freunde der Schweiz, for a copy of the article. In a memorializing letter to Augustus immediately following the demonstration, Böttger states that the teapot was made with the help of Herrn von Zschirnhausen [sic] („mit Bey Hülffe des Herrn von Zschirnhausen" fertiggestellt wurde). The source for this quote is a document in Staatsarchiv Dresden, Geheimes Kabinett, Loc. 1340: J.F. Böttgers u. Consorten Angelegenheiten, Vol. II, fol. 148. I would like to thank Dr. Mathias Ullmann, Chairman of the Tschirnhaus-Gesellschaft Dresden for communicating the archival location of the document. Böttger's statement shows that the relationship between Böttger and Tschirnhaus was one of collegiality and sharing of information.

15. The full text of the decree is given in Ref. 6, p 255. The text does not explicitly enumerate the projects and uses instead the phrase "tasks known only to us" (*Uns allein bekannte Verrichtungen*). They are discussed explicitly in the Steinbrück Report of 1717 (see Ref. 17 below).

16. On July 22, 1682, at the age of 31, Tschirnhaus became the first German national to be elected to the French Royal Academy.

17. I. Menzhausen, *Johann Melchior Steinbrück Bericht über die Porzellanmanufaktur Meissen von den Anfängen bis zum Jahre 1717; Kommentar, Transkription und Glossar*, Edition Leipzig, Leipzig, 1982, 47-48.

18. Ref. 14, p 21.

19. Ref. 7, p 375. Dr. med. Christoph Heinrich Petzsch (1692-1756), the presumed author of the document, uses vivid Latin prose to describe the outcome of these porcelain experiments: "…semidiaphanam tremuli narcissuli, ideam lacteam" or "appearing milky white like a translucent fluttering narcissus."

20. K. Berling, Ed., *Meissen China*, Dover Publications, Inc., New York, (unabridged reprint of the work originally published in English in 1910 under the title *Festive Publication to Commemorate the 200th Jubilee of the Oldest European China Factory, Meissen*, by the Royal Porcelain Manufactory, Meissen), 1972, 2. It should also be mentioned that while in Königstein, Böttger received several visits from Tschirnhaus. Following the visit by Tschirnhaus, Nehmitz, and Ohain at the end of June 1707, Böttger memorialized "mit dem Herrn von Schürnhausen [*sic*] alle Veranstaltungen verabredet zu einer sehr fleißigen Arbeith." (I have agreed with Tschirnhaus upon all arrangements for a very diligent work[plan]).

21. The list is discussed in Ref. 7, pp 188-189 (page numbers refer to the actual report, not the transcript).

22. C. C. Hudgins, "Chemistry in the New World," *Chem. Heritage*, **2007**, *25*, 20-26.

23. M. Martinón-Torres, T. Rehren, and I. C. Freestone, "Mullite and the Mystery of Hessian Wares," *Nature*, **2006**, *444*, 437-438.

24. M. Martinón-Torres, I. C. Freestone, A. Hunt, and T. Rehren, "Mass-Produced Mullite Crucibles in Medieval Europe: Manufacture and Material Properties," *J. Am. Ceram. Soc.*, **2008**, *91*, 2071–2074.

25. M. Martinón-Torres and T. Rehren, "Post-Medieval Crucible Production and Distribution: A Study of Materials and Materialities." *Archaeometry,* **2009**, *51*, 49-74.

26. Martinón-Torres et al. did observe highly elongated mullite crystals in areas of locally high feldspar concentration. These are the crystals shown in Fig. 5.

27. The reader is reminded that calcium sulfate in the form of gypsum was the typical flux used in early Böttger porcelain.

28. On January 19, 1719, less than two months before Böttger's death, Caspar Gottlob Bussius, treasurer of the Meissen Manufactory, claimed in a report to the Manufactory Commission (roughly equivalent to today's board of directors) that the credit for the invention of porcelain should properly go to Tschirnhaus and that following Tschirnhaus' death the secret of the porcelain composition (the *Arcanum*) was illicitly given to Böttger by Steinbrück, who was at the time the private tutor of Tschirnhaus' children. Dismissed at the time, the story was revived during the early 1900s by Curt Reinhardt and Hermann Peters (see for example: C. Reinhardt, "Tschirnhaus oder Böttger? Eine urkundliche Geschichte der Erfindung des Meißner Porzellans," *Neues Lausitzisches Magazin*, **1912**, *88*, 1-162; and also P. Diergart, "Was wissen wir gegenwärtig von der Erfindungsgeschichte des europäischen Porzellans? Mit Benutzung eines Manuskriptes des Herrn Hermann Peters-Hannover," *Mitteilungen zur Geschichte der Medizin und der Naturwissenschaften*, **1906**, *5*, 534-536. The date of the laboratory notebook page shown in Fig. 2 and the account given in the Wildenstein Petition (see Ref. 14) show that Böttger, Tschirnhaus, and their assistants already knew the recipe for porcelain during the second half of 1707, about a year before Tschirnhaus' death. The timeline for Bussius' conspiratorial hypothesis is therefore wrong but has nevertheless been repeated as recently as 1998 (see e.g., M. Schönfeld, "Was There a Western Inventor of Porcelain?" *Technol. Cult.*, **1998**, *39*, 716–729). A counterpoint is offered by Ulrich Pietsch, the director of the Dresden Porcelain Collection: U. Pietsch, "Tschirnhaus und das europäische Porzellan," in P. Plassmeyer and S. Siebel, Ed., *Ehrenfried Walther von Tschirnhaus (1651–1708): Experimente mit dem Sonnenfeuer*, Staatliche Kunstsammlungen, Dresden, 2001, 68-74. For a more up-to-date account see also U. Pietsch and P. Ufer, *Mythos Meißen*, edition Sächsische Zeitung, Dresden, 2008.

29. Alchemists and early chemists typically built the ovens used in their experiments themselves. A new design to

improve oven efficiency was published by Glauber under the name *Furni novi philosophici* (first edition, in German, 1646-49). Further improvements in oven construction were made by Kunckel as reported to Prince Elector Johann Georg II in 1675 (see Ref. 7, p 260). None of these designs could produce the temperatures needed for porcelain production. This explains Böttger's preoccupation with oven design during October/November, 1707.

30. Ref. 7, p 219.
31. Ref. 17, pp 76-79.

ABOUT THE AUTHOR

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REINVESTIGATING VESTIUM, ONE OF THE SPURIOUS PLATINUM METALS

James L. Marshall and Virginia R Marshall, University of North Texas, Denton

Introduction

In 1806 the Académie de France proclaimed that a new metal had been discovered in platinum (1):

> One writes from Germany that a chemist has discovered a new metal in small amounts in platinum. It was named Vestium from Vesta, the last planet [asteroid] discovered by Olbers. Consequently, platinum contains, 1. platinum. 2. palladium. 3. rhodium. 4. osmium. 5. iridium. 6. vestium. Other impurities were gold, iron, copper, titanium. . . . [authors' translation]

Three years later, in one of the shortest publications on record, it was announced by the Académie (2):

> On Vestium. This new metal has been reported as being isolated from platinum, but the experiments are not reproducible. We await further work. [authors' translation]

The case of vestium essentially lay dormant in the scientific literature until Weeks categorically stated in *Discovery of the Elements* in the mid-twentieth century (3):

> The Polish chemist, Jedrzej (Andrei) Sniadecki was the first to isolate the element now known as ruthenium, which he called vestium, though he later became convinced that this was not a new metal. . . . In Paris. . . . a commission composed of Berthollet, de Morveau, Fourcroy, and Vauquelin was unable to detect the new metal in their platinum. This so discouraged Sniadecki that he dropped all his claims and carried out no further experiments. There is no doubt, however, that he had isolated ruthenium.

One can search contemporary literature for details regarding vestium, but they are lacking. Nevertheless, the layman's literature accepts Sniadecki's discovery; for example, the Wikipedia entry is as follows (4):

> Sniadecki may have been the original discoverer of the element ruthenium in 1807, thirty-seven years before Karl Klaus.

(Karl Ernst Klaus, 1796-1864, is the historically accepted discoverer of ruthenium (5)). According to the Polish Wikipedia entry for Sniadecki (6):

> He discovered ruthenium (called vestium in an 1808 presentation about his work where he discovered it in crude platinum) only to find it was not officially confirmed. [author's translation]

Note there is no mention of Klaus. Should Sniadecki, instead of Klaus, in fact be credited with the the original discovery of ruthenium? What is the story?

The Rebirth of Vestium—How it Happened

In 1808 Jedrzej (Andrew) Sniadecki (1768-1838), a Polish scientist at the University of Vilnius (now Lithuania, formerly in the Polish-Lithuanian Commonwealth), published his paper (7), in which he described a "new metal" that he found in crude platinum in addition to the four (palladium, rhodium, iridium, and osmium) just discovered by the English scientists. He named this element vestium ("West" in Polish) in observance of the asteroid just discovered (Vesta, in 1807). After his discovery Sniadecki sent his 1808 report to the

French Academy and to the Russian Academy of Sciences. The French Academy promptly published the preliminary account (1). To validate his claim Sniadecki sent a sample of platinum ore to Paris, which was analyzed by Guyton, Fourcroy, and Berthollet (and nominally Vauquelin); but they could not reproduce the work (8), and Sniadecki's claim was rejected (2). Meanwhile, the Russian Academy reported Sniadecki's claim with the comment that it could not be accepted without verification, but no one did experimental work in an attempt to confirm vestium (9).

The French rejection did not really settle the issue. In spite of the grand reputation of French science at the beginning of the 19th century, the science citizenry outside Paris was well aware that the French Academy was not infallible in its chemical analysis (10). After Cronstedt discovered nickel in 1751, Sage and Monnet opined that the "new metal" was merely a mixture of cobalt, arsenic, iron, and copper—prompting Scheele (who discovered molybdenum in Köping) to write to Hjelm (who prepared an ingot of it on his forge in Stockholm) (11):

> I can already see the French hurrying to deny the existence of [our molybdenum].

Other hasty assessments of the French include Buffon's pronouncement that platinum was merely an alloy of iron, gold, and mercury (12) and Collets-Descotils' misidentification of del Río's "erythronium" as chromium after performing only three quick superficial experiments (13), thus "undiscovering" vanadium (14).

Unfortunately, Sniadecki could not reproduce his own chemistry (15). Before the initial reading in Paris he had attempted a retraction, but his brother Jan Sniadecki (1756-1830), who was rector of Vilnius University 1807-1815, urged him to persist. In a speech at a public meeting of the university, Jan boasted of this chemical achievement which elevated Jedrzej to the level of Klaproth and Vauquelin, the two best laboratory chemists in the world, and of Bergman (the mentor of Scheele) (11). After the French pronouncement, however, Jedrzej allowed the matter to drop, not even mentioning vestium in his own chemistry textbook (11, 15).

Figure 1. *Sniadecki's bust. The caption heralds him as "Vilnius professor of natural sciences 1797-1832, philosopher, head of the medical clinics. Artist Kazimieras Jelski. Terracotta."*

A century later, in 1907, Waclaw Kaczkowski, a dyestuff technologist from Warsaw, reopened the question and wrote an article (16) arguing that Sniadecki should have persisted in his claim. In fact, Kaczkowski contended, vestium was ruthenium, which by then had been known for six decades. A debate for and against Kaczkowski's idea ensued in the Polish scientific community (11). In 1937 Stanislaw Plesniewicz, a lecturer in the Warsaw Polytechnic Institute, urged Mary Elvira Weeks to include Sniadecki in her *Discovery of the Elements*. Although Weeks had not mentioned Sniadecki in her original article on the platinum group (17), she did add a paragraph about vestium in her book (3)—but with no chemical details, as she customarily did for other elements in that expansive book.

Reinvestigating Vestium

To explore the question of vestium with hopes of settling the issue, the present authors traveled to Vilnius, Lithuania. Here they visited the university where Sniadecki worked, and they consulted with scholars (15) familiar with Sniadecki's career. The first task was to obtain an accurate translation of Sniadecki's work, written in old Polish, which presented obstacles to a clear understanding of the experimentation. Fortunately, three separate and independent translations became available (15) and furnished a dependable account of Sniadecki's procedure:

First, Sniadecki boiled 400 g of crude platinum in nitric acid to remove mercury. Then he dissolved the residual ore in aqua regia, obtaining a solution and a residue. In the residue he identified and verified osmium and iridium. In the solution he identified contaminants iron, silver, lead, and the noble metals platinum, palladium, and rhodium—and vestium. The vestium was isolated as "red needles" (vestium chloride), which were not soluble in "spirit of wine" (ethanol) and which remained after alcohol extraction. Sniadecki performed several chemical tests to characterize the "new metal" to fill out his 26-page treatise (7). One who carefully reads Sniadecki's original paper finds irreconcilable differences between vestium and ruthenium. The main problem is

that vestium was found in the wrong fraction, i.e., in the aqua regia-soluble fraction. It is to be remembered that Klaus discovered ruthenium in the insoluble residue. Today ruthenium is known to be the least tractable of the platinum-group elements (18). Despite the fact that ruthenium is not soluble in aqua regia, proponents of vestium have claimed that Sniadecki's observations could be rationalized by the fact that Sniadecki "had only a small quantity of the metal at his disposal," and hence the minute quantity could be dissolved in aqua regia (16). Unfortunately, this argument of low concentration solubility is diametrically opposed to the fact that ruthenium chloride (either $RuCl_3$ or $RuCl_4$) is readily soluble in ethyl alcohol (11), whereas vestium chloride was not soluble (19).

Additional disparities are noticed, such as the reaction of vestium chloride with hydrogen sulfide to form an orange precipitate, whereas ruthenium chloride reacts to form a black precipitate (11, 19); and its reaction with ammonium chloride to form a lemon-yellow precipitate, while ruthenium chloride forms a black precipitate (11, 19). Arguments (16) have been made that these discrepancies arise from Sniadecki's vestium being "impure," but Sniadecki's orange and bright-yellow derivatives could, at the very best, contain only minute amounts of authentic ruthenium compounds which are black. In total, nine distinct differences between the chemical behavior of vestium and ruthenium have been documented (11), leading one to read with astonishment and amusement such comments as (16):

> . . comparison of the reactions of the two metals provides grounds for identifying vestium as ruthenium and thus crediting our great naturalist with yet another achievement in the field of science.

It is regrettable that proponents of vestium were generally not knowledgeable in platinum chemistry and that obvious inconsistencies with vestium were simply glossed over. It would be helpful to involve a specialist in platinum ore analysis in the debate, and as a matter of fact there was one, and he was outstanding: Orest Evgenevich Zvyagintsev (1894-1967), editor of the leading Russian platinum journal (20), coauthor of a series on ruthenium (21), and author of many articles on platinum geochemistry [a mineral has been named after him (22)]. Zvyagintsev's contribution to the debate was his matter-of-fact statement in 1957 that there was simply no similarity between vestium (whatever it was) and ruthenium (11).

So, what did Sniadecki have? The behavior of vestium does not correspond to that of any known element;

instead it mirrors a combination of several substances. Indeed, the history of platinum is replete with "discoveries" from platinum ore which were misidentifications, all mixtures. The list of mistakes includes not only Osann's irreproducible discoveries of four new elements [polinium, pluranium, two different rutheniums (23)] but also ilmenium, davyum, neptunium, uralium, amarillium, josephinite, and canadium, plus others that were never named—all of which were mixtures of metals and oxides of titanium, zirconium, silicon, iron, niobium, tantalum, tellurium, lead, tin, copper, the platinum-group metals, and perhaps other elements (24). The possibility of new element discoveries has always been alluring. Unfortunately, all too frequently elements have been identified without critical examination, even 20th-century "discoveries" such as alabamine, virginium, and illinium (25). The answer to the question "What is vestium?" remains unanswered—except one can say with certainty it is not ruthenium (26).

Sniadecki's Legacy

The legacy of Sniadecki lies in the many powerful contributions he made to the scientific community in Vilnius (8, 15). Born in Znin, Poland (half-way between Warsaw and Berlin), Jedrzej Sniadecki studied medicine in Krakow, Poland, and then in Pavia, Italy, where he graduated in 1793. Sniadecki admired Lavoisier and adhered to his principles; he wanted to meet Lavoisier but the French Revolution prevented this; instead he studied with Joseph Black in Edinburgh, Scotland in 1794. He was professor of natural sciences 1797-1832 at Vilnius (15). He and his brother introduced Polish into the lectures at the university; he wrote the first chemistry text in Polish. His famed book, *Początki chemii* (Introductory Chemistry), first written in 1800, has been used over a century (15). Sniadecki was a strict anti-phlogistonist and was informed about modern chemical theories. In his textbook he developed the general Polish vocabulary for chemical terms and nomenclature which are still used today (15). His laboratory and home still stand in Vilnius.
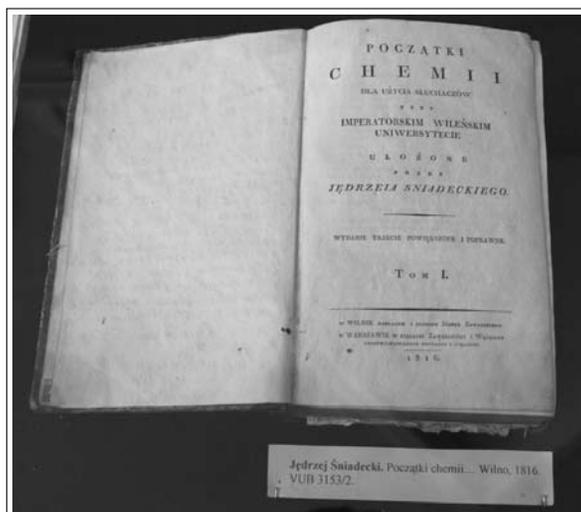
On September 28, 2008, the Jedrzej Sniadecki Lecture Hall (Auditorija) was dedicated at the Chemistry Faculty (Chemijos Fakultetas) at Vilnius University (Fig. 3). In the grand exhibit hall of St. John Church (Sv. Jonu Baznycia), the site of the original Vilnius University (Fig. 4), Sniadecki's bust (Fig. 1)is prominently displayed, as well as his famous Początki chemii (Fig. 2).

A Second "Discovery" of Vestium

In 1818, ten years after Snia-decki's claim, the German editor Ludwig Wilhelm Gilbert (1769-1824) announced (27) a new element discovered by Lorenz Chrysanth von Vest (1776-1840) of Graz, Austria. Vest was professor of botany and chemistry at the University of Graz (1812-1828) and later (1829-1840) Protomedicus (Chief Government Medical Officer) of Steiermark (Styria, in southeast Austria), attaining lasting recognition for his writings in botany and his contributions to public medical health in Steiermark

Figure 2. In the St. John's exhibit room is Sniadecki's famous introductory text, Sniadecki's famed book, Poczatki Chemii, first appeared in 1800 and used for over a century. It was the first general chemistry book written in Polish.

(28). His "new element" was found in a nickel ore of Schladming, Austria (27), 140 km west of Graz. Vest had originally proposed the name Sirium but adopted Vestium upon Gilbert's suggestion. [Gilbert was unaware of Sniadecki's work (29)]. Vest's article followed with a detailed analysis of his new metal (30), with an addendum that Sir Humphry Davy (1778-1829) had visited during his continental tour and had briefly studied the "new metal." Davy initially thought it might be tantalum but then changed his mind and took a sample away for further analysis in London (30). Thomson, editor of *Annals of Philosophy*, was quick to note that the discovery was in question because Vest had never obtained vestium free from arsenic, cobalt, and nickel (31); and in 1819 Michael Faraday (1791-1867), Davy's assistant, published an article announcing that vestium was only impure nickel (32), with minor amounts of cobalt, iron, and arsenic. Promptly, this "second" vestium was "utterly forgotten," never to be revived again (33).

Lessons from Vestium

In the excellent website Elementymology & Elements Multidict by the author Peter van der Krogt (34) lists over 200 "Names that did not make it," i.e., elements and/or element names which we do not recognize today as valid. Some of the names are archaic (e.g., columbium for niobium), but the majority are erroneous claims. Why were there so many? A more detailed analysis of the second vestium (sirium) may give us insight. A French editor

observed, immediately after Vest's announcement (35):

..as it now stands, nobody can give credit to M. Vest's Sirium, but must rather be impressed with his want of experience. As he appears not to know that nickel is not precipitated from its solutions by sulphuretted hydrogen [hydrogen sulfide], when they are acid, and that it is partially precipitated when they are neutral, we must beg him to repeat his experiments in order to discover whether his Sirium be not merely very impure nickel.. . .

Indeed, a chemist versed in inorganic qualitative schemes knows very well that the selective precipitation of metal ions with hydrogen sulfide—especially the nickel-cobalt subgroup—requires a very carefully adjusted pH (36). After ascertaining the major components (37), with his wry sense of humor Faraday described his analysis of 4.9 g of ore, how he carefully removed the arsenic, then the cobalt, finally the nickel, only to find that, "My Vestium entirely disappeared (38)."

Three years later Berzelius (1779-1848), the master assayer in Sweden, published an insightful discussion of the difficulties of analyzing ores of nickel (39). In this work, he advanced the art of nickel ore analysis to a sophisticated level, as Klaus had done for platinum ores. Berzelius studied the reasons why not only vestium, but also two additional substances from nickel ore had been misidentified as new metals. These two substances were "wodanium," from a Hungarian ore (40), and "nicolanum," observed "only in the presence of nickel ores (41)." He pointed out that not only alloys of two or more different metals, but also compounds of metals with arsenic or sulfur, can appear as unique metals. Consider, for example, niccolite ($NiAs$), a reddish-brown mineral with a metallic luster (42), which was originally confused with copper until Axel Fredrik Cronstedt (1722-1765) discovered nickel in 1751 (43).

Berzelius' treatise underscores the difficulties of analyzing new materials in the early years of qualitative analysis, during the late 1700s and the early 1800s, before sophisticated schemes were worked out and when

Figure 3. The old courtyard of Vilneus University, founded in 1579 and built around the Sv. Jonu Baznycia (St. John's Church) which is straight ahead. The location is on Universiteto Gatve. The building to the right has an old auditorium, akin to the one where Jedrzej Sniadecki's brother Jan, rector of the university, extolled the virtues of Jedrzej's vestium. Sniadecki, the "discoverer of vestium," had his laboratory 250 m to the east (straight ahead, past the church, out of view), on 2, A.Volano Gatve on the second floor of a building which is now the Lietuvos Respublikos Svietimo Ir Mosklo Ministerija (Ministry of Science and Education).

Figure 4. Grand Exhibit Hall, St. John Church

it was unknown which, and how many, elements were yet to be discovered. Even in the hands of experienced chemists, mistakes were easily made. This difficulty was understood by the broad scientific community, and it was common to send a specimen to experts for confirmation—and ideally to the masters, Klaproth of Berlin, Vauquelin of Paris, or Berzelius of Stockholm. In the case of Lorenz von Vest, there was good reason why he observed that the properties of vestium "were too much like those of nickel and cobalt to be separated (30)," for the "vestium" was a mixture of nickel and cobalt.

With the platinum group analytical difficulties were even sharper, and Sniadecki, a more experienced chemist, did not understand the mutual interferences of the chemically similar platinum metals that hindered quantitative separations. This research had to await Klaus, four decades later, who was able to work out simple, efficient separation schemes for their various combinations (44).

For Vest we understand the source of his errors, because several accomplished chemists studied his "vestium" and we have access to their analytical results. Regrettably, for Sniadecki's vestium careful analysis was never repeated with his ore. Furthermore, one cannot reexamine his chemical samples, because they were shipped to the University of Kiev (during Russia's annexation of Lithuanian territory), never to be seen again (11)— and we shall never know the identity of his "red needles."

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been named after the first two asteroids, Ceres and Pallas); Vest hesitated, fearing he might be accused of intentionally lending his own name to his new metal, but he relented and accepted Gilbert's suggestion. The English continued to use vestium and sirium interchangeably.

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36. Ref. 18, pp 188-258.

37. M. Faraday, "On Sirium," *J. Sci. Arts, R. Inst. Gr. Br.*, **1819**, *6*, 112-115.

38. M. Faraday, "On Sirium, or Vestium," *J. Sci. Arts, R. Inst. Gr. Br.*, **1819**, 7, 291-293.

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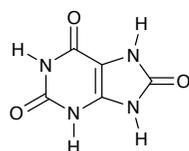
ABOUT THE AUTHORS

James L. Marshall and Virginia R Marshall, Department of Chemistry, University of North Texas, Denton TX 76203-5070; jimm@unt.edu. Dr. James L. Marshall received his Ph.D. in 1967 in organic chemistry from Ohio State University and joined the Department of Chemistry of University of North Texas in 1967, where he became engaged in research programs in nuclear magnetic resonance, conformational analysis, and material science. His many services have included chair of the department, chair of the ACS DFW section, and participant in the ACS Lecture Tour Series. Virginia R. Marshall received her M.Ed. with specialty in computer science in 1985 from Texas Woman's University and taught in the Denton I.S.D. for 20 years. The two married in 1998 and have been active ever since as a team in their "Rediscovery of the Elements" project, which by 2010 will culminate in their final publication covering eleven years of research.

# THREE CRUCIAL SCIENTIFIC OBSERVATIONS FROM MISTAKEN HYPOTHESES

M. John Plater, University of Aberdeen

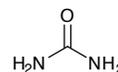## The Treatment of Mania with Lithium

In 1949 John Cade, a senior medical officer of the Victorian Department of Mental Hygiene, Australia, investigated the effects of lithium carbonate and lithium citrate on the mental state of patients suffering from mania or manic depression (1). This illness is sometimes known as bipolar disorder. Lithium was regarded as a controversial medication, which had resulted in the deaths of some patients and could sometimes cause unpleasant side effects. In the 19th century it was used for the treatment of gout and other ailments following the discovery by Garrod that lithium urate, a salt of uric acid, was the most soluble alkali metal urate. The presence of crystalline monosodium urate monohydrate (2) in the human body causes acute gouty arthritis, so the traditional use of lithium as a remedy for this has a theoretical basis. Pieces of cartilage with uric acid deposits were immersed in solutions of sodium, potassium, and lithium carbonate. Lithium carbonate was the fastest solution to dissolve the deposits. Enthusiasm for its use extended into other medications and also led to the widespread use of bottled curative waters, some of which are still marketed today, such as Perrier and Vichy, promoted at one time for their lithium content.
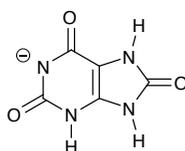
Cade carried out an experiment to determine whether uric acid was a toxic component of urea in manic patients. He wanted to determine whether this component might be the cause of mania. Unlike urea, uric acid is only poorly soluble in water, so the most soluble urate, lithium urate, was chosen. An aqueous solution of 8% urea saturated with lithium urate was injected intraperitoneally into some guinea pigs. The toxicity was less than expected. It appeared that the lithium might be exerting a protective effect, so further experiments were performed. Lithium urate was replaced with lithium carbonate. An 8% aqueous solution of urea kills five out of ten guinea pigs when injected intraperitoneally in doses of 1.25 mL per ounce of body weight. When 0.5% lithium carbonate in an 8% urea solution was injected in the same dosage, all ten animals survived. This showed that the lithium ion itself had a protective function against the convulsant mode of death caused by toxic doses of urea. This was an interesting and unexpected discovery which led to the next key experiment.

uric acid (lithium) urate urea

Cade proceeded to determine the effect of lithium salts alone on guinea pigs. When some animals were injected with large doses of 0.5% aqueous lithium carbonate solution, a key observation was made. After a period of about two hours the animals, still conscious, became lethargic and

unresponsive to stimuli for a few hours before returning to normal. Cade commented (1):

> It may seem a long distance from lethargy in guinea pigs to the excitement of psychotics, but as these investigations had commenced in an attempt to demonstrate some possibly excreted toxin in the urine of manic patients, the association of ideas is explicable.

Following this observation Cade wanted to try to use lithium salts for the treatment of mania. He also concluded that certain waters of wells in the British Isles, which were considered to have special virtue in the treatment of mental illness, had a real efficacy proportional to the lithium content of the waters. Ten manic patients were treated with either lithium carbonate or lithium citrate with remarkable results. The case study for one of them is reported below.

CASE II- E. A male, aged forty-six years, had been in a chronic manic state for five years. He commenced taking lithium citrate, 20 grains three times a day, on May 5, 1948. In a fortnight he had settled down, was transferred to the convalescent ward in another week, and a month later, having continued well, was permitted to go on indefinite trial leave whilst taking lithium citrate 10 grains three times a day. This was reduced in one month to 10 grains twice a day, and two months later to 10 grains once a day. Seen on February 13, 1949, he remained well and had been in full employment for three months.

All ten case studies are reported in Cade's original publication (1). Every patient showed a tremendous improvement. Lithium was introduced into medicine through a mistaken hypothesis. Today it is known as a "mood stabilizer" for people with mania. It serves to stabilize mood cycles by dampening high periods and easing low or depressive mood. Fortunately, some compounds that were developed for epilepsy like carbamazepine, trade mark Tegetrol, also function as mood stabilizers and can be taken alongside lithium for even better mood control (3). Lithium has enabled many individuals who suffer from manic depression to live relatively normal lives.

Cisplatin (II)
An in situ Drug from a Platinum Electrode

In 1965 the scientists Barnett Rosenberg, Loretta Van Camp, and Thomas Krigas of the Biophysics Department at Michigan State University, USA, investigated the effect of an electric current upon the growth of a suspension of bacteria (4). A special culture chamber was designed which contained platinum mesh electrodes.

The chamber was charged with a nutrient medium and inoculated with a species of *Escherichia Coli* and the bacterial population allowed to reach a steady state. The electric field was turned on at 1,000 cycles/sec for two hours. Platinum was chosen as the electrode material because of its chemical inertness, and the field was chosen to eliminate electrolysis effects and electrode polarization. Although these two precautions were taken, the scientists wrote (4):

> As we will show, both are mistaken ideas which led, via serendipity, to the effects described in this communication.

Microscopic examination of the effluent from the chamber showed that the *E. Coli* had ceased dividing and had begun to elongate. After just a few hours of electrolysis all the bacteria were in the form of long filaments that continued to increase in length rapidly with time. Even if the electric current was switched off the bacteria *continued to increase in length*. Oxygen was required to produce the effect. If nitrogen or helium was bubbled through the cell, the electric current had no effect upon the bacterial culture. Unexpectedly, a frequency of 500 c/s was the most effective in causing filamentous growth compared to the highest frequency used of 6,000 c/s. The lower frequency may allow more time for an active species to diffuse from the electrode surface so the concentration increases.

The filamentous growth observed by the scientists involved an inhibition of cell division but not of cell growth. In other words, the cells keep on stretching as they grow longer without dividing. Some agents known to cause filamentous growth were eliminated as possible causes here. These were ultraviolet light, temperature, pH, and magnesium ion. The investigators considered that a new chemical species might be generated in the electrolysis chamber, which was the causative agent. To test this hypothesis the nutrient medium was pumped into an electrolysis chamber and electrolyzed, after which it was pumped into a bacterial chamber with no electrodes. The electric current was only passed through the electrolysis chamber. If a new chemical species were formed in the nutrient medium in the electrolysis chamber that had a sufficiently long life time, it would still cause filamentous growth when added to the bacterial chamber. This proved to be the case. It caused elongation in the bacterial chamber, provided oxygen was present in the electrolysis chamber. If helium was bubbled through the electrolysis chamber, no elongation of cells occurred when the nutrient was transferred into the bacterial chamber.

The investigators showed by using a potassium iodide-starch test that an oxidant was being generated in the electrolysis reaction. Ordinary medium gave no reaction whereas the electrolyzed medium gave a positive test by turning from yellow to orange to blue after about five minutes. This oxidant might be the unknown *in situ-* formed reagent. A series of sensitive qualitative tests were used to detect possible oxidizing ions, all of which proved negative. Previously the investigators had passed an electric current through the nutrient medium. Now they took the known individual components of the medium, electrolyzed them separately, and tested for an oxidant. Results were negative with phosphate, sulfate, phosphate and glucose, phosphate, sulfate and glucose, sodium sulfate, and sodium carbonate. Positive results were obtained with ammonium and other chlorides. These solutions with chloride anions showed the characteristic yellow to orange to blue color changes with the starch/potassium iodide test. It was known that platinum electrodes can be attacked by an acidified chloride solution during electrolysis to form a compound of the formulae [PtCl$_6$]. A soluble platinum salt might therefore be the active agent. A solution of $(NH_4)_2PtCl_6$ tested positive with the potassium iodide/starch test, thus duplicating the series of color changes seen with the electrolyzed medium. Most importantly, inoculation of the bacterial culture chamber with a solution of $(NH_4)_2PtCl_6$ caused filaments to appear. The chemical needs only to be about 10 ppm to exert an effect. In the electrolysis experiments oxygen is vital and must somehow assist in the oxidation of the platinum electrode to generate $(NH_4)_2PtCl_6$.

From this breakthrough discovery a series of platinum compounds were tested for anti-tumor activity (5). Clinical trials began in the early 1970s with *cis*-Pt(II) $(NH_3)_2Cl_2$, with the outcome that cisplatin has become established as a valuable agent in the treatment of malignant teratoma or cancer of the testes. The compound $(NH_4)_2PtCl_6$, deduced to be present in the electrolysis nutrient, is in a higher oxidation state (Pt IV) and has a different structure from cisplatin; but since it is a mild oxidant it may get reduced *in situ* to generate square planar cisplatin.
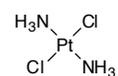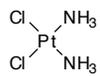
Transplatin   Cisplatin   Active anti-tumor species
(inactive)   (active)
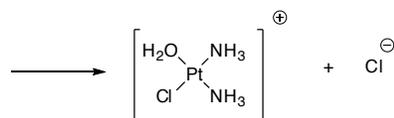
Cisplatin and the Active Anti-tumor Species

Since the discovery that cisplatin can interfere with cell division, investigators have tried to unravel the mechanism by which it works. As a neutral compound, it can readily cross cell membranes into cells. The interior of a cell membrane bilayer is nonpolar because of the lipid hydrocarbon chains, which can absorb neutral or nonpolar drugs like cisplatin. However, the chloride ligands are quite labile. The chloride ion concentration within cells is lower (4 mM) than in blood (104 mM). This favors hydrolysis and replacement of one of the chloride anions with water to give $[Pt(NH_3)_2(H_2O)Cl]^+$. This is an active species of the drug, which is a stronger coordinating agent because it is positively charged. Current opinion is that the platinum metal binds to some of the bases of a DNA strand and may bridge between them. In doing so it prevents the DNA from separating into strands, which is required for cell division to occur. It may work by changing the shape of the double helix and thus preventing a vital enzyme from recognizing the base-pair sequence.

In contrast to the flat *cis* isomer, the *trans* isomer exhibits no anti-tumor activity.

A New Drug for Treating Cancer
Heterocycles from EDTA

In 1969 the scientists Andrew Creighton, Kurt Hellmann, and Susan Whitecross, working at the Imperial Cancer Research Fund's department of chemistry and cancer chemotherapy, discovered anti-tumor activity in a series of compounds called *bis*-diketopiperazines (6). The initial hypothesis for discovering a new drug was to use a chelating agent that would bind to, and hence inactivate, trace metals that are vital to many enzymes inside cells. The cells would therefore die. The diagram shows how EDTA might bind to divalent metal ions M(II) by using its carboxylate side chains like claws to hold onto a metal ion, as depicted in a simplified X-ray crystal structure drawing of a metal complex of EDTA (7). Two carboxylate groups are ionized which balances the charge of the metal-ion in the center. The two nitrogen atoms which have lone pairs of electrons also coordinate making the complex even stronger. In total seven ligands bind to the metal ion: two carboxylates, two carboxylic acids, two tertiary nitrogen atoms, and a water.

EDTA   Possible EDTA metal complex
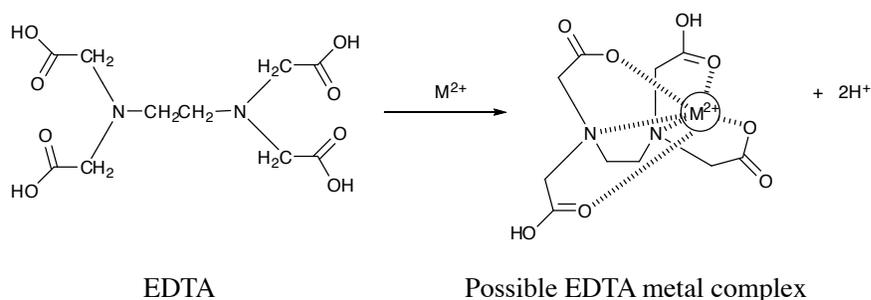
EDTA Binding a Metal-ion

EDTA, one of the strongest chelating agents for divalent cations, has no significant anti-tumor activity. This was readily rationalized because it is a charged polar molecule that would not easily cross through cell membranes. If a drug is to be absorbed and pass through a cell membrane into a cell, it should be nonpolar and quite "greasy." The investigators reasoned that if they prepared less polar derivatives of EDTA, these might penetrate cells more readily and break down into EDTA once inside the cell. These derivatives of EDTA would be *latent* precursors that are masking the desired molecule. The first two compounds synthesized and tested—the methyl and ethyl derivatives of EDTA—were inactive. The team then studied the reaction between EDTA and formamide in an attempt to prepare the tetramide. However, an unexpected product was formed: a diimide that showed promising screening results (8). This procedure is in fact a modification of one by J. R. Geigy (9), in which an extensive series of poly-N-diacetic acid imides are described as levelling agents, intermediates, textile auxiliaries, and curing agents. Both formamide, acetamide and urea can be used. Hence this very unusual reaction to convert iminodiacetic acids into diketopiperazines was already patented but for a different application.

Because of this discovery some further derivatives were made (10). A variety of acyclic analogs, in which the six-membered rings had been opened up, were inactive. This showed that the rings were important for the biological activity inside the cells and that they were not just allowing the compound to pass through the cell membranes. The incorporation of a methyl group—but not an ethyl group—at the central ethylene chain retained activity. These studies showed that a highly specific structure was required for anti-tumor activity. After publication of these results in 1969 the compound ICRF 159 was put on clinical trial. This led to its introduction for the treatment of acute myeloid leukemia and non-Hodgkin lymphomas (all forms of cancer) under the trade name of razoxane or razoxin.

This drug has no metal-ion chelating properties but was synthesized as part of a program to find a metal-ion chelating anti-tumor agent. The four arms of EDTA have been bound into six-membered heretocyclic rings with imide nitrogen atoms. These are less acidic than carboxylic acids, and geometry prevents them from simultaneously wrapping around a metal-ion like the carboxylic acids could. By an amusing twist of fate it was published in the journal *Nature*, along with the first metal-based compound to have anti-tumor activity, cisplatin.
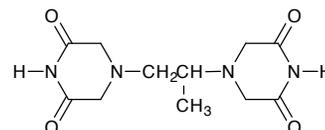
ICRF 159 Razoxane

Summary

Three examples of serendipitous discovery have been uncovered by the author after an extensive search of the literature over a number of years. They were selected from about 20 interesting examples, although a search engine analysis of the wider literature reveals hundreds of examples of publications with the word serendipity in the title or text. The common occurrence of serendipity in medicine, which is still underpinned by chemistry, is highlighted. Lithium and cisplatin (II) are inorganic compounds, whereas a *bis*-diketopiperazine is an organic compound that was prepared by chemical synthesis. There are numerous foundations and charities that fund medical research, probably because the public appreciate their role in health care and will provide financial support. But the public may not so easily grasp the role of chemistry in a medical discovery and hence may not appreciate its importance. Serendipity can help profile both chemical and medical research to a wider audience, and these examples illustrate that it can save lives and enhance the quality of life through anti-cancer therapy and the treatment of manic patients. The papers may have been based on mistaken hypotheses because the research plans were exploratory with an element of risk; but that thinking led to innovative discoveries. This

short synopsis highlights the need to fund basic blue sky research and to allow the development and exploitation of unexpected observations.

Origins of the Word Serendipity (11)

Horace Walpole (1717-97) fourth Earl of Oxford, son of Prime Minister Robert Walpole, connoisseur, antiquarian, and author of the famous gothic novel *The Castle of Otranto* and the 48-volume *Horace Walpole's Correspondence*, is credited with deriving the word serendipity from two letters that he wrote. The first (12), dated and addressed January 28, 1754, Arlington, [Piccadilly, London] was written to Horace Mann, an envoy in the service of King George II stationed in Florence. It was to acknowledge the safe arrival of a portrait of Bianco Capello, a 16th-century beauty and Duchess of Tuscany. His search for both a Capello and Medici coat of arms for the frame of the painting triggered his thoughts on serendip-

Horace Walpole, painting by John Giles Exkhardt, 1754

ity. He unexpectedly found a Capello coat of arms in a Venetian book with a fleur-de-lis attached to a blue ball. He recognized the fleur-de-lis as a Medici emblem and was persuaded that it was given to the Capello family by the Grand Duke in recognition of the marriage (12):

> This discovery indeed is almost of that kind which I call serendipity, a very expressive word…

From here he described an example of serendipity based on a fairy tale called *The Three Princes of Serendip*. The stories were published in Venice in 1557 by a printer Michele Tramezzino, who some believe was also the compiler of these ancient tales. Serendip is an old Persian or Arabic name for Ceylon. The episode with a camel—although Walpole confused it for a mule in his correspondence—inspired Walpole to derive the word serendipity (12):

> I once read a silly fairy tale called *The Three Princes of Serendip*: as their highnesses travelled, they were always making discoveries, by accident and sagacity, of things which they were not in quest of.

Walpole's key definitions for serendipity were "… discovery by accident and sagacity of things you are not in quest of…;" from a second line of thought "…*no*

discovery of a thing you *are* looking for comes under this description (12)." An instance of accidental sagacity "…was of my Lord Shaftsbury, who, happening to dine at Lord Chancellor Clarendon's, found out the marriage of the Duke of York and Mrs Hyde, by the respect with which her mother treated her at table."

The second letter, dated and addressed September 10, 1789, Strawberry Hill (14), [Twickenham, London] was written to a social reformer and religious writer Hannah More. He states (13):

> Nor is there any harm in starting new game to invention; many excellent discoveries have been made by men who were *a la chasse* of something very different.

His interest in the scientific method was also expressed here (13):

> I am not quite sure that the art of making gold and of living for ever have been yet found out: yet to how many noble discoveries has the pursuit of those nostrums given birth! Poor chymistry, had she not had such glorious objects in view!

The Oxford English Dictionary definition of serendipity is "The faculty of making happy and unexpected discoveries by accident." Some scholars believe this is different from the original derivation, but the OED has an explanation. Definitions of words can be "how words are or have been used, not how they ought to be used."

Walpole's Gothic mansion is currently under restoration by the Strawberry Hill Trust. Many of the contents, including the original letters, were sold to the Lewis Walpole Library, Farmington, CT/ USA. The Bianca Capello painting was sold from Strawberry Hill in 1842, and its whereabouts is currently unknown.

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WEBSITES, EMAILS

HIST: http://www.scs.uiuc.edu/~mainzv/HIST

HISTORY OF CHEMISTRY LISTSERVE: chem-hist@listserv.uni-regensburg.de

CHEMICAL HERITAGE: http://www.chemheritage.org

HISTORY OF SCIENCE SOCIETY: http://www.hssonline.org

HISTORY OF CHEMISTRY EuCheMs: http://www.euchems.org

David Katz's "History on Power Points": http://www.chymistry.com

HENRY EYRING: A MODEL LIFE*

K.A. Dambrowitz and S.M. Kuznicki, University of Alberta

Introduction

Henry Eyring was eminently quotable: of the many things he was credited with saying, a quote repeated by his student Joseph O. Hirschfelder in 1966 aptly describes the work ethic of this insightful and prolific scientist (1):

> A scientist's accomplishments are equal to the integral of his ability integrated over the hours of his effort.

Henry Eyring, with over 620 publications (2) and an H-index of 66 (3), was clearly both able and hard working. Eyring produced work that continues to directly influence scientific thought decades after its initial publication. He worked hard, thought deeply about the questions that caught his attention, respected the people around him, and produced work that redefined how the rates of chemical reactions were understood and modeled. One quantitative measure of the quality of that work is its continued relevance. Eyring's papers were cited 347 times in peer-reviewed journals in 2008, 27 years after his death (3). In fact, Eyring's work has been cited more than 225 times annually, every year since 1959 (3).

Henry Eyring's transition state theory, widely known as Absolute Rate Theory (ART), was initially published in 1935 (4). ART is recognized as one of the most important developments in chemistry in the twentieth century. The theory states that the mean lifetime of the activated complex is definite and controls the rate of a chemical reaction, and Eyring applied an unconventional combination of thermodynamics, quantum mechanics, and statistical mechanics to calculate the rate and concentration of crossing that potential energy barrier. Despite the accolades he received for ART, Eyring re-

mained engaged, hard working and humble throughout his life. He applied the principles of physical chemistry to broad-ranging questions that fired his imagination, but also taught introductory chemistry, passing his love and understanding of chemistry on to others, even during the final stages of his terminal illness. Approaching the world driven by childlike curiosity and an enduring belief that the truth is simple, he produced a body of work that continues to inform scientists from freshmen to senior researchers.

Biography

Henry Eyring was born at Colonia Juàrez in Chihuahua, Mexico in 1901, a first son and one of 18 children (2, 5, 6). When the successful ranching family was forced to desert their holdings and return to the United States during the Mexican Revolution, eventually settling in Pima, Arizona in 1914, Henry and his siblings learned how to work hard (5, 6). Hard work bred success; many of the Eyrings went on to prominent careers, including a university presidency and two other full professorships (E. M. Eyring, personal communication).

Upon completing high school in Thatcher, Arizona, Henry departed for the University of Arizona, where he earned an undergraduate degree in Mining Engineering (1923) and a Master's degree in Metallurgy (1924). Work experiences in both mining and metallurgy spurred Eyring to explore other fields of science, and he completed a Ph.D. in chemistry at the University of California at Berkeley under the supervision of Professor George Ernest Gibson. The focus of his Ph.D. research was the

Table 1. Selected events in the life of Henry Eyring

Year	Event
1901	Born in Chihuahua, Mexico
1912	Family departs Mexico, fleeing the revolution
1914	Family resettles in Pima, Arizona
1923	B.S. in Mining Engineering at the University of Arizona
1924	M.S. in Metallurgy at the University of Arizona
1927	Ph.D. in Chemistry at the University of California, Berkeley
1930-31	National Research Foundation Fellow at the Kaiser Wilhelm Institute, Berlin, Germany
1931-1946	Assistant, Associate and Full Professor of Chemistry at Princeton University
1935	Publication of "The Activated Complex in Chemical Reactions" in the Journal of Chemical Physics
1936	Publication of "Viscosity, Plasticity and Diffusion as Examples of Absolute Reaction Rates" in the Journal of Chemical Physics
1944	Publication of *Quantum Chemistry* (Wiley, NY)
1946-1981	Dean of Graduate School, Professor of Chemistry, and Distinguished Professor of Chemistry at the University of Utah
1963	President of the American Chemical Society
1965	President of the American Association for the Advancement of Science
1966	Awarded the National Medal of Science
1973	Publishes Paper #500
1979	Awarded the Berzelius Medal
1980	Awarded the Wolf Foundation Prize in Chemistry
1980	Dedication of the Henry Eyring Chemistry Building at the University of Utah
1981	Dies in Salt Lake City, Utah

ionization and the stopping power of various gases for α-particles from polonium (5).

In 1930 Eyring began work with Michael Polanyi at the Kaiser Wilhelm Institute in Berlin, funded by a national research fellowship. Together, Polanyi and Eyring developed a method for approximating the potential surface of a chemical reaction that combined theoretical calculations with empirical results (5). The combination of theoretical and empirical approaches is a recurring theme in Eyring's research (2). Eyring and Polanyi's application of quantum mechanics to chemistry garnered an invitation for Eyring to return to Berkeley for a year as a lecturer. During that year (1931), Henry and Mildred Eyring's first son Edward was born in Oakland, California (5).

Henry Eyring next moved to the Chemistry Department at Princeton University, where he remained for 15 years, earning the title of full professor. This very productive period included the publication of Eyring's two most cited papers, "The Activated Complex in Chemical Reactions" (4) and "Viscosity, Plasticity and Diffusion as Examples of Absolute Reaction Rates" (7), and of the standard text *Quantum Chemistry* (8). Two more sons Henry (1933) and Harden (1939) were born during this time (2, 5, 6).

Professor Eyring, invited to establish the Graduate School at the University of Utah, relocated with his family to Salt Lake City in 1946. During the period from 1946 to 1981, he continued to direct a prolific and highly collaborative research group (paper 500 was published in 1973) (6), served as the President of the American Chemical Society (1963), served as President of the American Association for the Advancement of Science (1965) (2, 5, 6), and published "Faith of a Scientist," a collection of essays on the topic of reconciling faith and science (9).

Henry Eyring's broad-ranging scientific contributions were recognized by his peers many times. His

honors included the Newcomb Medal in 1932, election to the National Academy of Sciences (USA) in 1945, the National Medal of Science in 1966 (presented by President Lyndon B. Johnson), and the Wolf Foundation Prize in Chemistry in 1980 (2). Eyring was particularly proud of the Berzelius Medal, presented by King Gustaf of Sweden in 1980. This medal is presented only once every 50 years by the Royal Swedish Academy of Science (2, 6). In 1980, when the chemistry building at the University of Utah was named in his honor, the 79-year-old Dr. Eyring responded with a speech including a quote combining his good humor with his abiding work ethic (10):

> I'll keep working as long as I can find my way to the chemistry building and somebody there will let me in. Now that my name is on the building, it should be a lot easier.

Professor Eyring kept that promise. In the final year of his life, he taught undergraduate chemistry, maintained an active research program, and collaborated on three new books (2). He died in December, 1981.

Some key events in Henry Eyring's life are listed in Table 1. Figure 1 is a photograph of Mildred Eyring taken by Henry Eyring in 1930 in Berlin. Figure 2 is a photo of Eyring with his three sons in Princeton in the winter of 1939 - 1940. More complete biographies of Henry Eyring can be found in print (2, 5, 6) and on the internet (11, 12).

Continued Impact of Absolute Rate Theory

Henry Eyring's most influential idea was the Absolute Rate Theory, first published in 1935 in the *Journal of Chemical Physics* (4). Eyring summarized the paper as follows (13):

> I showed that rates could be calculated using quantum mechanics for the potential surface, the theory of small vibrations to calculate the normal modes, and statistical mechanics to calculate the concentration and rate of crossing the potential energy barrier. This procedure provided the detailed picture of the way reactions proceed that still dominates the field.

The activated complex has a fleeting existence of only

Figure 1 – Mildred Eyring in Berlin, 1930**.** *The image is from the personal collection of E.M. Eyring.*

about 10^{-13} sec and is situated at the point of no return or of almost no return. It is much like any other molecule except that it has an internal translational degree of freedom and is flying apart. This concept describes any elementary reaction involving the crossing of a potential barrier. If the activated state is really a point of no return, there is no perturbation of the forward rate by the backward rate, so that the rate at equilibrium applies unchanged to the rate away from equilibrium.

In simple terms, this theory holds that atoms and molecules can collide and combine to form an unstable, high-energy complex. When the molecules fall out of this high energy state, they may do so as new and different molecules, or in their original states. The energy required to reach the activated state must be available if the molecules are to change into something new. This idea, which was radical when it was proposed in 1935, is now so firmly established in scientific thinking as to seem intuitively obvious. The papers published to explain the theory remain relevant and useful today. Their principles can be found in any introductory chemistry textbook, and their content continues to be regularly cited in the peer-reviewed literature. The two most influential publications describing ART were published in the *Journal of Chemical Physics* in 1935 and 1936 (4, 7) and were cited in the literature a total of 140 times in 2008 (3).

Continued Impact of Childlike Curiosity

As a graduate student at the University of Utah, one of the authors (S.M.K.) had the opportunity to spend time with Henry Eyring. What S.M.K. observed from these interactions was that Eyring was driven by childlike curiosity. In saying this, it is important to distinguish between two very different adjectives. Eyring was *childlike*, an adjective which describes some of the most valued characteristics of children: trust, guilelessness, curiosity, and openness. He was by no means *childish*, an adjective suggesting immaturity and silliness (14, 15). As Henry Eyring described himself (16):

> I perceive myself as rather uninhibited, with a certain mathematical facility and more interest in the broad aspects of a problem than the delicate nuances. I am

more interested in discovering what is over the next rise than in assiduously cultivating the beautiful garden close at hand.

Eyring's curiosity made him extraordinarily open to new fields of thought and exploration. He loved to think about new problems that caught his imagination. He himself illustrates this point with an oft-told story of walking through a rose garden at Princeton with Albert Einstein during the Second World War. The garden had been replanted with field crops. Professor Eyring plucked a sprig and asked Professor Einstein to confirm what it was, but Einstein didn't know. Eyring sought out a gardener, who replied: "It is soybeans." Einstein was too busy thinking about other things, but for Eyring,

Figure 2 – Hal, Harden, Henry and Ted Eyring in Princeton during the winter of 1939 to 1940. *The image is from the personal collection of E.M. Eyring.*

"what gain[ed] attention [wa]s not just propinquity, but interest." (17, 18).

One outcome of Eyring's broad scientific curiosity was effective collaboration with scientists from many disciplines. He published extensive work in the field of physical chemistry but also contributed to the disciplines of astrophysics, biochemistry, biology, chemical education, geology, medicine, molecular biology, and textiles (2).

Eyring's curiosity was not universally admired. Some colleagues, in nominations prepared for various awards, including the Nobel Prize, made comments that reveal a subtle contempt for his simple and curiosity-driven approach to scientific problems. The authors of the comments cited below express reservations about Eyring's approach to scientific problems, despite his obvious success (19):
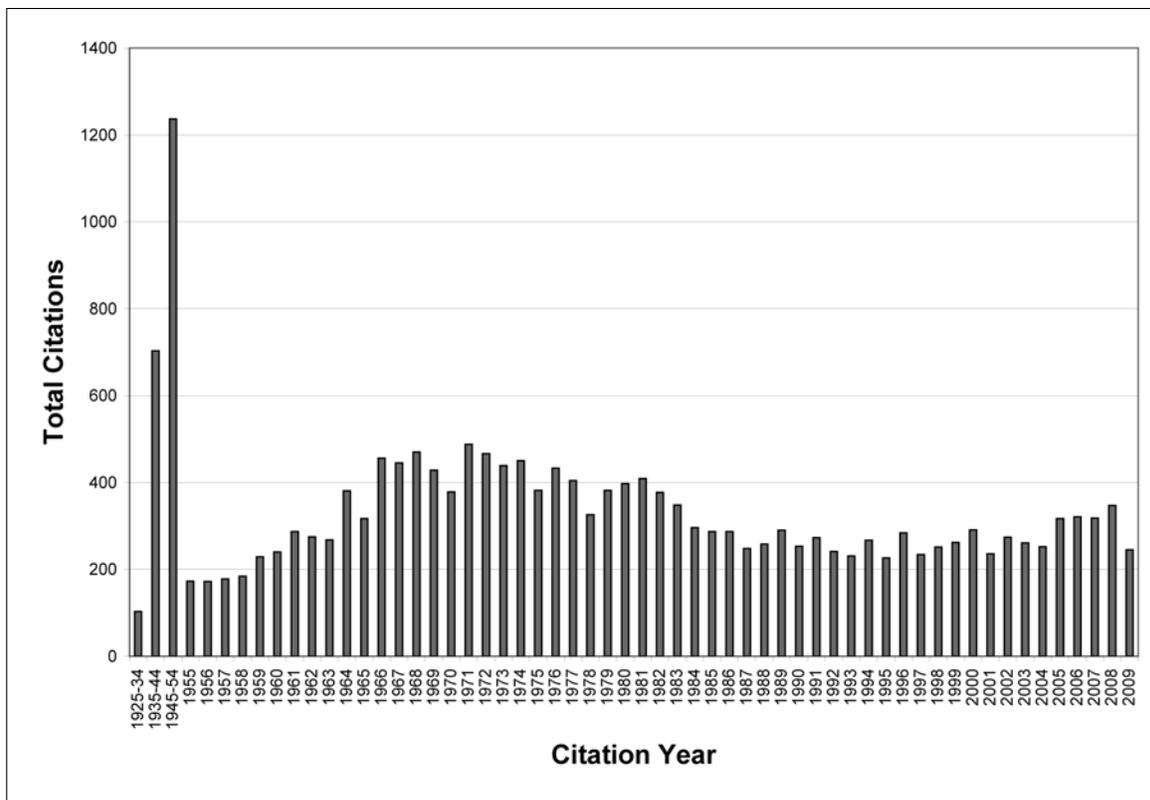
Figure 3. Annual research citations for Henry Eyring. *This citation history was generated from statistics that were accessed August 2, 2009 from the Web of Science (TM), a Thomson Reuters Citation atabase (Thomson Reuters, 2009), and is based on the 488 publications icluded in the Web of Science (TM) Dstinct Author Setfor Henr Eyrn*

Table 2. Citation statistics for the 10 most-cited publications of Henry Eyring*

Publication Name	2005	2006	2007	2008	2009	Total Citations	Average Citations per Year
Combined Citations for all Publications	**317**	**321**	**318**	**347**	**245**	**19525**	**229.71**
J.Chem.Phys., 1936	51	52	47	61	35	1530	20.40
J.Chem.Phys., 1935	58	70	55	79	57	1528	20.37
P.N.A.S. USA, 1952	3	7	9	3	4	789	13.60
J.Phys.Chem., 1954	32	20	19	26	17	551	9.84
Z.Phys.Chem, 1931	11	10	11	6	11	425	5.00
Chem. Rev., 1935	14	17	11	14	12	338	4.51
Phys. Rev., 1932	0	3	4	1	1	327	3.85
J.Chem.Phys., 1937	5	5	4	5	4	313	4.17
J.Phys.Chem., 1937	3	4	2	2	0	306	4.08
J. Phys. Colloid Chem., 1949	1	4	2	3	2	298	4.89

*Statistics were accessed August 2, 2009 from the Web of Science (TM), a Thomson Reuters Citation database (Thomson Reuters, 2009). Citation totals are based on the 488 publications included in the Web of Science (TM) Distinct Author Set for Henry Eyring.

His approach to every problem is fresh, original and frequently unorthodox. He tends to discover the facts rather than read what others have found.

He paints with a broad brush. It is interesting that it comes out so well.

The continued impact of Eyring's scientific contributions would suggest that following his childlike curiosity and applying himself to the questions that interested him constituted an effective strategy.   Figure 3 shows Eyring's annual research citations. His citations reached a level of 229 per year in 1959 and have remained very high ever since, even though his last papers were published in 1982 (3). Table 2 summarizes the recent and total citations for Eyring's most cited publications. Despite the length of time since these influential papers were first published, they clearly remain relevant to researchers (3).

Truth is Simple

Eyring, a man who believed that veracity and simplicity were closely related, advocated in one author's (S.M.K.) presence that if something was true, it could be expressed in simple terms. This is not to say that Eyring's scientific contributions were simplistic. On the contrary, his work is sophisticated and complex, although he was a proponent of simplicity.

Simple Truths in Research

Although not all scientists possess the mathematical skill required to understand the details of Eyring's work, the simply stated core truth of his Absolute Rate Theory provides a good starting place to think about how chemical reactions work. In the preface to *Quantum Chemistry* published in 1944, Eyring wrote (20):

No chemist can afford to be uninformed of a theory which systematizes all of chemistry even though mathematical complexity often puts exact numerical results beyond his immediate reach.

This remains true today.

Henry Eyring's thoughts on model building and hypothesis design also remain relevant across many disciplines. In his own words (21):

In model building it is convenient to start out with the following hypotheses:

(a) There is always a model that will explain any related set of bonafide experiments.

(b) Models should start out simple and definite enough that predictions can be made.

(c) A model is of limited value except as it correlates a substantial body of observable material.

(d) Models that suggest important new experiments, even if the theory must be modified, can be useful.

A well designed model can be proved or disproved, debated, tested, and improved. No matter what field of science, a simple approach to model building can be very powerful.

Simple Truths in Teaching

Professor Eyring was a teacher who asserted that deep and sophisticated understanding of complex material is

a prerequisite to a simple explanation of that information. One principle that he passed on to his family was that (22):

> If you can't explain something to an eight-year-old, you don't really understand it yourself.

Eyring often used analogies to explain complex ideas to nonscientific audiences and to students from outside the field of chemistry. His simple explanations made a scientific understanding of the principles of chemistry accessible to a broad range of people and inspired great praise from his students (6). Eyring also inspired learning in his sons. Edward, seen in Figure 4 as a toddler watching the eclipse, became a Professor of Chemistry. Hal is currently First Counselor in the First Presidency of The Church of Jesus Christ of Latter-Day Saints, while Harden was Assistant Commissioner of Higher Education for the State of Utah upon his retirement in 2009 (E.M. Eyring, personal communication).

Simple Truths in Faith

Henry Eyring was an unapologetic man of faith. Though it may not have been respected by all his colleagues or supported by all of his fellow believers, Eying also took a simple, but not simplistic, approach to reconciling faith and science. Eyring believed that, although faith and science might seem to be in conflict, this apparent conflict did not negate either human pursuit, but simply underscored the incomplete human understanding of both. For him both true science and true religion are concerned "with the eternal verities of the universe" (23). In his own words (24):

> Is there any conflict between science and religion? There is no conflict in the mind of God, but often there is conflict in the minds of men.

For Eyring, apparent contradictions between scientific results and the teachings of his faith community would be resolved by an eventual understanding of the truth (25):

> I am a dedicated scientist and the significant thing about a scientist is this: he simply expects the truth to prevail because it IS the truth. He doesn't work

Figure 4 – Sharing his scientific curiosity. *Edward (left) and Henry (right) Eyring view an eclipse in 1932. The image is from the personal collection of E.M. Eyring.*

very much on the reactions of the heart. In science, the thing IS, and its being so is something one cannot resent. If a thing is wrong, nothing can save it, and if it is right, it cannot help succeeding.

Simply Respecting Everyone: Brother Amott, USPS, Ph.D.

Eyring encouraged his students to treat everyone with respect (1) and clearly led by example. When he was the Dean of the Graduate School at the University of Utah, the U.S. Postal Service delivered the mail directly to the Dean's Office, twice each day. The mailman who delivered the Dean's mail for 20 years, known to the Dean's secretaries as Brother Amott, always stopped to speak to the Dean and his influential and hard working secretaries. When it came time for the mailman to retire, Eyring decided to exercise his authority and arrange for Brother Amott to receive an honorary doctorate directly from the Office of the Dean, in recognition of his service to the University of Utah, in particular to the Graduate School. This story, which typified Professor Eyring's respect for others, caught the imagination of the Salt Lake City press and caused quite a stir (E. M. Eyring, personal communication).

Conclusion

Professor Eyring published over 600 scientific articles and more than a dozen textbooks over his 50-year career (2). He established the Graduate School at the University of Utah and educated countless graduate and undergraduate students (2, 5). He wrote essays and texts reconciling the pursuit of scientific knowledge with faith in God (9, 24). His collaborators included biologists, chemists, physicists, and medical researchers. He thought broadly, and brought innovative questions and solutions to the many fields that inspired him. Eyring's work continues to be actively cited in the research literature, nearly 28 years after his death (3).

Eyring was hard working and insatiably curious. He was also a proponent of simplicity. As one author (S.M.K.) learned from time spent with Professor Eyring (26):

Henry Eyring saw himself as simple. Great ideas come from simple people. It is simple ideas that can actually change the world. Henry Eyring instinctively knew the truth when he saw it. You know the truth when you see it. The truth is always simple. The lesson of Henry Eyring's life is that simple people, just like you and me, can change the world. We do it a little bit every day. And we have the potential to change the world much more, if we can better understand and use our unique gifts.

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Scientific Objects and their Materiality in the History of Chemistry

Workshop at the Max Planck Institute for the History of Science
Berlin, Germany, June 24-26, 2010

BACKGROUND

Concepts such as the atom, element, or phlogiston have laid the groundwork for chemical research in defining the units of ordering systems, constituting the goals for material production, serving as limitations to the extent of chemical practice, or having crucial heuristic roles. And all of them have experienced variation, redefinition, development, suppression, and sometimes even extinction in the course of history. It is the aim of this conference to track down the history of such superordinated scientific concepts and objects, and to contribute to the understanding of their working modes.

PROGRAM

Topics may center on one of the following concepts/objects. This list is meant as being indicative, not exclusive:

- earth, air, water, fire, ether

- sal, mercur, sulfur

- phlogiston, caloric, oxygen, lumière

- element, compound, composition, mixture, alloy • electron, atom, bond, molecule, structure • polymer, colloid, crystal, glass • salt, base, acid • metal, halogen, rare earth • gas, liquid, solid, plasma • natural product, synthetic product • supramolecular, nano • pure, impure • chemical reaction

The workshop will consist of about 15 precirculated papers. Inquiries should be sent to carsten. reinhardt@uni-bielefeld.de

Michael Gordin (Princeton), Ursula Klein (Berlin), and Carsten Reinhardt (Bielefeld)

LOST ARTIFACTS?
The Anna Lea Painting

As noted below in the response to the previous column, the F. J. Moore Portrait Collection at MIT is apparently no more, though an examination of its holdings, as reproduced in the book by Smith (1), shows that most were not unique, one-of-a-kind items and that both copies and originals of the various photographs, lithographs, paintings, statues, etc. are to be found elsewhere; so the loss for the history of chemistry community, though unfortunate, is not irretrievable. There is, however, one possible exception to this statement, which is reproduced in the accompanying figure. This appears on page 124 of the Smith book and carries the title "Founders of the Coal-Tar Dye Industry: The Synthesis of Alizarin," as well as the following extended caption:

From a painting in the possession of the Chemistry Department of the Massachusetts Institute of Technology. The title of this picture and the subjects named [left to right: Graebe, Hofmann, and Liebermann] are more or less conjectural. It is an oil painting by Anna M. Lea, dated 1869. It was on January 11, 1869 that Graebe and Liebermann, at a meeting of the Berlin Chemical Society, with Hofmann as the presiding officer, announced their discovery of the synthesis of alizarin and prepared the dye before the audience. This was an epochal date and made a sensation throughout the chemical world. Efforts to learn the history of the painting and how it came into the possession of MIT have been fruitless to date. Anna Lea was painting in Dresden and Paris in 1869. "Her father through his business interests had something to do with coal-tar dyes," writes a member of the family. President Crafts of MIT [and of Friedel-Crafts reaction fame] resided in Paris for twenty years (1874-1891) carrying on his chemical researches and may have secured the painting.

A search by Deborah Douglas of the MIT archives and museum has failed to uncover the current location of the painting, which is apparently no longer in the possession of MIT or its chemistry department. Does this painting still exist and, if so, where is it presently located?

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GRAEBE   HOFMANN   LIEBERMANN
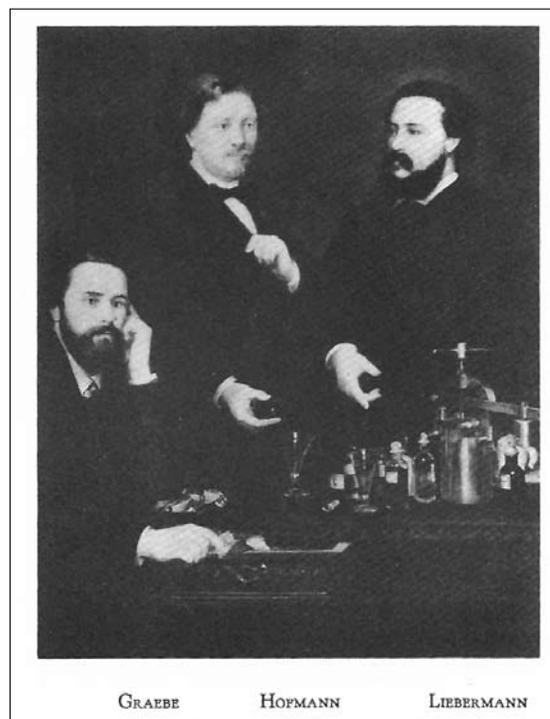
Readers having information relating to the above artifacts or questions of their own which they would like to see addressed in future columns should send their comments and questions to Dr. William B. Jensen, Oesper Collections, Department of Chemistry, University of Cincinnati, Cincinnati, OH 45221-0172 or email them to jensenwb@ucmail.uc.edu.

RESPONSE TO THE PREVIOUS COLUMN

(**2009**, *34*, 61)

At the suggestion of Ronald Smeltzer, an email correspondence was initiated with Deborah Douglas, the current Curator for Science and Technology at the MIT Museum. Though able to uncover documents collaborating Smith's account of how the Moore Portrait Collection came into being, she reports that no traces of it are currently to be found at MIT, whether in the chemistry department, the archives, or the museum. This raises the question of how severe this loss is to the history of chemistry community, the answer to which forms the basis of this issue's column as given above.

FUTURE ACS MEETINGS

March 21-25, **2010**—San Francisco, CA

August 22-26, **2010**—Boston, MA

March 27-31, **2011**—Anaheim, CA

August 28-September 1, **2011**—Chicago, IL

March 25-29, **2012**—San Diego, CA

August 19-23, **2012**—New York, NY

April 7-11, **2013**—New Orleans, LA

September 8-12, **2013**—Indianapolis, IN

March 16-20, **2014**—Washington, DC

September 7-11, **2014**—San Francisco, CA

March 22-26, **2015**—Denver, CO

August 16-10, **2015**—Boston, MA

March 13-17, **2016**—San Diego, CA

August 21-25, **2016**—Philadelphia, PA

April 2-6, **2017**, San Francisco

September 10-14, **2017**, St. Louis

BOOK REVIEWS

Chemistry & Art. *Further Adventures of a Chemist Collector*. Alfred Bader, Weidenfeld & Nicolson, London, 2008, x + 246 pp, ISBN 978-0-297-85512-5, £18.99.

This publication is the sequel to Alfred Bader's first book, titled *Adventures of a Chemist Collector* (Weidenfeld & Nicolson, 1995). As readers (and movie goers) will always appreciate, Dr. Bader provides a brief, two-page summary of the earlier book. Born in Vienna in 1924, the young Alfred in 1938 was spirited out on the first *Kindertransport* leaving Vienna, interned briefly as an "enemy alien," landing in a Canadian prisoner of war camp, and then being accepted to Queen's University in Kingston, Ontario (one of the greatest "investments" ever *unknowingly* made by a university). From there followed major steps: enrolling at Harvard and earning a Ph.D. with Louis Fieser, meeting Isabel Overton in 1949, falling in love yet unable to wed because of perceived religious issues, and starting the Aldrich Chemical Company in 1951—the gold standard in fine chemicals for generations of organic chemists, including this reviewer. Marriage to Helen Daniels followed in 1952, the births of David and Daniel, divorce in 1981, and marriage to Isabel in 1982. As Aldrich prospered, Dr. Bader indulged an early interest and assembled a world class collection of paintings with particular strength in seventeenth-century Dutch masters including Rembrandt. Aldrich catalogs of this era featured beautiful, full-color reproductions of gems in the Bader collection as cover art. Even today, one occasionally finds these collectable catalogs on Ebay. Merger to form Sigma-Aldrich in 1975 was not ultimately as happy a union as anticipated and, in 1992, Dr. Bader was "expelled" (his term) from the company. Freed from the grind of business and business politics, Alfred Bader turned his formidable knowledge and entrepreneurial and management skills toward collecting and dealing in art masterworks as well as a range of philanthropic causes.

In reviewing of the present book, it is fair to say that chemistry plays only a minor role in it. There is a fairly complex mystery involving art as well as chemistry related in Chapter 9 (*Prussian Blue*). A painting titled *A Chemist's Laboratory* in the Museum of the History of Science at the University of Oxford is said to depict Sir Humphry Davy conducting an experiment with an assistant. The painting is signed and dated "LR 1827" and reproduced in Plate 48. (This book contains 81 glossy plates, and more than half are excellent photographs of paintings). The questions include: Who is the artist? Is this an original subject or a derivative? Is it indeed Humphry Davy? Or is it William T. Brande, Davy's successor at the Royal Institution in 1813? Is the young assistant in fact Michael Faraday, who had strong associations with Brande as well as Davy? To make matters more interesting, Dr. Bader was contacted by an art dealer in North Carolina, who sold him a somewhat larger version of the same scene that more clearly depicted the mixing of two solutions to produce a blue precipitate (Plate 50). At one point, Dr. Bader offered a £1,000 award to the person who could solve the puzzle or most contribute to its solution. I will not spoil the fun by disclosing the (likely) solution. Chapter 15 is a photographic reprinting of a 1998 article authored by Dr. Bader and published in the *Bulletin for the History of Chemistry*. Its topic is the connection in chemical symbolism between William Joseph Wiswesser and the

nineteenth-century chemist Josef Loschmidt. During the 1960s, Wiswesser developed the Wiswesser Line Notation (WLN), which provided a simple way to describe any chemical structure in printable line notation. WLN was employed in Aldrich catalogs. Wiswesser admired Loschmidt, whose depiction of benzene anticipated that of the more well-known Kekulé.

The largest portions of the book, however, describe Dr. Bader's adventures (once again) in collecting, verifying, buying, and selling great paintings, primarily those of the seventeenth century as previously noted. Now, it is fair to say that an "absolutely pure" chemist might find this material irrelevant and perhaps even a bit boring. However, this reviewer is considerably "impure" and eclectic in interests and suspects there are numerous like-minded chemists among the potential readership of this book. I have collected rare books in chemistry and alchemy for over three decades. So the "inside game" of auctions, including strategic positioning behind opposing bidders, consortia of purchasers, dealing with auction houses on unsold items, verifying provenance, and just "plain old *hondling*" (*hondling* is a Yiddishism for bargaining) make for enjoyable reading. Since my purchases are usually three to four orders of magnitude lower in price than those of Dr. Bader, he is my surrogate for flights across the Atlantic and visits to the elite dealers, auction houses, and scholars.

There are eighteen chapters in this book, and some briefly relate deep friendships as well as Alfred's and Isabel's dedication and decision making in the cause of philanthropy: Jewish philanthropies, the American Chemical Society's Project SEED for economically-disadvantaged high school students interested in science, efforts to promote the well-being of Israeli Arabs, aid to the Roma people. The Helen Bader Foundation, administered by son Daniel, is another effective charitable organization;

and Queen's University has received major contributions including funding of its new chemistry building, donations of artwork worthy of any great museum, and the 140-room, fifteenth-century Herstmonceux Castle in England dedicated to international and interdisciplinary learning (see Plate 55, itself a photographic artwork). These points are made with a quiet pride rather than self proclamation—all in all a life well lived. That is not to say that Dr. Bader does not enjoy some S*chadenfreude* at the expense of those at Sigma Aldrich, who treated him so rudely, or the occasional unprincipled art dealer. What is abundantly clear is that Dr. Bader is a passionate man of generous spirit. Here is my own experience (and proper disclosure): a few years ago, I requested permission to reproduce in full color a print from the Collection of Isabel and Alfred Bader of the 1671 oil painting *The Alchemist*, by Hendrick Heerschop for a pictorial book I was writing. Although I had very briefly met Dr. Bader a few years earlier in Milwaukee and certainly also knew that his business was not in need of my funds, I followed the publisher's protocols in formally requesting permission and offering to pay a fee. Here was the delightful response:

> Dear Dr. Greenberg, Why should I charge you for a reproduction which it gives me great pleasure to send you, enclosed..With best wishes, Alfred. Bader.

In summary, although chemistry and chemical history account for only a fraction of this book's content, the book provides a peek at many wonderful paintings, an enjoyable and rarified view of the backrooms of the powers that collect, buy, and sell these paintings, and further insight into a major figure in the practice of late twentieth-century chemistry. *Dr. Arthur Greenberg, Department of Chemistry, University of New Hampshire, Durham, NH 03824*

EL COLOR LÍQUIDO. Instrumentos y útiles de la colorimetría en el siglo XIX. Lluis Garrigós-Oltra, Carles Millán-Verdú, and Georgina Blanes-Nadal, Publishing AguaClara, Alicante, 2008, 311 pp, ISBN 84-8018-270-9.

Three representatives of the History of Chemistry, currently professors in the University of Alcoi, bring us this book on the instruments used for colorimetric analysis over time. The authors come from different scientific and technical areas—chemistry, physics, and engineering—but conduct their research in the History of the Sciences and the Technologies. They publish their findings in books and journals of quality, and some of these publications, like those from professor Blanes-Nadal, deal with the history of colorimetry.

There is little in the way of literature and historical studies on the twentieth century design and development of chemical analysis with optical instruments, and even less on the history of how instrumentation was being designed as the different methods of colorimetric analysis were emerging. This lack is due to the interest of industry, and in some cases of public health, in executing rapid tests at the expense of the accuracy of the results, as well as to the fact that this has been an area little cultivated by the historians of science and technologies. Therefore, it is not surprising that the practical applications of colorimetry during the middle of the 19th century remain unnoticed today. In its practical applications, colorimetry assisted the oil and sugar industry, aided in determining the potability of drinking water, or in analyzing the fat content in milk. This was possible because colorimetry is an instrumental technique whose aim is to measure the absorption of visible light by a pure substance or a mixture or a solution.

This book is a good and accurate contribution to the recovery of a scattered, or with respect to some concepts and instruments, nonexistent record of the hereditary toolbox of colorimetry. The authors have been moved to write this book in order to incorporate these materials in a history of analytical chemistry, which is being approached after the parsing of classical sources, while also incorporating new historical, scientific, and technical perspectives. The authors overcame serious difficulties in order to draft a number of valuable pages as they have described in the preface (pp 14-15).

The authors have also had the good sense to contextualize the capital importance that the outlined tools have for museums of science and technology, as well as for their intrinsic historiography. The exploitation of the niche which is presented in this book has not thus far been a priority of these museums, whose tasks are more oriented to the teaching of science than to its history. Thus, it is to be granted that, in the prologue, the former director of the National Museum of Science and Technology in Madrid, Amparo Sebastian Caudet, shows that the museum is interested in the instrumental heritage from industry, university, and research centers. Nevertheless, we, the historians of science and technology, still long for greater attention from both national and regional authorities on this subject.

Divided into nine chapters, the book covers, from the beginnings of the nineteenth century, the usefulness of colorimetry in quantitative chemical analysis, revising the original use of color as an analytical technique, without forgetting the discussions raised between Houtou of Labillardére and Payen about the titration of chlorine dissolved in water and of charcoal as a decolorizer. The entry about photometry by light absorption and the description of *the Cianometer of François Aragó* serve to display devices like those designed by Descroizilles and Gay-Lussac for the volumetric analysis of chlorine.

If colorimetry means measurement of color, one must collect, describe and classify the instruments used; but, before that, it is also necessary to know their working foundation and explain the theoretical concepts on which they are based. The authors serve this purpose by explaining in detail the law of Lambert-Beer: its development, shaping, and interpretation, together with an outline of the optical parts of the spectrometer of Patterson.

The authors demonstrate their historical knowledge when reviewing the history of the early colorimeters (among them: Payen, Labillardére, Collardeau) and also when describing their theoretical and practical foundations. A special dilution colorimeter appeared near the middle of the nineteenth century, and its first use is attributed to Carl Heine. This colorimeter was used for the analysis of steel (Blodget Britton's colorimeter), for the measurement of Cu (II) (Bishop's colorimeter), for the quantification of bromine dissolved in water (Jacquelain' colorimeter), for the analysis of indigo (Salleron's colorimeter), for the content of salicylic acid in wine (Remont's procedure), for a rapid check for the coloration of wine (Dujardin' colorimeter), in the sugar industry (Pellet-Demichel's colorimeter), and for the quantification of iodine in a solution (Garraud's colorimeter).

In the decade of the 1860s the Duboscq colorimeter

appeared; this is the longest used instrument in the history of colorimetry, which, with improvements, was used until the 1940s. Chapter 5 is centered around this instrument. A history of balance colorimetry is presented, by covering the colorimetric proposals of Casaseca, Müller, Stamm, and Dehms, and ending with the already mentioned Duboscq colorimeter. The appearance of this instrument forced the modification of the optics of the colorimeter of Stammer and the introduction of improvements in the prototypes with which the new colorimetric era was initiated: the colorimeters of Günsberg and Wolff. The end of the century was accompanied by the emergence of low-cost and noncommercially manufactured instruments (for instance, that of Giannetti), and of some commercial ones (those of Gallenkamp, Laurent, Pelline, and Krüss).

Colorimetric methods were advancing in lockstep with the advances in the scientific and technical knowledge of chemistry; thus, in the twentieth century there arose a number of colorimetric methods applied to the determination of a wide range of chemical species. Although commercial manufacturers offered modern instruments to researchers and research laboratories, their price forced the potential users in many cases to build the instruments themselves. Among the variables involved in the colorimetric processes, one finds the colorimeters of Bottomley, Mills, Harvey, Davis, Leeds, Stokes, and Müller; the chromometers of Stead and Ridsdale; the reagents of Nessler; and the Nessler and Hehn tubes. A technique to determine the degree of dissociation of solutes enabled the invention of the colorimeters of Donan and Bayley, the latter one being used to detect Cu (II) ions (cuprimeter). The technique was also used for the assessment of the alkalinity of water, among other applications. To measure the purity of industrial alcohols, the diafanometer of Savall was employed, and for very dilute solutions one could use the colorimeter of Nugues.

From the outset the colorimetric technique attracted the interest of commercial manufacturers of analytical instruments. Thus, I believe it is necessary to make a thorough study of the relationships between theoretical science, applied science, economics, and society by using this certain fact to draw other conclusions. This is especially significant nowadays, when there is so much said about the interest of society for certain areas of scientific, technical, sociological and humanistic knowledge.

The technique of determining the color of liquids was responsible for the interest of some companies in publishing catalogs of their instruments, as was the case, among others, of the company The Tintometer Limited, which did so with the intention of providing its distributors with information related to how the different colorimeter models would fit the specific needs of researchers and industrialists. The study of the colorimetric characteristics of drinking water (chemical and organoleptic behavior) was of concern for the technician in charge of the fabrication of instruments in the second half of the twentieth century, and from this emerged the colorimeters of Bowdtich, Ledds, Croque, Holding and Tidy, R. P. Wilson, and Engler. There followed also the colorimetric scale of Falkoner King; the measurement of the color of wine resurfaced with the manufacture of the chromatometer of Andrieu, the wine-colorimeter of Salleron and the colorimeter of Papasogli. The color of blood was measured with the *hemocromatometer* of Harem.

One of the contentious issues in the early development of color theory was the question of the existence of a given set of colors. On this issue the authors present a brief but rich history of the development of ideas and theories for the standardization of color, from what was believed in the early Middle Ages up until the present. With the colorimetric base of Lovibond, the colorimeter that bears his name was fabricated, and it is given wide coverage. Under this scheme the authors describe the colorimeter of Procter as a modification of the previous tintometer.

The last chapter, devoted to the transparency of solutions, leads to the presentation of *lactoscopios* and other related instruments, and ideas which have been modernized with respect to the originals: the *nephelometry, diafanometry*, and *difusometry*. Some of these devices were used for quick detection of milk fraud with the *lactoscopio* of Donné. The authors signal that the success of *lactoscopios* has been dependent on the country where they have been considered; but still, there are several models which have been employed: those of Vogel, Heusner, Feser, Heeren, and Mittelstrass. *Hematoscopios* were also used in hematology.

Everything that is presented in the book serves to introduce the wide dissemination and application which colorimetry has had in the analysis of organic and inorganic substances, living or inert.

We have at hand a work which is an essential addition to the history of the broad field of chemical analysis. Today's students are only familiar with modern laboratories, equipped with sophisticated spectrophotometers. For this reason it is particularly fortunate that there are

works like the one here reviewed, which serve to present an understanding of the past, to study the present, and to foresee the future, these being the fundamental issues to be pursued in the historical study of any discipline.

The present generation seems to lack interest in history, sees and reads only what is strictly contemporary, and generally only grasps a history of the immediate past. At the same time there are growing numbers who want to learn about the past, lest they be condemned to repeat it without knowing that it is repeated, and therefore to become mere epigones. Many of today's "creators," usually those who believe themselves to be the most innovative and modern and who allow themselves to ignore as outdated that which is a little older than they themselves, generate stale, repetitive, trite questions. With a mixture

of naivety and arrogance, they have decided there are no lessons from the past, that history will be born or reborn with them. Whoever wants to cultivate a science should quickly absorb what has preceded it, to avoid being unknowingly anachronistic.

We have no doubt that this scenario will not evolve among the young students who are taught the provenance of the knowledge they are learning, that everything has its own history and that before them, many others spent many efforts in the advancement of science. The reviewer expresses this hope as an added incentive for readers to gain such an experience after the reading of this book. *Manuel Castillo Martos, Professor of History of Science at the University of Seville*. [The editor expresses deep gratitude to Dr. Gorka Peris for invaluable assistance in the editing of the English version of this review.]

The Rise and Decline of Colloid Science in North America, 1900-1935: The Neglected Dimension. Andrew Ede, Ashgate, Aldershot, Hampshire, UK and Burlington, VT, 2007, 208 pp, ISBN 978-0-7546-5786-6, $99.95.

The study of colloids was one of the most vital and attractive subjects for chemists during the first three decades of the twentieth century. Wolfgang Ostwald, the German leader of colloid chemistry, defined colloids as dispersed systems consisting of particles of a size too small to be seen microscopically and too large to be called molecules (or, what he called "the World of Neglected Dimensions"). The study of the neglected dimensions, or colloid science, rapidly grew as a promising scientific discipline, especially in the United States. In his present book, Andrew Ede focuses on the study of colloid science in North America from 1900 to 1935. The book stemmed, with some minor changes, from his Ph.D. dissertation, "Colloid Chemistry in North America, 1900-1935. The Neglected Dimension," submitted to the University of Toronto in 1993. In his words, "In 1920, colloids were the hottest topic in American science, whether it was chemistry, physics, or physiology. Fifteen years later, colloid science was in almost complete retreat" (p 2). In this book he attempts to answer how and why the field gained such a high status and then degenerated.

The colloid science boom reached its peak in America in the 1920s, as reflected by the flood of literature on colloids and the large number of practitioners. During the decade, according to Ede, a minimum of twenty percent of American research chemists were working on colloids or colloid-related topics. In 1916 the National Research Council organized a Committee on the Chemistry of Colloids as the major organ to encourage and promote research and education in this field. Many American universities began to offer courses in colloid chemistry. The annual National Symposium on Colloid Chemistry was first held in 1923. The American Chemical Society created its Division of Colloid Chemistry in 1926.

European influence is apparent in its development. The rise of colloid chemistry coincided with the expansion of physical chemistry. America's leading colloid chemists, such as Wilder Dwight Bancroft at Cornell and James William McBain at Stanford, were students of Wilhelm Ostwald, Wolfgang's father and the founder of physical chemistry. Another of Wilhelm Ostwald's students, the German Herbert Freundlich, was invited as a guest of honor to the third National Colloid Symposium, and later became a professor at the University of Minnesota. These colloid chemists were actually physical chemists by profession. Wolfgang Ostwald's series of lectures on colloids in America drew considerable attention. Theodor Svedberg, the Swedish colloid chemist,

spent two terms at the University of Wisconsin where, together with his American disciples, he developed his ultracentrifuge for the study of proteins. Bancroft's *Journal of Physical Chemistry* carried a large number of articles on colloids.

Ede explains the rise of colloid research within a broader context as well. It took place during the Progressive Era, a time when there was explosive growth in American science and industry. The study of colloids, then, was a largely untouched area of research and could be conducted at a low cost. The field offered American researchers an ample opportunity to contribute to the international scientific community when resources were limited. The utility of colloid chemistry also made such research attractive during a period of industrialization. The mobilization of science during World War I further enhanced the status of colloid chemistry, which formed an important area of wartime research on gas and masks.

By 1935, however, colloid science had come under attack from outsiders and suffered embarrassment caused by members within the colloid ranks. While other areas of chemistry continued to expand, work on colloids declined. The National Research Council omitted colloid chemistry from its annual review of American chemistry. Colloid research failed to achieve an institutional niche. Why did this happen? Despite the alleged grand scope and high expectations for colloid science, it turned out that it covered only limited areas of research with success. No general consensus was reached regarding basic theories and methodology in the colloid community. For example, the isolationist Bancroft believed that colloids were unique and that colloid science must have unique laws. By claiming this, he marked his approach toward colloids as being largely qualitative. Bancroft's harsh critic, Jacques Loeb, was eager to make colloid research more quantitative by applying Donnan's equilibrium to colloid membrane behavior. The unionist Loeb believed that colloids were not unique and that colloids could be studied in terms of existing physical-chemical principles. Singling out Bancroft as the scholar responsible for the decline of American colloid science, Ede spends Chapter 8 delineating Bancroft's ill-fated attempt to apply a colloid theory to cure insanity, drug addiction, alcoholism, and allergies—all of which came to naught and only created a social stigma for colloid science. In this way, the study of colloids ended up consuming itself. Here, Ede employs the metaphor of ouroboros, a dragon-like creature that swallowed its own tail and disappeared, in that the research program "disappeared, consumed by the very act of studying colloids" (p 1).

Yet, a critical blow came rather from outside: the emergence of macromolecular chemistry, led by the German organic chemist Herman Staudinger. In Staudinger's view, colloidal particles were not the aggregates of small molecules held together by physical forces, as most colloid chemists argued, but were, in many cases, "macromolecules" that were composed of between 10^3 and 10^9 atoms linked together by the normal "Kekulé" bonds. Chapter 9 vaguely outlines the conflict between the micelle theory versus the macromolecular theory, but does not expound on how American colloid chemists reacted to the macromolecular theory and changed their minds. No mention is made of Wallace Hume Carothers and Paul J. Flory, who pioneered American macromolecular chemistry at DuPont, although Ede describes some work by DuPont's colloid researchers, including Victor Cofman, Elmer O. Kraemer, and J. Burton Nichols, in other chapters.

Today's colloid researchers might be bewildered by the author's use of the ouroboros metaphor for the rise and decline of colloid science. Unlike ouroboros, colloid science did not disappear, but rather continues to live on. Although the popularity and status it enjoyed in the 1920s are no longer evident and its scope and definition have been changed, the legacy that colloid chemists of the time bequeathed has been succeeded and developed into various works such as the DLVO theory (which explains the stability of colloids) advanced in the late 1940s, and the surface forces apparatus (SFA), an instrument for the direct measurement of surface forces made in the early 1970s.

Ede bases his narrative principally on published sources. However, he should also have examined a rich store of manuscripts, such as the Wilder Dwight Bancroft Papers at Cornell University, the Jacques Loeb Papers at the Library of Congress, and the Wolfgang Ostwald-Martin Fischer Correspondence at Wittenberg University, Ohio. Ede also should have consulted a number of important works on the history of colloid chemistry and macromolecular chemistry that appeared after he completed his 1993 dissertation, but well before the 2007 publication of its book version. It is also a pity that there are many typographical and grammatical errors, which should have been eliminated through the editorial process. Aside from these shortcomings, *The Rise and Decline of Colloid Science in North America* does provide us with a good survey of the history of American colloid science as a useful starting point for further study. *Yasu Furukawa, Nihon University.*

RECOLLECTIONS

Kasimir Fajans

Fajans was a gift to the University of Michigan from Hitler's Nazi Germany. A brilliant but flawed man who was his own worst enemy, he, almost simultaneously with Rutherford and Soddy, formulated the laws of radioactive transformations. Rutherford, and later Soddy, were recognized by being awarded the Nobel Prize. Fajans never was, possibly because of the enemies he acquired. One illustration of Fajans' self-inflicted trouble: he argued in print with the famous Linus Pauling again and again, not always using good judgment about the wording of his arguments. Pauling was my "scientific grandfather," and it was clear to me that Pauling, despite certain intemperate actions in his later years, was a truly great man. Editors, of course, also recognized his stature and began to reject papers written by Fajans. Yet it struck me that in his arguments with Pauling, Fajans had been correct perhaps more than half the time. He simply didn't understand how to argue in a civil manner.
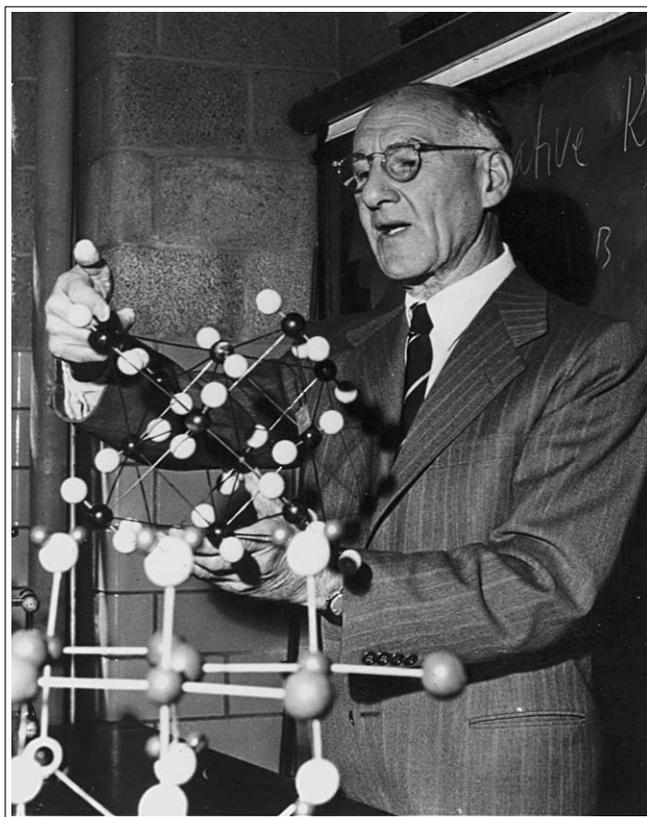
As far as Nobel prizes are concerned, there is another story besides that involving Rutherford and Soddy. One day Fajans told me about what happened when he had a young assistant investigate some aspects of the precipitation of silver halides. This assistant came to him and showed him a remarkable color change when a certain dye was present as the endpoint was passed in a titration of a halide solution into a silver solution. Fajans told me that the assistant wasn't very bright and had no idea of what happened; but Fajans remarked that he, himself, understood immediately. The dye later came into general use in analytical determinations of silver, and was known as the Fajans' indicator. After Fajans told me the name of this not very bright assistant, namely Odd Hassel, I realized that Fajans had had another brush with the Nobel Prize—inasmuch as Hassel later went on to win it in1969!

I had been lucky enough to have had two courses from Fajans, one in the first semester of physical chemistry as an undergraduate, and one on thermodynamics as a graduate student. Fajans spoke English with such a thick accent that it took awhile to learn to understand him. Furthermore, his lectures tended to be very disorganized. Even so, Fajans had the knack of getting to the heart of subjects. I developed a love of thermodynamics from Fajans. It wasn't always clear even to Fajans how some subtle aspects of thermodynamics worked, but Fajans never tried to bluff his way out of the problem as some professors do. For example, in the graduate course, Fajans told us about various electrochemical cells that operated with gravity providing the driving force. One of these cells seemed very strange to me, so I asked him to explain how it worked. He was at a loss, so, after class, he asked me to follow him. We went to his office, which was piled high with all manner of journals and apparatus. He went to a particular stack of yellowing journals, reached up high into the pile and quickly removed one. It contained the original article on that very cell! How Fajans knew exactly where to look when it was obvious that those journals hadn't been touched for years, defied my imagination. He asked me whether I read German (the language of the journal). When I responded, "not really," he told me to read the article and report on it during the next class!

When I was invited to join the Michigan faculty, I was surprised and disappointed by the absence of discussions at the end of seminars in physical chemistry. At Iowa State University where I had been, such discussions were spirited, and useful to students. What had happened was that when Fajans was an active member of the faculty, he made such outrageous and often nasty statements after seminars that the rest of the faculty thought it best to keep quiet. Well, I felt that keeping quiet after seminars was quite the wrong way to behave. So I always raised questions at seminars and, bit by bit, the other faculty members began to, as well. What a dampening influence Fajans had been. He had so very much to offer, yet the way he expressed his ideas was almost totally counterproductive.

Fajans was always interested in new structural results because they enabled him to sharpen his already very keen ideas about structure and bonding. One day I put into his mailbox a reprint reporting a rather strange structure I had determined. Fajans walked in before I left, took a quick look at the reprint, then came over to me and bellowed "How could *you*, a student of mine, publish a resonance structure in your paper? I once thought about resonance theory for five minutes, and realized it was nonsense!" First of all, while it was true that I had taken two courses from Fajans, I had never been a research student of his. Second, this outburst revealed how little Fajans understood quantum mechanics because the formulation of resonance theory by Pauling had a firm basis and provided useful insights into many molecular properties. Actually, Fajans considered that theoretical chemistry, particularly quantum chemistry, had no place in chemistry. Chemists were supposed to study and understand molecules from the standpoint of their observed behavior

In parties at his home, Fajans was the very model of a gracious European host. One could ask for no finer a gentleman in such situations. But in his professional dealings with others, he suffered terrible lapses of judgment in his uncivil behavior. For example, A. D. Walsh had published some brilliant work showing how qualitative aspects of molecular orbital theory could help one quickly predict structural trends in molecules. He formulated what became known as the Walsh Rules. One day Michigan was fortunate enough to get Walsh to present a seminar. Fajans was present, and so was I. Walsh began by pointing out how prescient Fajans had been in formulating his "Quanticule Theory" of molecular binding and how closely related it was to molecular orbital theory. He went into some detail to show examples. One would have thought that Fajans would be extremely pleased by this gracious acknowledgment of his creativity. But no, Fajans became enraged and angrily argued that Walsh didn't interpret his quanticule theory quite exactly as he meant it to be interpreted. Fajans had so very much to offer the world that it is a tragedy he made it difficult for the world to appreciate him.

—*Lawrence S. Bartell, Philip J. Elving Collegiate Professor of Chemstry, Emeritus, University of Michigan.*

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2.   G. W. Wheland, *Advanced Organic Chemistry*, Wiley, New York, 1949.
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