

Determining the Effects of Wöhler's Synthesis of Urea

Clarke Knight • IB Extended Essay • May 2010 • 3,997 words

Explanations for the existence of 'living' versus 'non-living' entities have been posited since ancient times. Vitalism was a school of thought that defined living organisms beyond physical, chemical, or biological terms. Proponents of vitalism believed that life required a 'vital principle,' 'vital force,' 'vital spark,' 'vital energy,' 'élan vital,' or 'soul.' This 'force' however, could not be seen by those who sought to describe it but nonetheless was the quality believed to divide all matter into two categories: the living (vital force present) and the dead (vital force absent). Living beings contained an irreproducible essence making them qualitatively distinct from non-living matter. Accordingly, life emerged from some mystical impulse beyond the material or physical world. Life required divine intervention.

As such, the ideas of science and religion have been intertwined for centuries. The unraveling of these ideas may have started with Aristotle, as the "precursor of all vitalistic theories until the most recent times" (Driesch, 1914). Aristotle believed that the universe was rational and by applying logical reasoning, the basis of all science, one could understand the universe (Armstrong, 1994). As early as 300 B.C., Aristotle categorized natural objects as animal, plant, or mineral. Further attempts to reconcile the religious concept of vitalism with emerging scientific models can be traced to the thirteenth century, where translations of early Greek philosophies (Plato, Aristotle, et al.) show that logical reasoning was used as a tool to understand life forces.

Most importantly, religious thinkers like Thomas Aquinas (1225-47) attempted to "integrate the new philosophy with the Western Christian tradition" (Armstrong, 1994) in his life's work *Summa Theologica*. In it, he lists rational proofs of God's existence to link his religious faith with his scientific studies.

Centuries before Friedrich Wöhler performed his urea experiment, Aquinas recognized a difference between the living and the dead and then separated the living into categories: "Simple things do not differ by added differences – for this is the property of compounds. Thus man and horse differ by their differences; rational and irrational...it is better to say that they are, not different, but diverse" (Aquinas, In: 1947). Therefore, according to Aquinas, two living creatures can be made of diverse substances. While it is obvious a horse is not the same as a man, they are not made of different kinds of materials. In modern terms, all matter can be broken down into elements like carbon, nitrogen, or hydrogen, and these elements do not have some sort of preference for the type of substance they will comprise (like a horse, man, or rock). For instance, atoms that make up the stars are the same materials that can be found in human blood.

By the 1600's, models of matter were defined based on their behavior to heat, and two forms of matter were identified: inorganic and organic. Inorganic materials could be melted and recovered when the heat source was removed, but organic materials could not be recovered. Vitalists believed that not only were living organisms made of more complex substances, they were made of different qualities of substances, i.e. ones that could not be heated and be restored to the original form. The essential difference between organic and inorganic materials, according to the above definition, was a vital force, present only in organic material. Vitalism gave rise to the inorganic/organic distinction.

Beyond the obvious influence of religion on human actions, a belief in divine influence can be seen in the emerging principles of science into the nineteenth century. Before the microscope and other technologies allowed for observation of microbes, the leading 'creation' theory in Western thought was spontaneous generation: life originated from inanimate objects. Aristotle first postulated this theory and "as a general rule, then, all testaceans grow by spontaneous generation in mud" (Thompson, D'Arcy & Wentworth, 2007). This idea contrasts with the notion of vitalism in that organic substances were made from other organics, while spontaneous generation held that organics could come from non-organic material (mice could result from dirty clothes, for example). However, spontaneous generation was derived from "widely held cultural and religious beliefs of the time" (Levine & Evers, 1999). Over 600 years after Aquinas, Louis Pasteur demonstrated biogenesis – a theory that states living organisms do not impulsively arise from non-life – and through 'germ theory' in 1864 permanently ended previous arguments for spontaneous generation.

The conceptual gap between organic and non-organic, the living and the dead, continued for centuries and was not fully closed in Wöhler's time. Physiological chemists of the early nineteenth century wanted to show that the organic compounds of living organisms were simply the result of chemical processes. "Berzelius argued in 1836 that chemistry could account for all of the reactions occurring within living organisms, and that organic and inorganic processes differed only in complexity" (Bechtel & Richardson 1998). Berzelius continued: "there is no special force exclusively the property of living matter which may be called a 'vital force'" (Bechtel & Richardson, 1998). While vitalism gave rise to organic and inorganic distinctions, chemistry reshaped the singular religious argument with alternative explanations of 'life.'

For the emerging scientists of the eighteenth and nineteenth centuries, the question may have been what level of vital forces could be tolerated. Often vital forces were invoked when technology or explanations were lacking (Betchel & Richardson, 1998). For example, the greatest challenge of biology was to explain development from an egg to an organism. When faced with physiology, the production of an organic form defied chemical explanations of the day. As an elderly man, Berzelius reverted to old conservative ideas (Kauffman & Chooljian, 2001), and he believed that "in living nature the elements seem to obey entirely different laws than they do in the dead..." (Berzelius, 1847). This was a vitalist stance.

Many feel that the separation between people and animals or living organisms and dead substances was created by humans to justify their supremacy on earth. It follows then that the distinction between a man, horse, and rock as made by Aquinas, a deeply religious man, was so he could understand man's purpose in life. He believed that humans were made in God's image (and vastly different from a lowly animal or inanimate object) and thus must be different in some fundamental way.

Christian literalists scorned many new scientific discoveries

because they contradicted or could not be reconciled with the Bible. Literalists believed that the entire Bible was true, word for word, and any scientific contradiction of 'fact' could nullify the entire book. It was imperative to the Church that no conflicting scientific views became accepted by the masses, lest the Church would look like fools. To make matters worse for the Church, the new Age of Reason was dawning quickly in the early seventeenth century, making any "religious mythology vulnerable to the new science" (Armstrong, 1994). Those questioning the Church ran the risk of being ostracized or excommunicated because "excessive intellectualism [was] damaging to the faith" (Armstrong, 1994). On the eve of some of the greatest scientific advancements after the Middle Ages, the Church tried desperately to cling to tradition, becoming the pillar of immutable thought in the Western world.

Some scientists like Galileo tested the limits of Church doctrine by showing, with evidence, that the Earth was not the center of universe but rather revolved around the Sun. Nicolaus Copernicus was the first to announce his findings in the publication of *De revolutionibus*, which used mathematics, as well as a new definition of gravity, to explain why the Sun must be the center of the universe (Hannam, 2005). Others, like Galileo, were sentenced to "indefinite imprisonment" by the Inquisition (Armstrong, 1994) for supporting this radical idea. The Church's conservative viewpoint made it difficult for scientists like Copernicus and Galileo to share their ideas and advance knowledge. Because church leaders acted defensively when new scientific ideas were proposed, they alienated many followers and opened the door for a new group of nonbelievers: atheists.

Progress in areas of science in the beginning of the nineteenth century created a "new spirit of autonomy and independence" (Armstrong, 1994) that allowed many of the faithful to become atheists. The nineteenth century has been called the "best-documented moment of widespread doubt [in religion] in human history" (Hecht, 2003). Scientists and philosophers like Freud, Marx, Darwin (and Wöhler) "forged philosophies and scientific interpretations of reality which had no place for God" (Armstrong, 1994). Slow progress towards this separation of Church dogma and science had its roots in early chemistry and geology. James Hutton (c. 1790) and Charles Lyell founded uniformitarianism, which was also in marked conflict with scripture. What made Lyell's principle of uniformitarianism unorthodox was that it explained geology through natural processes: the building of mountains and the shaping of seas was independent of God's direct hand (Scott & Eldredge, 2005). Resultantly, God was rendered useless, a conclusion that ignited opposition.

According to the vitalist idea of life, matter that comprises living organisms has a vital force that is lacking in non-living objects. Organic matter could only be created from organic matter since inorganic matter lacked the vital force required for life. In 1828, Friedrich Wöhler synthesized urea, an organic compound, using inorganic material, and showed for the first time that a natural (organic) chemical could be recreated in a laboratory. "This refuted once and for all the doctrine that the synthesis of organic compounds requires a special force" (Schlick, 1925 In: Feigl & Brodbeck, 1953).

Although Wöhler's experiment is arguably one of the most elegant and important in the nineteenth century, little is known about Wöhler's personal opinion on the matter. In a letter to Berzelius, Wöhler excitedly wrote, "I can no longer, so to speak, hold my chemical water and must tell you that I can make urea without needing a kidney, whether man or dog..." (Benfey, 2005). While Wöhler's achievements as a chemist were many, synthesis of urea proved to be the most controversial experiment of his life and marked the beginning of the formal branch of research known as organic chemistry (Warren, 1928).

Contemporaries called Friedrich Wöhler's synthesis of urea in 1828 without the aid of a kidney "epoch-making" (Von Hofmann, 1882) and "little less than a miracle" (Remsen, 1882-83). Before Wöhler's discovery, vitalism was the dominant theory in chemistry. With this breakthrough, Wöhler put the principles of alchemy and vitalism to rest and set the stage for modern chemistry. Wöhler described his experimental results as "more noteworthy inasmuch as it furnish[ed] an example of the artificial production of an organic, indeed a so-called animal substance, from inorganic materials" (Leicester & Klickstein, 1956).

Some scientists of the day disagreed that Wöhler actually 'synthesized' an organic substance from dead, inorganic substances. This stance would lead to the belief that Wöhler simply transformed one organic substance to another, and therefore the experiment was classified as a failure. One such critic, Douglas McKie, stated that "he could make urea without a kidney or a living creature, be it man or dog... but, be it noted, not without dried blood, horns, hoofs, and such 'organic' originals." McKie made further allusions by stating, "among the hoofs, the cloven one of vitalism is surely not difficult to detect here" (McKie, 1944). McKie insinuated that Wöhler was under the influence of the devil during his synthesis of urea. While Wöhler's experiment did use cyanogen, a substance prepared from the oxide of mercury in dried blood, the objection that these substances still contained a 'vital force' was unsupported. The properties of cyanogen as prepared in Wöhler's experiment are described in Webster's A Manual of Chemistry as 'inorganic' and thus devoid of all so-called life forces (Webster, 1839). George Kauffman stated, "Wöhler's synthesis of urea belongs to a small group of classic experiments that have radically changed our view of the world, opened up new paths of research..." (Kauffman & Chooljian, 2001).

Advocates of vitalism believed in variations of the core tenets, which led to levels of confusion in the doctrine. For example, Xavier Bichat, a French anatomist from the eighteenth century stated, "urine, indeed, the saliva, or the bile indifferently taken from such or such a subject, may be analyzed, and hence results in our animal chemistry; but such a chemistry is the dead anatomy of the fluids, not a physiological chemistry" (Gold, 1827). A contradiction appears between the vitalists, McKie and Bichat, on whether the blood used in Wöhler's experiment was organic or inorganic. While McKie says that fluids like blood are "organic," there is discord with Bichat's view that "bile" and other such animal fluids are "dead." Thus, at least according to Bichat, the starting materials of Wöhler's experiment were in fact not alive and did not contain any vital forces.

Other scientists, most notably Henri Bergson who coined 'élan vital' or vital impetus to explain creation, believed that "we

have succeeded in reproducing artificially... certain facts of organization, such as indirect cell division and protoplasmic circulation" (Bergson, 1922). Hence, even those proponents of vitalism conceded that biological (organic) processes can be duplicated in the laboratory. Bergson and other scientists thought it possible that future science could advance enough to create complete living organisms, and that the only obstacle was lack of technology, not the impossibility of the principle. The resulting conflict among vitalists was about when substances contained the vital force, and these uncertainties in principle among leading vitalists paved the way for the explosion of scientific thought following Wöhler's experiment.

In the nineteenth century, explanations of life increasingly developed from chemical and mechanistic views, not along traditional religious or metaphysical paths. Science started to break away from the yoke of religious doctrine at the time of Wöhler's synthesis to develop on its own terms. Yet, science and religion have always been linked closely, and there will probably continue to be undertones of religion in the advancement of scientific thought because they are competing ideas that provide an explanation of the world. The difference between science and religion is that the foundations of science are built on quantitative or empirical evidence while principles in religion are held true because people have faith in them. Still, Wöhler's experiment shook the scientific community, as many of his contemporaries and even his mentor Berzelius were stupefied by his findings.

How can the laws of science be used to show, with convincing arguments, the flaws in the concept of a vital force flowing through living organisms? The alleged 'death' of vitalism was not accepted quietly or easily, and Wöhler himself recognized the implications of his discovery. Wöhler said, "the great tragedy of science [is] the slaying of a beautiful hypothesis by an ugly fact" (Jaffe, 1936).

One of the most interesting arguments for vitalism is the notion that the absence/presence of the vital force attributed to living organisms cannot be proved and thus vitalism could indeed be correct. This 'leap of faith' is not an objective explanation, but one based on belief. An argument based on the conviction that something cannot be disproved is not credible evidence in favor of that argument. Rather, logical arguments with a foundation of collected facts, like those found in scientific theories and mathematical proofs, give sound reasoning. As even Aquinas believed, understanding of scientific theory would be obvious to the observer or could be understood through its religious explanation, a belief in the "higher science" (Aquinas, In: 1947). So, Aquinas reassured the common layperson (and maybe himself) that in the event a scientific concept proved too difficult to grasp, the crutch "God did it" would be suitable rationale. Conversely, scientific reasoning does not have a security blanket to cover up what is unexplainable. In fact, a sound scientific explanation must satisfy "certain conditions of adequacy," the explanation must be (a) derived logically from the information gathered; (b) contain general laws and at least one statement which is not a law (to distinguish an explanation of observations from the laws themselves); and (c) be capable of experiment and/or observation (Hempel and Oppenheim, 1948). Ernst Mayr said that vitalism, "virtually leaves the realm of science by falling back on an unknown and presumably unknowable factor" (Bechtel and Richardson, 1998).

Vitalists believed that the 'vital force' could not be directly seen or observed. The same is also true of gravitational and electromagnetic fields. The difference between the notion of 'vital forces' and gravitational or electromagnetic fields is the latter are measurable, predictable, and can be explained by general law (Hempel and Oppenheim, 1948). Because vital forces cannot be tested, measured, or observed, they have been rendered devoid of all empirical meaning. No general law, credible experiment, or quantitative data has been gathered by vitalists to prove the existence of such a 'force.' As such, vitalism does not fulfill any of the requirements of scientific rigor. The conviction of vitalists that a 'force' builds up simpler substances into more complex ones is a tautological explanation of the properties of vitalism because explanatory power does not reside in the concept itself. For example, when defining a word, one does not use the word itself in the definition because that does not reveal anything new about the subject. Much like a definition does not repeat the actual word, scientific principles do not use the idea of the same principle in the explanation, but instead draw their description from other laws and facts. Vitalism has limited information to call upon, making it an endless loop of ideas that are difficult to define on their own terms. As Daniel Dennett states, "vitalism - the insistence that there is some big, mysterious extra ingredient in all living things - turns out to have been not a deep insight but a failure of imagination" (Dennett, 2005).

The end of the belief in spontaneous generation in 1864, coupled with Wöhler's experiment (in 1828) that subverted the explanatory power of vitalism, cleared the way for new concepts in science. Other scientific principles were established that might not have been published (or even conceived of). For instance, could Darwin's theory of evolution have been developed and accepted if vitalism were still held to be true? Even with vitalism, Darwin may have still conducted the research on the Galápagos and published his work, but it could have been rejected (or suppressed) by the community of vitalists. The underlying principle of vitalism, based on the premise that living matter has a soul, was not compatible with the process of Darwinian evolution whereby species evolve over time. For example, advocates of a vitalistic concept of 'evolution' believed that the eyes of man and the octopus must have followed dissimilar paths of development, even though the eyes have anatomical likeness, because mechanisms of chance variation were not 'satisfactory' in explaining the similarity in the eyes. This example has been used as evidence that there was an "'undivided original vital impulse' which so acts on inert matter as to create appropriate organs for the function of vision" (Nagel, 1953 In: Feigl and Brodbeck, 1953). Here, the vitalist view of creation assumed a magical transfer of 'life energy,' while Darwinian evolution used observation and testable hypotheses to illustrate life processes. Some described Darwinian evolution as different because he "specif[ied] the processes" of evolution and his theory was not similar to older theories because his was "an enlarged scientific knowledge" (Merton, 1973). The doctrine of vitalism and Darwinian evolution are incompatible with each other. Consequently, Darwin's publication of *The Origin of Species* lessened the credibility of vitalistic arguments that were still present in the scientific world.

Another scientist who separated religious thought and science was Charles Lyell (1797-1875). Lyell, a budding geologist who studied the theory of catastrophism before converting to uniformitarianism, faced the challenge of disconnecting the Bible from geological phenomena. William Buckland, Lyell's mentor, "tried to link catastrophism to the Bible, looking for evidence that the most recent catastrophe had actually been Noah's flood" (Lindberg, 2009). Lyell studied the Earth and came to understand that changes in geology occurred over extremely long periods of time, contradicting the religious notion that the Earth developed in a few thousand years. It was Lyell's goal to have geology "built on observation and not susceptible to wild speculations or dependent on the supernatural" (Lindberg, 2009). His theories in turn "deeply" affected Darwin (Lindberg, 2009), who "envisioned evolution as a sort of biological uniformitarianism" (Lindberg, 2009). The public found Lyell's and Darwin's theories heretical, and their ideas may not have come to fruition as quickly without the end of vitalism.

There were some who still clung to a religious definition of life even in the beginning of the twentieth century. One "scientist," Duncan Macdougall, tried to prove the existence of the soul by placing dying patients on a scale and taking their mass before and immediately after death. Macdougall found that each of the five patients tested lost around an ounce of mass immediately after death (Macdougall, 1907). The fact that Macdougall appropriated mass (around 21grams) to the 'soul' goes against the very definition that the soul is a mass-less abstraction. Despite Macdougall's findings, there have been no credible tests to indicate a human soul.

For many scientists in the past centuries, vitalist ideas were perhaps unsatisfactory positions they held while on the pathway to scientific understanding. Joseph Keating discussed vitalism as "a form of bio-theology." He stated, "vitalism is that rejected tradition in biology which proposes that life is sustained and explained by an immeasurable, intelligent force or energy. The supposed effects of vitalism are the manifestations of life itself, which in turn are the basis for inferring the concept in the first place. This circular reasoning offers pseudo-explanation, and may deceive us into believing we have explained some aspect of biology when in fact we have only labeled our ignorance. Explaining an unknown [life] with an unknowable... is absurd." (Keating, 2001). Other contemporary historical writers say vitalism belongs in the "trash heap of history" (Dennett, 2005).

God may not be as all-powerful as He once was in the hearts and minds of those in the West, but He still played an important role in people's lives, including the scientists whose research challenged religious faith. Almost every scientist of the day (seventeenth – twentieth centuries) believed in some notion of a higher power, which means the idea of God influenced (to some degree) the thinking of new rationalists. Chemists like Wöhler were raised in religious homes, and in the aftermath of his synthesis he probably remained a believer. The foundations of Christian belief, as the one and only explanation of the world, were deeply entrenched in the public's mind. It took the work of many scientists like Louis Pasteur, Friedrich Wöhler, Charles Lyell, Charles Darwin, and others to change the way religion and science were perceived by the masses.

Their work separated Church dogma from the theories and laws of science.

Unfortunately, many believe the modern age of science is over, and that the postmodern age of apathy toward science has commenced. Postmodernists do not universally extol the scientific method, or accept the work of the aforementioned scientists, despite their historic and transformative contributions. Ironically, postmodernists believe we may never have complete knowledge, yet they rebuke the work of scientists who strive to gain understanding of the natural world. For instance, some postmodern 'sociologists' believe disease and biology are unrelated and that disease is merely a social phenomenon – a ludicrous concept to many scientists.

But what then is life? How did it all begin? And does the scientific method involve some level of faith? Certainly science does not have answers for everything, and many important questions cannot be framed in a scientific context. However, vitalism in itself must be given credit; it acted as a catalyst for the initial questioning of "truths" and had value addressing what was not yet fully understood. In a similar vein, this project shows that the most dangerous threat to knowledge is not ideas like vitalism, but the certitude with which proponents cling to such ideas. But the biggest irony of all, one that may surprise philosophers and scientists alike, is that Wöhler's watershed experiment for science used cyanogen, a main component of urine. Of all the places to start solving the riddles of life, one would probably not expect to find it in their toilet.

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