

WILHELM HEINTZ (1817-1880) AND THE CHEMISTRY OF THE FATTY ACIDS (1)

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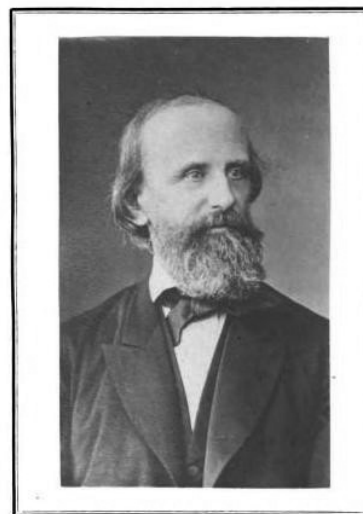
Introduction

In 1855, Otto Erdmann, the editor of the *Journal für praktische Chemie*, asked Wilhelm Heintz at the University of Halle to submit a review article summarizing his lengthy investigation of the fats and fatty acids. Beginning in the mid-1840s, Heintz had subjected these compounds to their most thorough investigation since Michel Eugène Chevreul thirty years earlier, and he redefined the criteria for identifying them as chemical species. Spurred by difficulties in purifying fats isolated from human fatty tissue, Heintz's research program demonstrated convincingly that well established fatty acids long thought to be pure were in fact mixtures of other known fatty acids. Heintz argued, furthermore, that a sharp melting point after repeated crystallization could no longer serve as a sufficient criterion for their purity and introduced a new method for establishing the purity of the fatty acids (2).

Although little known today, Wilhelm Heintz was an extremely productive chemist during the nineteenth century. At the time of his death in 1880, Heintz had authored over 200 publications, primarily in physiological chemistry, but also on mineral analysis, improved techniques for elemental analysis, and organic chemistry. His relative obscurity perhaps derives from a number of factors, including his position at Halle, one of the smaller, less prestigious universities in Germany, where he did not have the resources to direct a large research group. His only significant student was Johannes Wislicenus (1835-1902), to whom we owe the only major account

of Heintz's life (3). Heintz also emphasized primarily empirical investigation and wrote little on theoretical matters except during a short dispute in 1864 with Vladimir Markovnikov on the constitution of the ethyl glycol amides, when he was among the first chemists to use Aleksandr Butlerov's new term "chemical structure" (4). Nearly all of Heintz's published work consisted of journal articles, and he published only one book, a textbook of animal chemistry, in 1853 (5).

Wilhelm Heintz



Wilhelm Heintz

geb. am 4. Novbr. 1817. gest. am 2. Decbr. 1880.

Figure 1. Wilhelm Heintz (1817-1880), from Ref. 3.

Heintz was born in Berlin, the son of a businessman, and followed an unusual path to a university career in chemistry. He was initially apprenticed to a pharmacist, but soon decided against a career as a pharmacist in favor of chemistry. Since he had not completed his education at the Gymnasium for normal entrance to the university, Heintz prepared for and passed the matriculation exam in October 1840, when he immediately enrolled at the University of Berlin (6). He attended lectures from J. H. F. Link in pharmacy and natural history, Heinrich Dove in physics, Eilhard Mitscherlich and Heinrich Rose in chemistry, and Johannes Müller in physiology. He became friends with many of Müller's students, and in January of 1845, he was the only chemist among the co-founders of the *Deutsche physikalische Gesellschaft zu Berlin* with Emil du Bois Reymond, Ernst Brücke, Karl Knoblauch, Wilhelm Beetz and Gustav Karsten. During this time, he also met and became friends with Hermann Helmholtz, and by the late 1840s, had established himself as a significant member of the Berlin circle of up and coming physical scientists, including DuBois-Reymond and Helmholtz.

Heintz worked in Rose's laboratory, studying inorganic compounds such as alumina and iron oxide, asbestos, properties of glass in the electroscope, and dyestuffs. For his dissertation, which he completed in February of 1844, Heintz turned to saccharic acid (7). Although he did not formally complete a *Habilitationsschrift*, by late 1845, Heintz already had thirteen publications and a small private laboratory in his parents' house where he offered instruction in qualitative analysis to a small number of students. He was therefore granted the *venia docendi* (the right to lecture at the university) by ministerial dispensation, and in 1846 Heintz was appointed to the medical faculty as a lecturer in physiological and animal chemistry at the institute of clinical medicine directed by Johann Lukas Schönlein (1793-1864) at the Charité hospital in Berlin (8).

Throughout his career, Heintz's major interest was in physiological and animal chemistry, especially the chemical composition of animal fluids. Between 1845 and 1850, he published 26 papers that described novel methods for isolating and identifying components of various animal fluids, especially human urine. He introduced a new method for the quantitative determination of urea in normal and diseased urine by measuring the quantity of ammonia formed by decomposition, discovered the presence of creatine in urine and studied the composition of urine sediments (9). In other papers, he described methods for determining the composition of ash residue

from bones and animal substances, characterized stomach acid, analyzed the composition of the fluid found in a hydantoin cyst, and the milk from the "cow tree" of Venezuela (10). On the basis of this work, Heintz was called to the University of Halle in 1851 to succeed Richard Marchand, where he remained until his death in 1880.

Heintz's Fat Kingdom

When he moved to Halle, Heintz turned his attention to the chemistry of the animal fats, or the "fat kingdom" (*Fettreich*) as he affectionately called it. The animal fats had first been extensively studied nearly forty years earlier by Chevreul, who published his results first as a series of papers in the *Annales de chimie* and then in an 1823 book, *Chemical Research on the Fatty Bodies of Animal Origin* (*Recherches chimiques sur les corps gras d'origine animale*) (11). Chevreul separated animal fats into distinct compounds with a definite composition. He found that saponifying each of these animal fats formed a "sweet principle" to which he gave the name "glycerin" that combined with a few common fatty acids that he named stearic, oleic, and margaric acids. Chevreul also found spermaceti to saponify, but instead of the "sweet principle," it contained a substance that resembled alcohol, but with a significantly higher molecular weight, which he called "Ethal," that combined with various fatty acids to form spermaceti. He also isolated another fatty substance that he could not saponify that he named cholesterine (cholesterol). Chevreul used a variety of novel techniques, including elemental analysis, fractional solution and crystallization. He also used the melting point both to identify and judge the purity of the fats and fatty acids he isolated. Highly admired at the time, Chevreul showed that the fats were subject to systematic chemical analysis and obeyed the laws of chemical combination (2). Chevreul's work provided the basis for further investigation of fats and oils, and when Heintz entered the field, chemists had identified many new fats and fatty acids, all defined by their melting point and chemical composition. Furthermore, in 1853, the young Marcelin Berthelot further demonstrated by synthesis that fats are triglycerides, when he combined glycerine with various combinations of three fatty acids (12).

Heintz became interested in the fatty acids through his friend, the physiologist Ernst Brücke, who had worked in his laboratory during the 1840s with a project on the composition of human fat. Brücke had assumed that human fat consisted of the fats margarin and olein, and should therefore produce margaric acid on saponifi-

cation, but he had repeatedly obtained a fatty acid with a melting point below that of margaric acid. Brücke would abandon this project sometime in the mid-1840s, before he left Berlin in 1848 for the University of Königsberg, but the line of investigation resulting from Brücke's unexpected difficulty would eventually, as Heintz wrote in 1855, "make questionable the existence of all the [fatty acids] as chemically pure bodies" (13). Heintz published the results of this research between 1851 and 1857 in a series of lengthy articles in his preferred journal, *Poggendorff's Annalen der Physik und Chemie*. As Wislicenus noted, Heintz's articles gave a "clear picture of Heintz's working style," and he reported carefully the "path followed by experimental investigation" without sparing the reader any detours and errors along the way (14).

Heintz's own narrative suggests that he continued Brücke's project nearly immediately, even though his first full publication on fats did not appear until 1851 (15). Brücke's difficulties suggested to Heintz that human fat must contain an additional solid fat that on saponification produced an additional solid fatty acid that could not be separated from margaric acid by "simple crystallization" (*bloßes Umkrystallization*) (16). Heintz slowly cooled a sample of human fat below 0°C, separating any solidified fats from the remaining liquid, and eventually concluded that human fat consisted of a mixture of at least six different fats, including margarin, palmitin, olein, and a new fat he named anthropin. Saponification of the margarin prepared from human fat produced margaric acid, but the composition and melting points of these acids suggested they were still impure.

This circumstance connected with the fact that the previously applied methods of separating fatty acids applied to human fat has not once resulted in the pure preparation of any of the fatty acids, compelled me to seek another separation method. I have had a lengthy, repeated struggle to use the ordinary, conventional separation techniques on the fatty acids, but always with no success, as [should be] expected, because it is well known how extraordinarily similarly, one could almost say identically, the compounds of the various fatty acids behave with the same foundation towards means of resolution (17).

Heintz's frustration finally eased in 1848, when he encountered an article by Liebig on a new method for separating valeric, butyric and acetic acids by conversion to their salts with sodium carbonate followed by distillation (18). In any mixture of these three acids, Liebig found that butyric and valeric acid distilled first, always leaving the acetic acid behind, even though it had the

lowest boiling point of the three components. Heintz explained this—as Liebig had not—by suggesting that the butyric and valeric radicals had a lesser affinity for the sodium, allowing the separation to take place (19).

This train of thought led me to test the idea if it would not be possible simply to separate such substances (*Körper*) from one another by their degree of affinity, when their properties are so similar, both in a pure state (*im freien Zustand*) and when combined with other substances, that they were previously inseparable or only partially separable. I thought right away about the solid fatty acids, with which I have occupied myself for so long without success, precisely because the previously applied methods were quite imperfect.

The fatty acids could not easily be distilled, but Heintz could take advantage of the differential solubility of their salts, and he settled on treating the fatty acids with lead acetate. He would later use magnesium and barium salts, but the method remained the same (13). Heintz dissolved the fatty acid in minimal hot alcohol and slowly added a solution of lead acetate in approximately half the stoichiometric amount. On cooling, the fatty acid with the greatest affinity for lead precipitated as the lead salt. The precipitate was then filtered and acidified to yield the acid, and the filtrate treated again with lead acetate. This process was repeated until the melting points of the obtained fatty acids remained constant (20). Heintz found that he could separate mixtures of three or more acids by this method, and the results suggested that mutton tallow and spermaceti were more complicated mixtures than earlier assumed. Heintz noted that the "quality" (*Güte*) of this method was justified by the isolation of a new fatty acid from anthropin that he named anthropic acid (*Anthropinsäure*).

In 1852 Heintz extended these preliminary results. Because he had found human fat to contain margaric, palmitic and anthropic acids, he expected sheep tallow to have a similar composition because it contained similar fats. His results were confirmed, but in an unexpected way. In the attempt to isolate anthropic acid from saponified mutton tallow, Heintz found that the melting point continually increased on repeated recrystallization of the fraction, and in several of the recrystallizations, he noticed the precipitation of small amounts of margaric and stearic acid. "The results of these experiments," Heintz wrote, "finally gave me the notion that anthropic acid, despite its great ability to crystallize, may be a mixture of stearic and margaric acid" (21). Heintz therefore mixed stearic acid with varying amounts of margaric acid, and noticed that even a small amount of

stearic acid changed the appearance of the margaric acid crystals, which eventually entirely lost their crystalline properties. A solid mixture of 11 parts margaric acid and 6 parts stearic acid appeared “exactly like the acid I had named anthropic acid,” and had the same melting point (22). “Pure” anthropic acid was therefore simply a mixture of stearic and margaric acids.

Furthermore, Heintz noted that palmitic acid seemed to be ubiquitous when handling anthropic acid, such that he “could not resist the suspicion” (*der Vermuthung nicht mehr erwehren*) that margaric acid itself was nothing more than a mixture of stearic and palmitic acid. Heintz found that a mixture of 7 parts palmitic acid and 5 parts stearic acid resulted in a compound, “which in all of its properties, especially in the crystalline form as it solidifies and in the melting point, coincides with anthropic acid.” A mixture of ten parts palmitic acid and one part stearic acid, “possessed *all the properties* of margaric acid,” in both melting point and crystalline form (23). As the portion of stearic acid increased, the melting point continued to decrease to a minimum, when it increased again and assumed the appearance of anthropic acid. “This experiment with palmitic and stearic acid with different origins has been repeated so often,” Heintz wrote, “that I can no longer doubt [these results]” (24).

These results completely changed the composition of both human fat and mutton tallow. The fats anthropin and margarin did not exist. Human fat consisted only of stearin and palmitin, which contained palmitic and stearic acids, and human and mutton fat differed only in the proportion of stearin and palmitin. The results also cast doubt on the composition of spermaceti, which Heintz had shown earlier to consist of ethal and six fatty acids, including margaric acid. (25).

Spermaceti, the Rule of Four, and Melting Point Depression

Before returning to spermaceti, Heintz turned to the fatty acids contained in butter. Already in 1844, Joseph Lerch had identified four fatty acids in butter (26):

Buttersäure (butyric acid): $C_8H_8O_4$

Capronsäure (capronic acid): $C_{12}H_{12}O_4$

Caprylsäure (caprylic acid): $C_{16}H_{16}O_4$

Caprinsäure (capric acid): $C_{20}H_{16}O_4$

Heintz isolated four more fatty acids, doubling the number in butter to eight, and noted that palmitic acid

was present in the greatest quantity:

Myristic acid: $C_{28}H_{28}O_4$

Palmitic acid: $C_{32}H_{32}O_4$

Stearic acid: $C_{36}H_{36}O_4$

Arachidic acid (*Butinsäure*): $C_{40}H_{40}O_4$

Heintz noted that the composition of these acids seemed to follow a general law, “that the saponification products of fats contain only those acids whose number of carbon atoms is divisible by four” (27). This implied that any known fatty acid that did not follow this law would be a mixture of fatty acids that did. This was true for margaric and anthropic acids (both with 34 carbons). It also suggested that some fatty acids created by saponification of spermaceti, cetyl acid, with 30 carbons, and cocinic acid, with 26 carbon atoms, must be mixtures of other fatty acids that obeyed the “law of four,” and Heintz obtained ten pounds of spermaceti to investigate further (28).

Heintz’s results on spermaceti appeared as a two-part article in 1854. He collected the fatty acids separated from the ethal and submitted them to fractional precipitation, slowly adding ethanol and removing the resulting precipitate in twenty fractions. Because it “would be an endless task” (*endlose Arbeit*) to subject each of these fractions individually to additional fractional crystallization, Heintz combined fractions with similar melting points for crystallization. This work proved painstaking; Heintz recrystallized the solids from the first six fractions fifteen times, until the amount was too small to continue. The earliest fractions from the initial precipitation produced the acids with the highest melting points, and in subsequent fractions the melting points decreased. From the stable melting points of the acids from the various combined fractions, Heintz concluded that spermaceti contained only four fatty acids that fully confirmed his rule of four (29):

Stearic acid ($C_{36}H_{36}O_4$): m.p. 69.2°

Palmitic acid ($C_{32}H_{32}O_4$): m.p. 62°

Myristic acid ($C_{28}H_{28}O_4$): m.p. 53.8°

Lauric acid (*Laurostearinsäure*,
 $C_{24}H_{24}O_4$): m.p. 43.6°

There remained, however, a single fraction with a melting point of 32.3°, lower than pure lauric acid. This suggested a fifth component with a lower melting point, but acids isolated from the subsequent fractions had a

higher melting point, making this fraction an exception to Heintz's general observation that all the later fractions contained acids with lower melting points. This "left only the suspicion" that this fraction was another mixture of two fatty acids in the correct proportion to produce a lowered, but sharp melting point, just as the mixture of palmitic and stearic acid had produced margaric acid. Heintz therefore systematically mixed the following pairs of the four fatty acids in various proportions to determine their melting point:

Stearic/palmitic acids (C_{36}/C_{32})

Palmitic/myristic acids (C_{32}/C_{28})

Myristic/lauric acids (C_{28}/C_{24})

Stearic/myristic acids (C_{36}/C_{28})

Palmitic/lauric acids (C_{32}/C_{24})

Stearic/lauric acids (C_{36}/C_{24})

The melting points for the various combinations suggested that "analogous mixtures of different acids behave in a completely analogous way" (30). For mixtures of acids that differed in composition by four carbon atoms (the first three combinations above), a mixture of 70% of the acid with the lower carbon content and 30% of the acid with the higher carbon content always resulted in the lowest melting point. Furthermore, the melting point of palmitic acid was lowered by the same amount if mixed with the same proportion of either stearic acid (containing four more carbon atoms) or myristic acid (containing four fewer carbon atoms) acids. The same was true for myristic acid. Mixtures consisting of two acids that differed by eight or twelve carbons followed a similar rule. If the melting point was plotted against composition, Heintz wrote (31),

in all cases the curve will first sink below [the value of] the lower melting compound, and then turns upward, cutting the abscissa and then slowly climbing above it. This curve remains almost the same for every two acids that differ by four or eight carbons. But the greater the difference of composition of the two acids, the sooner the curve reaches its the lowest point.

But this new law still did not explain the fraction that melted at 32.3°C. Heintz now suspected that this could be a mixture of three acids that increased by four carbon units in sequence (such as stearic, palmitic and myristic acids). Heintz took a fixed mixture of palmitic and myristic acid and combined it with varying amounts of stearic acid, and another fixed mixture of myristic

and lauric acid with varying amounts of palmitic acid. The melting points of these mixtures "fully confirmed" Heintz's initial suspicions, as one of these mixtures proved to have a melting point of 32.2°C.

Heintz concluded that the law he had established in his study of butter had general consequences, and the fatty acids in spermaceti also followed the "rule of four." There was no need to postulate a fifth fatty acid, and all four acids present contained a multiple of four carbon atoms. Heintz went on to list the many known fatty acids that did not fit the "rule of four" and suggested that they must be mixtures of known acids. By 1855, therefore, Heintz had reached two major conclusions: 1) fats consisted of a small number of fatty acids, and that these acids always contained a multiple of four carbon atoms, and 2) that mixtures of fatty acids produced a lowered melting point that sometimes remained quite sharp, giving a false sense of their purity. Furthermore, the degree of melting point depression followed a general law, according to the proportion of fatty acids that differed in composition by four carbon atoms. In 1857, Heintz completed his investigation by synthesizing the "true" margaric acid with 34 carbon atoms and found its properties very different from the original margaric acid (32).

Heintz recognized that the presence of a sharp melting point in these mixtures could be due to a new pure chemical compound created on mixing the acids, but he rejected this possibility for two reasons. First, the mixtures with the lowest possible melting point did not appear to have a unique form when they solidified, and they appeared completely uncrystalline. The only exception to this was, not surprisingly, margaric acid, which, according to Heintz, produced long needles on crystallization, and "possesses a much greater ability to crystallize" (*besitzt viel grössere Krystallisationsfähigkeit*) than either pure stearic or palmitic acid (33). Heintz's second argument is complex and difficult to follow, but in essence he suggested that the proportions required to produce the lowest possible melting point did not "correspond to a weight proportion (*Gewichtsverhältniß*) of simple molecular numbers (*Atomzahlen*)" (34). The possibility of creating a new compound on mixing fatty acids seemed even more unlikely when Heintz considered that three fatty acids could mix to lower the melting point even further. "It is therefore certain," wrote Heintz, "that the physical behavior of the molecules (*Atome*) alone is the reason for the observed phenomena" (35).

Simple Substances, Melting Points and Chemical Species

Heintz's work on fats was only a fraction of his total research output, but it reflects his general emphasis on the empirical investigation of animal fluids with little reliance on theory beyond calculating molecular formulas. It certainly was his most significant and enduring accomplishment, even if his name is no longer recognized today. Separating these acids was painstaking work, with melting points that often differed only a fraction of a degree. Accounts of Heintz's work acknowledged his "astonishing perseverance" and "great virtuosity with which he manipulated his method." An 1881 commenter in *Nature* remarked that Heintz's work "form[s] essentially the basis of our present knowledge of the fats and the fatty acids" (36). Heintz's painstaking work on differentiating the fatty acids also resembles Emil Fischer's more famous later investigation of the isomeric sugars. Yet, unlike Fischer, who had van 't Hoff's theory to guide him on the total number of possible stereoisomeric sugars, Heintz had no theoretical guidance as to how many fatty acids there could be until he derived the rule of four.

Heintz's research on fatty acids illustrates a number of issues in nineteenth century chemistry. First, consider Heintz's technique for separating the fatty acids and the criteria for chemical identity—how do chemists identify a unique chemical species? In his 1854 paper on spermaceti, Heintz concluded that the long accepted method for preparing pure compounds, repeated recrystallization until the melting point no longer changed, was no longer adequate. Heintz wrote in 1854 (37)

Until my work no other means of purification was recognized other than recrystallization. If the melting point by repetition of this operation no longer changed, it was safe to conclude the purity of the acid. My investigations have demonstrated that this conclusion is not correct under all conditions. But I have previously learned a method for the case when recrystallization does not suffice to establish an acid's purity, and with its assistance, [I] demonstrated that margaric, cetyl and anthropic acids are mixtures.

In other words, "simple crystallization" (*bloß Umkrystallization*) could not guarantee the formation of a single pure compound, no matter how uniform and regular the crystals appeared to be, or how sharp and unchanging the melting point. The only way to assure purity, according to Heintz was repeated fractional precipitation of the fatty acids to reach a constant melting point.

In 1823, echoing Lavoisier, Chevreul had written that the identity of any chemical species is "based on experiment and should not be considered as absolute but purely as the result of the means employed" (38). Heintz's method of fractional precipitation demonstrated that margaric and anthropic acid were no longer "simple substances," in Lavoisier's sense of the term. Heintz himself was fairly surprised at the appearance of yet another new separation method, remarking that (39)

since chemistry became a science, it was the most enthusiastic goal of everyone who set it as their life's work, to complete and increase the methods of investigation. One would hardly think that even now it is still possible to devise methods that are entirely new in their principles.

As a sign that Heintz thought his fractional precipitation method was significant, his first 1851 paper on the fatty acids discussed exclusively the origins and effectiveness of this new method.

Another significant result of Heintz's work was what he termed the "law" of melting point depression, an extensive quantification of the effect of impurities on melting points. In his 1823 book, Chevreul had compiled an extensive table that displayed a regular increase in melting point in mixtures of oleic and margaric acids. Although he did not find a mixture with the lowest possible melting point, Chevreul demonstrated that the melting points gradually increased from approximately 0°C (99% oleic acid) to 55°C (99% margaric acid) (40). Heintz did not mention Chevreul's table, but was directly influenced by Johann Gottlieb's 1846 paper on the fatty acids isolated from goose fat. Gottlieb had saponified goose fat and isolated both stearic acid (*Talgsäure*) and margaric acid, but he was initially confused, because his first fraction melted at 58°C, a value below the melting point of both stearic and margaric acids. Gottlieb therefore deliberately mixed the two acids and found that the melting point was often below 60°C, and compiled a table of melting points as a function of composition to avoid errors and correlate the melting point with composition (41). Whereas Gottlieb had only mixed stearic and margaric acids, Heintz expanded Gottlieb's results significantly by determining the melting points of various combinations of stearic, palmitic, lauric and myristic acids, and deriving a general law describing the relationship between composition and the maximum melting point depression (42). Both Gottlieb and Heintz drew an explicit analogy between the melting point depression in fatty acids and a similar phenomenon that occurred in mixtures of certain metals. Heintz noted (43)

The mixing of two metals often results in a significant lowering of the melting point, and if a third [metal] is added, the melting point often goes significantly lower. I remember here especially the mixture of metals reported by Rose, Newton, and Lichtenberg, made of lead, tin, and bismuth, that melts in boiling water.

Heintz's use of melting points to identify fatty acids as chemical species raises broader questions about the general adoption of melting points as an identification technique in chemistry. In his 1851 paper on the composition of human fat, Heintz described his careful measurement of the temperature of fat as it solidified around the bulb of a thermometer, determining the freezing temperature when the liquid fat became transparent. He also determined the melting point of the same fat in a capillary tube, and then measured the temperature at which it re-solidified on cooling (44).

On two other occasions, in 1852 and 1855, Heintz described in detail his method for determining accurate melting points. His thermometer was made by the prominent glassblower Heinrich Geisler, and had a small bulb (10 × 4 mm), allowing it quickly to assume the surrounding temperature. The scale was divided into 1/5°C increments, and allowed him to establish temperatures within 1/20°C with the naked eye (45). To take a melting point, Heintz first melted the acid in a water bath and sucked some of the molten solid into a "capillary tube with the thinnest possible walls, made from already thin-walled gas inlet tube." The acid solidified in the capillary tube and it was then attached to the thermometer such that it touched the bulb. The assembly was then placed in a beaker (*Becherglas*) full of water and the temperature gradually increased to the moment when the acid became transparent where the capillary touched the bulb of the thermometer. This temperature was then the melting point of the acid (46).

Heintz emphasized that it was important to have a fully calibrated, accurate thermometer, since small differences in melting point could indicate a substantial difference in the purity of the sample, and that no other methods would be sufficient for determining purity of the fatty acids, for "otherwise agreement with my results will be difficult to obtain, and the melting point might indicate a pure acid, when it certainly is not" (47). Heintz's detailed description of his melting point technique would seem to indicate its novelty, and Wislicenus and Richard Meyer suggested later that Heintz was among the first chemists to use the constancy of the melting point as a criterion for a compound's purity (48). But this is clearly

not true, as Heintz himself explicitly noted that the accepted technique for identifying purity of the fatty acids was repeated crystallization until a constant melting point was reached (49).

The origins of the melting point as an accepted standard for chemical species identification remain unclear. Melting points for inorganic compounds do appear in textbooks fairly early. In the first volume of his 1821 *Lehrbuch*, Berzelius listed the melting points of mercury, wax, tin, lead, copper and iron, and in his 1844 textbook, Eilhard Mitscherlich listed the melting points of sulfur, selenium and phosphorous (50). The first use of melting points for organic compounds is more difficult to determine. Chevreul himself, of course, recorded specific melting points as identifying properties for the fats and fatty acids, and in their 1832 paper on the benzoyl radical, Liebig and Wöhler casually mention the melting point of benzamide as 115°C (51). It may be that fatty acids were routinely characterized by melting point following Chevreul's example, and chemists used melting points for other organic compounds only irregularly.

Literature references to early techniques for measuring melting points seem to be even more obscure than the first literature appearance of melting points. Berzelius, Mitscherlich, Liebig and Wohler, and Chevreul did not describe their technique for measuring melting points, or even discuss it as a novel means of identification, suggesting that melting points were already used for identification by the 1820s, and the technique for measurement was not unusual enough to discuss. On the other hand, Heintz thought his technique for measuring melting points original enough to describe in detail twice (52). Heintz therefore appears to belong to an existing tradition of measuring and using melting points, but we are still far from understanding the process by which this technique, and its counterpart the boiling point, became standardized among chemists for defining a chemical species (53).

References and Notes

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8. R. Meyer, *Vorlesungen über die Geschichte der Chemie*, Akademische Verlagsgesellschaft, Leipzig, 1922, p 165; Ref. 3, p 3124.
9. W. Heintz, "Ammoniakgehalt des Harnes," *Zeit. ges. Naturw.*, **1855**, 5, 366-369; W. Heintz, "Auffindung des Kreatins im Harne," *Ann. Chem.*, **1847**, 70, 466-480; W. Heintz, "Rechtfertigung der Methode, den Harnstoff aus der Quantität des aus ihm erzeugten Ammoniaks zu bestimmen," *J. prakt. Chem.*, **1847**, 41, 282-284; W. Heintz, "Über die harnsauren Sedimente," *Ann. Chem.*, **1845**, 55, 45-78; W. Heintz, "Über die quantitative Bestimmung des Harnstoffs, des Kalis und Ammoniaks im Harne," *Pogg. Ann. Phys. Chem.*, **1845**, 66, 114-160.
10. W. Heintz, "Quantitative Bestimmung der Aschenbestandtheile thierischer Substanzen I," *Pogg. Ann. Phys. Chem.*, **1847**, 72, 113-155; W. Heintz, "Quantitative Bestimmung der Aschenbestandtheile thierischer Substanzen II," *Pogg. Ann. Phys. Chem.*, **1848**, 73, 455-461; W. Heintz, "Untersuchung des flüssigen Inhalts der Echinococcenbälge (Hydatinbälge) einer Frau Echinococcenflüssigkeit," *Jenaische Ann. Phys. Med.*, **1850**, 1, 180-191; W. Heintz, "Zusammensetzung der Knochenerde," *Pogg. Ann. Phys. Chem.*, **1849**, 77, 267-287; W. Heintz, "Bestimmung des Harnstoffs im Harn und Zusammensetzung des salpetersauren Harnstoffs," *Berichte der Berliner Akademie*, **1845**, 277-282.
11. M. E. Chevreul, *Recherches chimiques sur les corps gras d'origine animale*, Levrault, Paris, 1823. M. E. Chevreul, *A Chemical Study of Oils and Fats of Animal Origin*, translated by G. R. List and J. Wisniak. AOCS Press, Urbana, 2009. On Chevreul, see Costa, Ref. 2, and A. J. Dijkstra, "How Chevreul (1786-1889) Based His Conclusions on His Analytical Results," *Oleagineux, Corps Gras, Lipides*, **2009**, 16, 8-13.
12. A. J. Roche, *Nationalizing Science: Adolphe Wurtz and the Battle for French Chemistry*, MIT Press, Cambridge, MA, 2000. pp 200-201.
13. W. Heintz, "Ueber die Fette," *J. prakt. Chem.*, **1855**, 66, 1-51, p 3. A slightly modified version appeared later in the *Zeitschrift für die gesammten Naturwissenschaften*. W. Heintz, "Über die Fette," *Z. ges. Naturw.*, 6, **1855**, 279-307.
14. Ref. 3, p 3131. "klare Anschauung von der Art, wie Heintz arbeitete," ... "Experimentaluntersuchung verfolgten Weg."
15. Heintz's earliest communication on the fats, concerning tallow, appeared in 1849 in the proceedings of the Prussian Academy. W. Heintz, "Beobachtungen über das Schmelzen von Stearin aus Hammeltalg," *Monatsberichte der Königlich Preußischen Akademie der Wissenschaften zu Berlin*, **1849**, 222.
16. W. Heintz, "Ueber die Zusammensetzung des Menschenfetts," *Pogg. Ann. Phys. Chem.*, **1851**, 84, 238-261, p 239.
17. *Ibid.*, p 244. "Dieser Umstand verbunden mit dem, dass die bisher angewendete Methode der Scheidung der fetten Säuren, auf die aus dem Menschenfett gewonnenen angewendet, nicht einmal die Reindarstellung auch nur einer derselben gestattet, nöthigte mich, nach einer andern Trennungsmethode derselben zu forschen Lange und vielfach habe ich mich bemüht, die gewöhnlich gebräuchlichen Principien der Scheidung auf die feiten Säuren anzuwenden, aber stets ohne Erfolg, wie zu erwarten, weil ja bekannt ist, wie außerordentlich ähnlich, man möchte fast sagen gleich, sich die Verbindungen der verschiedenen feiten Säuren mit derselben Basis gegen Auflösungsmittel verhalten."
18. J. Liebig, "Ueber die Trennung einiger Säuren der Reihe $(\text{CH})_n\text{O}_4$," *Ann. Chem.*, **1849**, 71, 355-357.
19. W. Heintz, "Ueber eine neue allgemeine Trennungsmethode solcher Körper, welche sich in ihren Eigenschaften sehr nahe stehen," *Pogg. Ann. Phys. Chem.*, **1851**, 84, 221-237, pp 225-226. "Diese Gedankenfolge, deren allgemeines Resultat also das war, dass bei jener von Liebig angegebenen Scheidungsmethode der Verwandtschaftsgrad von wesentlichstem Einfluss ist, führte mich auf die Idee zu versuchen, ob es nicht gelingen sollte, eben durch den Grad der Verwandtschaft solche Körper von einander zu trennen, deren Eigenschaften sowohl, wenn sie sich im freien Zustande befinden, als wenn sie an andere Substanzen gebunden sind, sich so nahe kommen, dass man sie bisher nicht oder nur unvollkommen zu scheiden vermochte. Ich dachte hierbei zunächst an die festen fetten Säuren, mit denen ich mich schon seit längerer Zeit erfolglos beschäftigte eben weil die bis dahin angewendeten Methoden so höchst unvollkommen waren."
20. Ref. 19, pp 226-227.
21. W. Heintz, "Über die Zusammensetzung des Hammeltalgs, des Menschenfetts und des Wallraths," *Pogg. Ann. Phys. Chem.*, **1852**, 87, 553-587, pp 571-572. "Diese Resultate meiner Versuche brachten mich endlich auf den Gedanken, dass die Anthropinsäure ungeachtet ihrer grossen Fähigkeit zu krystallisiren, ein Gemenge von Stearinsäure und Margarinsäure seyn möchte." Heintz noted that had the amounts of anthropic acid from human fat been greater, he would have noticed it was a

- mixture much earlier. It was the quantities of anthropic acid from mutton tallow that allowed him to determine that it produced two fractions with similar melting points but different compositions.
22. Ibid., p 572. "durchaus wie die Säure, die ich Anthropin-säure genannt hatte."
 23. Ibid., p 573. "welches in *allen Eigenschaften*, namentlich in der Art zu krystallisiren, wenn es aus dem geschmolzenen Zustande in den festen übergeht, und im Schmelzpunkt, der bei $56^{\circ},3$ C. liegt, mit der Anthropinsäure übereinstimmt." Heintz's emphasis.
 24. Ibid., p 574. "Dieser Versuch ist mit Palmitinsäure und Stearinsäure von verschiedenem Ursprung so oft wiederholt worden, dass ich ihn nicht mehr bezweifeln kann."
 25. W. Heintz, "Über den Wallrath," *Pogg. Ann. Phys. Chem.*, **1852**, 87, 21-44, 267-293.
 26. J. Lerch, "Ueber die flüchtigen Säuren der Butter," *Ann. Chem.*, **1844**, 49, 212-31. Formulas are given using Heintz's atomic weights, where C = 6 and O = 8.
 27. W. Heintz, "Über die Butter," *Pogg. Ann. Phys. Chem.*, **1853**, 90, 137-165, p 162 "daß in den Verseifungsprodukten der Fette überhaupt nur solche Säuren vorkommen, deren Kohlenstoffatomzahl durch 4 theilbar ist." This corresponds to the modern "law" that naturally occurring fatty acids usually exist in multiples of two, although modern methods have detected small quantities of fatty acids with an odd number of carbon atoms.
 28. Ibid., p 163.
 29. W. Heintz, "Über den Wallrath," *Pogg. Ann. Phys. Chem.*, **1854**, 92, 429-451; 588-612, pp 440-441. Myristic acid was first isolated from nutmeg by Lyon Playfair in 1841, but Heintz renamed it. L. Playfair, "Ueber das feste Fett der Muskatbutter," *Ann. Chem.*, **1841**, 37, 152-164.
 30. Heintz, Ref. 29, p 591. "analoge Gemische der verschiedenen Säuren vollkommen analog verhalten."
 31. Heintz, Ref. 29, p 593. "Will man den Einfluss der Mischung auf den Schmelzpunkt der Säuregemische durch Curven ausdrücken, und verlegt man zu dem Ende den Anfangspunkt derselben von der leichter schmelzenden Säure ausgehend, in die Abscisse, so wird in allen Fällen die Curve zuerst unter dieselbe herabsinken, dann sich wieder nach oben wenden, die Abscisse schneiden und nun allmähig über dieselbe hinaussteigen. Diese Curve bleibt für je zwei Säuren, die sich um C_4H_4 und die sich um C_8H_8 unterscheiden, nahezu dieselbe. Je grösser aber der Unterschied der Zusammensetzung: der beiden Säuren ist, um so früher tritt der tiefste Punkt der Curven ein."
 32. W. Heintz, "Ueber die Margarinsäure," *Pogg. Ann. Phys. Chem.*, **1857**, 257-289. Modern methods have detected small amounts of a naturally occurring fatty acid with 17 carbons.
 33. Ref. 13, p 7.
 34. Heintz, Ref. 29, p 595. "Es müßten ferner die Verhältnisse, in welchen die beiden Säuren gemischt werden müssen, um ein Gemisch darzustellen, das einen möglichst niedrigen Schmelzpunkt besitzt, dem Gewichtsverhältniß einfacher Atomzahlen entsprechen, was ebenfalls nicht zutrifft." Heintz is using the word "Atom" here in the modern sense of "molecule."
 35. Ref. 13, p 17. "Es ist demnach zweifellos, dass nicht in der Bildung chemischer Verbindungen, sondern in dem physikalischen Verhalten der Atome allein der Grund für die beobachteten Erscheinungen gesucht werden muss."
 36. "erstaunlicher Ausdauer" Wislicenus, Ref. 3, p 3126. "... hohe Virtuosität, zu welcher er die Handhabung [manipulation] dieses Verfahrens ausbildete," E. v. Meyer, in E. Korschelt, et al., *Handwörterbuch der Naturwissenschaften*, vol. 5, Fischer, Jena, 1914, p 300. T. H. N., "Wilhelm Heintz," *Nature*, **1881**, 245-246, p 245.
 37. Heintz, Ref. 29, p 598. "Bis zu meinen Arbeiten hat man aber kein anderes Reinigungsmittel gekannt, als das Umkrystallisiren. Wenn der Schmelzpunkt durch Wiederholung dieser Operation sich nicht mehr änderte, so glaubte man auf die Reinheit der Säure schliessen zu dürfen. Dass dieser Schluss nicht unter allen Umständen richtig ist, haben meine Untersuchungen dargethan. Ich habe aber schon früher ein Mittel kennen gelehrt, um in dem Falle, wenn das des Umkrystallisirens nicht ausreicht, sich doch von der Reinheit einer Säure zu überzeugen, und mit Hülfe desselben die Gemischtheit der Margarinsäure, Aethalsäure, Anthropinsäure dargethan." Heintz, Ref. 13, p 3. "Man hatte bis dahin für die Reinheit einer fetten Säure nur das eine Merkzeichen, dass durch Umkrystallisiren ihr Schmelzpunkt nicht mehr erhöht werden konnte."
 38. Ref. 11, p 301. This passage was emphasized by Chevreul.
 39. Ref. 19, p 221. "Seitdem die Chemie sich zu einer Wissenschaft zu erheben anfang, war es das eifrigste Bestreben aller derer, welche sie zu fördern zu ihrem Lebensziele setzten, die Methoden der Untersuchung zu vervollkommen und zu vermehren. Man sollte daher kaum glauben, dass jetzt noch es möglich ist, eine in ihrem Principe gänzlich neue Methode zu ersinnen."
 40. Ref. 11, 82-83. The melting point of oleic acid is $13-14^{\circ}C$, and therefore a liquid at room temperature.
 41. J. Gottlieb, "Untersuchung Des Gänsefettes und der Oelsäure," *Ann. Chem.*, **1846**, 57, 33-67, pp 34-37.
 42. Although he did not use the term, Heintz is describing what today is called the eutectic point of a mixture.
 43. Heintz, Ref. 29, p 597-598. "Die fetten Säuren verhalten sich daher durchaus ähnlich wie die Metalle. Durch Vermischen von zwei Metallen sinkt der Schmelzpunkt oft bedeutend und wenn noch ein drittes hinzugesetzt wird, so geht der Schmelzpunkt häufig von Neuem bedeutend herunter. Ich erinnere hier nur an das Rose'sche, Newton'sche, Lichtenberg'sche Metallgemisch, das aus Blei, Zinn und Wismuth bestehend, im kochenden Wasser schmilzt." Unfortunately, neither Heintz nor Gottlieb gave a literature citation for this curious phenomenon.
 44. Ref. 16, p 239. "Wurde etwas desselben auf einer Thermometerkugel geschmolzt, so war es beim allmähigen Erkalten noch bei $50^{\circ}C$. dünnflüssig, wurde aber allmähig immer dicklicher, überzog sich bei $46^{\circ}C$. mit einer Haut,

- floss bei 45° C. nicht mehr, wurde aber erst bei 42°-43° C. trübe und undurchsichtig. Diese Erscheinung wiederholte sich vollkommen mit einer neu dargestellten Portion dieses Fettes. Wurde dagegen sein Schmelzpunkt bestimmt, indem man es in einem Capillarrohr unter Wasser erhitze, so wurde es erst bei 53° C. flüssig, die geschmolzene Masse trübte sich jedoch erst wieder bei 44° C.”
45. Ref. 21, p 583.
46. Ref. 13, p 23. “möglichst dünnwandiges Capillarrohr, das man durch schnelles Ausziehen eines schon dünnwandigen Gasleitungsrohrs erhält.” Heintz did not use the modern standard of reporting a melting point range.
47. Ibid. “sonst eine Uebereinstimmung mit meinen Resultaten schwerlich erzielt werden würde, und man daher nach dem Schmelzpunkt eine Säure für rein halten würde, die es keineswegs ist.”
48. Meyer, Ref. 8, p 165. Wislicenus, Ref. 2, p 3126.
49. W. Heintz, “Über die Fette,” *Zeit. ges. Naturw.*, **1855**, 6, 279-307, p 280
50. E. Mitscherlich, *Lehrbuch der Chemie*, Mittler, Berlin, 1844, pp 50, 61, and 64; J. Berzelius, *Lehrbuch der Chemie*, 6 vols. Vol. 1, Macken, Reutlingen, 1821, pp 38-39.
51. Liebig and Wöhler wrote simply: “At 115°C [benzamide] melts to a water-like liquid, which congeals by cooling to a large-leaved crystalline mass, ...” J. Liebig and F. Wöhler, “Untersuchungen über des Radikal der Benzoesäure,” *Ann. Pharm.*, **1832**, 3, 249-287, translated in O. T. Benfey, Ed., *Classics in the Theory of Chemical Combination*, Dover Publications, New York, 1963, p 29. Timmermans implies that Liebig and Wöhler were the first to use the melting point, although he does not present a systematic study of the literature. J. Timmermans, *The Concept of Species in Chemistry*, translated by R. Oesper, Chemical Publication Company, New York, 1963. See also W. B. Jensen, “Melting Points and the Characterization of Organic Compounds,” *J. Chem. Educ.*, **2009**, 86, 22-23.
52. Heintz’s description of his melting point technique is the earliest I have seen, although almost certainly there must be earlier descriptions. Later descriptions of melting point apparatus include J. Piccard, “Zur Bestimmung Des Schmelzpunkts,” *Berichte*, **1875**, 8, 687-689, and C. F. Roth, “Ein neuer Apparat zur Bestimmung von Schmelzpunkten,” *Berichte*, **1886**, 19, 1970-1973. In 1893, Walther Nernst wrote a comprehensive survey on boiling and melting points, but did not extensively discuss techniques. W. Nernst and A. Hesse, *Siede- und Schmelzpunkt, ihre Theorie und praktische Verwerthung mit besonderer Berücksichtigung organischer Verbindungen*, Vieweg, Braunschweig, 1893.
53. The most comprehensive studies of thermometry are by Chang and Middleton, but neither discusses the melting point. H. Chang, *Inventing Temperature: Measurement and Scientific Progress*, Oxford University Press, New York, 2004. W. E. K. Middleton, *A History of the Thermometer and Its Use in Meteorology*, Johns Hopkins University Press, Baltimore, 1966. For an excellent discussion of chemical species identity, see J. Schummer, “The Impact of Instrumentation on Chemical Species Identity from Chemical Substances to Molecular Species,” in P. J. T. Morris, Ed., *From Classical to Modern Chemistry: The Instrumental Revolution*, edited by P. J. T. Morris, pp. 188-211, Chemical Heritage Foundation, Philadelphia, 2002.

About the Author

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