

Preformationism vs. Epigenesis

Preformationism and epigenesis are two competing theories of embryonic development. Preformationism is the view that an organism, in some sense, is preformed from origination; and that development is mere growth, unfolding, and solidification of a miniature being into adult form. Epigenesis, on the other hand, is the view that the organism is not fully formed at the beginning of embryonic development; rather, its form arises gradually, changing shape and acquiring its adult parts over time. This paper tracks the historical developments of the debate, leading up to the present day; and will argue that 21st century research thus far best supports a middle ground: the epigenesis of something preformed.

I. Ancient history.

Pre-Aristotelians lacked an organized and generally accepted theory of generation and of development. Throughout this period, nevertheless, one finds certain common questions and certain shared thematic answers, such as: do both parents contribute equally to conception, or does one parent have greater efficacy over the other?; what determines the sex of offspring?; and, why do children typically resemble their parents? Answers included the full range, from the belief that semen contained all of the essential characteristics, needing only a place to grow (Aeschylus, 525-455 B.C.; Euripides, 480-406 B.C.); to the notion that sex differentiation was a function of the temperature of the womb (Empedocles, 490-430 B.C.). Although neither explicitly preformationist nor epigenesist, within the various thematic answers can be found a theoretical opposition which may be called by its modern names, preformationism and epigenesis.

Aristotle (384-322 B.C.) was the first to present a systematic theory of embryonic development. Aristotle is the progenitor of the epigenesis thesis, the main rival to preformationism, that organisms arise from unformed material and develop gradually over time. In his text, *On the Generation of Animals*, Aristotle argued that, either all of the parts of an organism (such as the heart, lung, liver, eye, and all of the rest) come into being together or they come into being in succession;

based in part on observations of embryos from a multitude of different organisms, Aristotle was able to deny that all of the parts of an organism come into being together, “That the former is not the fact is plain even to the senses, for some of the parts are clearly visible as already existing in the embryo while others are not; that it is not because of their being too small that they are not visible is clear, for the lung is of greater size than the heart, and yet appears later than the heart in the original development.” To Aristotle, then, being arises in the same way as the knitting of a net, gradually acquiring the parts that make it what it is. In order to explain how this epigenetic process of development is driven, Aristotle posited a soul. All organisms, Aristotle claimed, possess a soul that resides within the material body from inception, and which is responsible for guiding the epigenetic process of development. Aristotle's theory of epigenesis, among his thoughts on form and matter, formed the core of biological thought for hundreds of years; ideas about generation changed very little from the time of Aristotle to the 17th century.

II. 17th Century.

In 1651, English physician William Harvey (1578-1657), with the publication of *On the Generation of Animals*, was the first naturalist to argue that all living beings arose from eggs in a manner in which complexity of form gradually appeared where uniformity previously existed. To test his ideas, he devised an experiment using deer that he had mated. He dissected deer uterus after fertilization had occurred and searched for an embryo, but was unable to find evidence of the developing embryo in the uterus until weeks after mating had taken place. In addition to his experiments on deer, Harvey constructed experiments whereby he monitored the development of the fetus of chicken embryos from fertilization to hatching. He logged the progress of embryonic development, noting that the chicken, starting off as undifferentiated and homogenate material, only gradually developed into a functional fetus. On the basis of his observations, Harvey concluded that epigenesis followed generation. Harvey's conclusions were in sharp contrast to other leading scientists of his time.

Jan Swammerdam (1637-1680), a pioneer of microscopy, was a severe critic of Harvey. Writing of Harvey's idea of epigenesis, Swammerdam remarked that it was a notable demonstration of humanity's capacity for error, or for weak and imperfect reason. He is often considered the modern founder of preformationism. Based on meticulous studies of insects and amphibians, Swammerdam urged instead that, in development, the same organism persists through its various stages (egg, larva, pupa, and adult), and that each stage was packaged within each other like a nest of boxes. He believed on the basis of his demonstrations that living things developed within eggs, that no new parts were formed during insect metamorphosis, and that growth was merely an increase in the parts already present.

Another pioneer in early microscopy, Italian embryologist Marcello Malpighi (1628-1694), reinvigorated Swammerdam's preformationism¹. In 1672, Malpighi published the first microscopic account of chicken development, which showed that the unincubated chicken egg possessed a great deal of rudimentary structure from its onset. In 1694, Nicolaas Hartsoeker (1656-1725), Dutch mathematician, physicist, and outspoken proponent of preformation theory, published his *Essai de Dioptrique*. His major contribution to embryology was his observation of human sperm cells, the first to be seen under a microscope. While observing human sperm under a microscope, Hartsoeker claimed that he saw tiny men inside of the sperm. Referring to his little person as *petit l'enfant* ("the little infant") or *le petit animal* ("the little animal"), Hartsoeker furnished an image of a tiny human being curled up inside of a sperm cell (Figure 1). Now referred to as a *homunculus*, Hartsoeker's sketch became iconic of 17th century preformation theory. The scientific reputation

¹ Contrary to popular belief, Malpighi's work does not, in general, support preformationism (Adelmann 1966). This is evident in that, Malpighi recognizes that there is no structure comparable to an embryo which is to be found in an unfertilized egg; of a subventaneous egg, he remarked, "when torn open revealed no structure peculiar to and different from it." Nevertheless, his observation of the existence of rudiments of important organs in unincubated chicken eggs provided reason to question epigenesis.

of Swammerdam, Malpighi, and Hartsoecker, among others, largely prevented the theory of epigenesis from gaining ground, allowing preformationism to prevail.

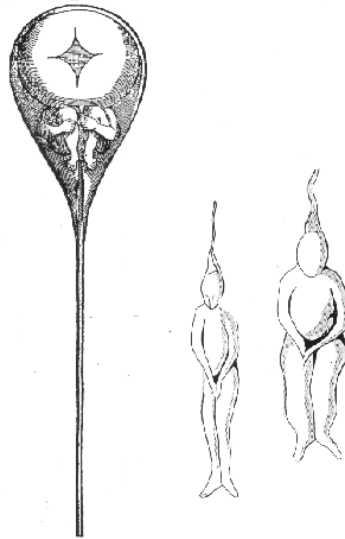


Figure 1. Homunculi in a sperm cell (Hartsoecker, 1695).

III. 18th Century.

Ideas from the 17th century were of great influence to the succeeding era. By the beginning of the 18th century, the theory of preformation was widely accepted and had become the dominant model of embryonic development. Clashes between preformationists and epigenesists, nevertheless, carried on. Central to these debates were Albrecht von Haller (1708-1777), a Swiss anatomist, physiologist, and naturalist; and Caspar Friedrich Wolff (1734-1794), a German physiologist and one of the founders of embryology.

In 1758, Hallar published *Sur la formation du coeur dans le poulet*, a work devoted to embryological development and in which a detailed account of preformationism was defended. In it, Hallar provided results from his extensive microscopic experiments on incubated chicken embryos. He claimed his researched demonstrated that the chicken existed within the egg prior to fertilization. His proof was in his discovery of membrane-continuity, which convinced him completely and

finally of the truth of preformationism. Membrane-continuity consisted in evidence that the membrane of the yolk of an incubated egg was an outgrowth of the membrane of the chicken's small intestines, and that its blood vessels were also a continuation of the chick's. If the egg yolk and the membrane, which existed in the egg previous to impregnation, are of one piece with the developing chick, then, Haller argued, so too must the embryo have been created previous to impregnation, even if the embryo was too small to be seen. Through the use of more elaborate microscopy, Wolff was able to disprove that membrane-continuity was as Haller had described.

One year after Haller had announced his support for preformationism, in 1759, Wolff published his doctoral dissertation *Theoria Generationis*, where he revived the ideas of Aristotle and Harvey, and where he strongly endorsed the theory of epigenesis. Using advanced microscopy, Wolff first studied plant development. He discovered globules within plants that were capable of differentiating into stems, leaves, and other plant tissues. He observed that a plant root is able to regenerate a whole new plant if its stem and leaves are removed, despite it having had already been differentiated. Using similar methods of observation, Wolff later provided evidence that the development of animals, particularly chickens, came from the growth of embryonic layers of cells, thereby invalidating the theory of preformation. Wolff's views, although logical and persuasive, were not well received and were not the intended death knell of preformationism, for one main reason: Wolff, like Aristotle before him, invoked a causal agent, the *vis essentialis*, or essential force, to explain how organisms develop from their initial unformed liquid states into a adult.

The Haller and Wolff debate over embryological development can be viewed as a controversy of philosophical difference. The 17th and 18th centuries coincided with the Scientific Revolution. This was a period of great turmoil and of dramatic intellectual revolutions, a period during which developing technology helped to generate innovative ideas and novel knowledge that ultimately supplanted medieval and ancient views, ushering in the fundamental concepts of modern science. Cartesian mechanistic materialism ascended into popularity, displacing the classical

worldviews presented in the works of Aristotle, Ptolemy, Galen, and the like. As naturalistic models rose to fame, preformationism presented itself as the only viable model of development. As Stephen Jay Gould (1941-2002) notes, preformationism represented the very best of the Newtonian mechanistic paradigm, even if it conflicted with the strong empirical evidence purveyed by Wolff and the like. To understand this, consider the crucial philosophical disparity underlying preformationism and epigenesis: either the parts of an organism are present at generation, or the fertilized egg is at first without form. But if the egg is formless, then some external force must be faithfully imposing design upon matter, consistently guiding formation from egg to adult, "If the egg were truly unorganized, homogeneous material without preformed parts, then how could it yield such wondrous complexity without a mysterious directing force?" (Gould 1992) But the Enlightenment period was not fond of mysterious, directing forces. As a consequence, preformationism prevailed.

IV. 19th and 20th century.

By the 19th century, microscopy tools and techniques had improved drastically. In the 1830s, achromatic microscopes were introduced, which allowed for more precise observation of embryonic development. This allowed for the development of cell theory by 1839.

In 1838, German botanist Matthias Jakob Schleiden (1804–1881) discovered that cells were the basic unit of the structural elements of plants. German physiologist Theodor Schwann (1810–1882) extended Schleiden's conclusion in 1839 to include animals, "the elementary parts of all tissues are formed of cells".

In the 1850s, Robert Remak (1815–1865), Rudolf Virchow (1821–1902), and Albert Kölliker (1817–1905) established that all cells come from preexisting cells, thus completing classical cell theory.

By late 19th century, preformationism had been largely discarded in the face of cell theory; the conflict between preformation and epigenesis was put aside. The mechanistic models from the preceding era were abandoned in light of the new understanding of embryonic development that cell theory had provided. Scientists

now understood that “they need not treat living organisms as machines, nor give up all hope of ever explaining the mechanisms that govern living beings.” (Magner 2002) A new form of preformationism, however, was on the horizon.

In 1866, Gregor Mendel (1822-1844) published *Experiments on Plant Hybridization* in the *Proceedings of the Natural History Society of Brunn*. In his paper, Mendel delivered evidence for the combinatorial rules of inherited traits. Using pea plants that he grew in the garden of his monastery; Mendel carefully pollinated the plants, saved seeds to plant separately, and analyzed the succeeding generations. He self-pollinated the pea plants until they bred pure, or until they consistently gave rise to similar characteristics generation after generation; to ensure purity, each line was bred for at least two years. He studied seven distinct and easily recognizable characters of the pea plants: the smoothness of the seeds (round vs. wrinkled), the color of the seed albumen (yellow or green), the color of the seed-coat (white or grey), the form of ripe pods (inflated or constricted), the color of unripe pods (yellow or green), the position of the flowers and the pods on the stems (axial or terminal), and the height of the plants (dwarf or tall). In one experiment, Mendel pollinated a purple-flowered plant with pollen from a white-flowered plant, and he observed that the resulting plants had purple flowers. In another experiment, Mendel cross-pollinated yellow-seeded pea plants with green-seeded pea plants. Every pea-seed in the first generation crop was yellow. In the second generation, however, some of the resulting seeds were green. Mendel counted the number of yellow to green peas and noted a 3:1 ratio. For each character studied, he noticed that the characteristics of the second-generation offspring consistently showed a 3:1 ratio. Further breeding showed that some traits were dominant and could mask the effects of other traits (like tall or yellow), while others were recessive (like dwarf or green). It also revealed that different traits don't blend: they are inherited independently of each other from parents as discrete units. Establishing himself as the father of modern genetics, Mendel deduced the following five points,

1. *Genes exist.* There are hereditary determinants: the inheritance of a trait is determined by *units* or *factors* that are passed from parent to offspring. These *units* or *factors* are now called genes.
2. *Genes exist in pairs.* Alternate phenotypes of a single character are determined by alleles (different forms of a single gene). In adult pea plants, each gene is present twice in each cell, constituting a gene pair; each gene pair can be of the same alleles or of different alleles of that gene.
3. *The law of segregation.* During gamete (egg and sperm) formation, each member of each gene pair segregates from the other member.
4. *Gametic content.* Each gamete carries only one member of each gene pair.
5. *The law of independent assortment.* The union of two gametes to form a zygote is random: alleles of different genes combine independently of one another during gamete formation.

At the beginning of the 20th century, Mendel's ideas were independently confirmed by three separate researchers (Carl Correns, Hugo de Vries, and Erich von Tschermak).

In 1902, Walter Sutton (1877–1916), American geneticist and physician, hypothesized that chromosomes are the physical basis of inheritance². He concluded his landmark paper, *On the morphology of the chromosome group in Brachystola magna*, with, "I may finally call attention to the probability that the association of paternal and maternal chromosomes in pairs and their subsequent separation during the reducing division... may constitute the physical basis of the Mendelian law of heredity." Sutton further developed his hypothesis in his 1903 paper, *The chromosomes in heredity*.

In 1910, while heading a fly lab (*Drosophila*), Thomas Hunt Morgan (1866-1945), American evolutionary biologist, geneticist, and embryologist, encountered a white-eyed mutant male among red-eyed wild types. First generation crosses between the mutant and the wild type produced all red-eyed progeny; second

² Theodor Heinrich Boveri (1862-1915) was a German biologist. He is also credited with independently demonstrating that chromosomes are the vectors of heredity.

generation crosses produced some white-eyed flies. This led Morgan in a series of papers, *Sex Limited Inheritance in Drosophila* (1910) and *Random segregation versus coupling in Mendelian inheritance* (1911), to conclude: 1) that genes reside on chromosomes; 2) that each gene resides on a particular chromosome; and 3) that some traits were sex-linked. This fully linked to chromosomes to Mendelian inheritance.

In 1933, Belgian biochemist Jean Brachet (1909-1988) demonstrated that there was an increase in DNA during the synthesis of nuclear material³. He also observed that there was a correlation between the amount of cytoplasmic RNA and the synthesis of proteins. His findings implied that DNA is found in chromosomes and that RNA is required in protein synthesis.

In 1941, two leading American geneticists, Edward Lawrie Tatum (1909-1975) and George Wells Beadle (1903-1989), made a crucial discovery: they showed that genes encode for proteins, and formulated the hypothesis known as the "one gene, one enzyme" hypothesis.

The 20th century was a time of great discovery for the burgeoning field of Genetics. In the 20th century, the following facts were learned: that there are genes, that genes are located on chromosomes, that genes on chromosomes are the units of inheritance, and that genes are responsible for encoding proteins. At a time when proteins were already thought to be the basic building blocks of life, the true causative forces in the cell; it's easy to see how a new form of preformationism came about: genes, which are the units of inheritance, are the precursors to proteins, which are the molecular basis of traits; genes, then, correlate with characters in organisms; in this way, in some sense, organisms are therefore *preformed* in the egg within their genetic composition. As Richard Lewontin (1929-present) accedes, "There is no essential difference, but only one of mechanical detail, between the view that the organism is already formed in the fertilized egg and the view that the complete blueprint of the organism and all the information necessary to specify it is

³ Torbjörn Caspersson (1910-1997) was a Swedish cytologist and geneticist. He made similar observations independent of Brachet.

contained there.” (2002) By the mid 20th century, this notion of preformationism prevailed.

IV. Present day.

The end of the 20th century up to present day brought about challenges to genetic preformationism.

Stem cell research revealed that genes do not determine cellular fate: positional information within the organism directs and decides differentiation. This was demonstrated, among other places, in 2004 *in vivo* by Chanvivattana, Y. et al.. Experimenting on the root epidermis of *Arabidopsis*, Chanvivattana et al. showed that hair-forming and non-hair-forming cells are under strict control of positional information; any changes in positional information would alter the fate of the cell.

In 2007, Craig Venter (1946-present), American biologist, published a breakthrough paper, *Genome transplantation in Bacteria: Changing One Species to Another*, in *Science* magazine. In it, he described the process of genome transplantation whereby a whole genome from one species is transformed into another species. He demonstrated genome transplantation using bacteria. He successfully isolated the *Mycoplasma mycoides* genome and transplanted it into *Mycoplasma capricolum* recipient cells. Some take Venter’s genomic transplantation as proof that genetic preformationism is valid: one species was transformed into another, and the only thing that changed was the genome itself; therefore, the genome is the driving force of the cell, the blueprint which contains all the information necessary for cellular reprogramming. Venter’s transplantation success, however, depended largely on using two closely related species of mycoplasma. If Venter had attempted his transplantation using two divergent species, it would have failed⁴.

⁴ Nuclear mitochondrial and nuclear-cytoplasmic incompatibility is an established result from numerous inter-species somatic cell nuclear transfer experiments. Inter-species somatic cell nuclear transfer embryos usually fail to fully develop due to incomplete reprogramming of donor cell. Nuclear-mitochondrial and nuclear-cytoplasmic incompatibility is a demonstrated reason for failure.

After Venter's initial study, he attempted to transplant an isolated *M. mycoides* genome from a yeast clone, but met failure. Venter and his group determined that the failure was a result of methylation (bacterial cells are known to use methylation to protect their genomes from degradation). In subsequent studies, methylase enzymes were isolated from *M. mycoides* and used to methylate the *M. mycoides* genome isolated from yeast. When the genome isolated from yeast was methylated in vitro, it successfully transplanted, proving that methylation is crucial not just for genome transplantation, but for viable cellular function.

Venter further determined that the DNA of the donor genome had to be supercoiled; if it weren't supercoiled, it would not transplant.

DNA methylation is a biochemical process that adds a methyl group to a nucleotide. It plays an important role in the development of an organism, and it is one of several mechanisms that a cell uses to alter gene expression. Methylation is known to be involved in numerous cellular processes, including embryonic development, genomic imprinting, X-chromosome inactivation, and preservation of chromosome stability (by controlling telomere length and telomere recombination). It always occurs within CpG islands (regions in which a cytosine nucleotide is located next to a guanine nucleotide). CpG islands are known to be methylated by a class of enzymes called methyltransferases. Methylation, by altering the native structure of the nucleotides, modifies gene expression by interfering with the cellular machinery which carries out transcription. CpG islands are also known to respond to environmental factors. In 2002, Cooney et al. demonstrated that dietary supplements could increase DNA methylation in mammals, and thus alter expression of the agouti gene, which impacted the fur color, weight, and propensity to develop cancer of subsequent offspring.

DNA supercoiling refers to the conformation that DNA may take, either to the over- or under-winding of a DNA strand. DNA conformation is known to facilitate biological functions, including DNA recombination, replication and transcription. Certain enzymes, such as topoisomerases, have been shown to be able to cause DNA to become either negatively or positively supercoiled. Additional studies have demonstrated that exposure to environmental stimuli can result in modifications to

DNA arrangement. Goldstein and Drlica showed, for example, that bacterial DNA supercoiling varies with temperature.

Therefore, 1) all the information necessary for an organism is not contained within the genome itself, and 2) the environment is not just a set of enabling conditions. Positional information, methylation, and supercoiling work in concert with the genome, encoding their own pieces of information. It might still be argued that the genome *predetermines* the organism to the extent that it limits the organism's range of expressible possibilities (as epigenomic modifications and positional information, while certainly informative and influential, are still always acting on or within the confines of the genomic sequence). This calls for a preformationism of degree, which seems most suited to the evidence at hand.⁵

DRAFT

⁵ It's interesting to note that, if we choose classical logic, then for both preformationism and epigenesis, either it obtains or it does not, and both cannot have the same truth value; but, if we go fuzzy, vague, multi-valued, or paraconsistent; then, not only need not preformationism exclude epigenesis (i.e., both may obtain); but, for both preformationism and epigenesis, neither it nor it not need obtain (i.e., there can be degrees of obtainment). In this way, our commitments to logic, by necessarily imposing a range of propositional values, limits our conceptual possibility and therefore delineates the very world that we live in. To accept the notion of an epigenesis of something preformed, then, might require the dismissal of classical logic.

References

- Adelmann, H. Marcello Malpighi and the Evolution of Embryology. Ithaca: Cornell University Press; 1966.
- Aristotle. On the Generation of Animals. Trans. Arthur Platt. eBooks @ Adelaide. 2007. <http://ebooks.adelaide.edu.au/a/aristotle/generation/>
- Aulie, RP. "Caspar Friedrich Wolff and his Theoria Generationis', 1759". Journal of the History of Medicine and Allied Sciences (1961) XVI (2): 124-144.
- Baxter, AL. "Edmund B. Wilson as a Preformationist: Some Reasons for His Acceptance of the Chromosome Theory". Journal of the History of Biology Vol. 9, No. 1, pp. 29-57 (1976)
- Bowler, P. "Preformation and Pre-Existence in the Seventeenth Century: A Brief Analysis". Journal of the History of Biology Vol. 4, No. 2, pp. 221-244 (1971)
- Buettner, K. "Jan Swammerdam", Embryo Project Encyclopedia. 2007. <http://hdl.handle.net/2286/embryo:124753>
- Campbell, K et al. "Nuclear-cytoplasmic incompatibility and inefficient development of pig-mouse cytoplasmic hybrid embryos." *Reproduction*. Aug;142(2):295-307 (2011)
- Chanvivattana, Y. et al. "Interaction of Polycomb-group proteins controlling flowering in Arabidopsis." *Development* 131, 5263–5276 (2004)
- Cobb, M. "Malpighi, Swammerdam and the colourful silkworm: replication and visual representation in early modern science." *Annals of Science* Volume: 59, Issue: 2, Pages: 111-117 (2002)
- Cooney, CA, Dave, AA, and Wolff, GL. "Maternal Methyl Supplements in Mice Affect Epigenetic Variation and DNA Methylation of Offspring". *Journal of Nutrition* 132 (8 Suppl): 2393S–2400S. (2002)
- Cosmo, A.DI. et al. "First results about topoisomerase activity in *astacus astacus* and *austropotamobius pallipes* as a biomarker for crayfish viability." *Bull. Fr. Pêche Piscic.* (2004) 372-373 : 401-408
- Costa, S. and Shaw, P. "Open minded' cells: how cells can change fate." *Trends in Cell Biology*, Volume 17, Issue 3, 101-106, 1 2007
- Crowa , E and Crowa , J. "100 Years Ago: Walter Sutton and the Chromosome Theory of Heredity". *Genetics*, Vol. 160, 1-4, January 2002

Egger, G., et al. "Epigenetics in human disease and prospects for epigenetic therapy." Nature 429, 457–463 (2004)

"Embryology - History Of Embryology As A Science".
<http://science.jrank.org/pages/2451/Embryology-History-embryology-science.html>

Gilbert, SF. Developmental Biology. 6th edition. Sunderland (MA): Sinauer Associates; 2000.

Gonzalo, S. et al. "DNA methyltransferases control telomere length and telomere recombination in mammalian cells." Nature Cell Biology 8, 416 - 424 (2006)

Gould, SJ. Ever since Darwin: reflections in natural history. New York: Norton; 1977.

Griffiths AJF, Miller JH, Suzuki DT, et al. An Introduction to Genetic Analysis. 7th edition. New York: W. H. Freeman; 2000.

Harvey, W. The works of William Harvey. Trans. Robert Willis. Philadelphia: University of Pennsylvania Press; 1989.

"History of Genetics - Gregor Johann Mendel, Rediscovery, The Chromosome Theory Of Heredity, Culture Of Heredity, Fine Structure Of The Gene".
<http://science.jrank.org/pages/7723/History-Genetics.html>

Jones, P. A., & Baylin, S. B. "The fundamental role of epigenetic events in cancer." Nature Reviews Genetics 3, 415–428 (2002)

Kandel, E. "Thomas Hunt Morgan at Columbia University".
<http://www.columbia.edu/cu/alumni/Magazine/Morgan/morgan.html>.

Lawrence , C.R., "Albrecht von Haller", Embryo Project Encyclopedia. 2008.
<http://hdl.handle.net/2286/embryo:125318>

Lawrence , C.R., "Hartsoeker's Homunculus Sketch from Essai de Dioptrique", Embryo Project Encyclopedia. 2008. <http://hdl.handle.net/2286/embryo:125308>

Lawrence , C.R., "Nicolaas Hartsoeker", Embryo Project Encyclopedia. 2008.
<http://hdl.handle.net/2286/embryo:125306>

Lawrence , C.R., "Preformationism in the Enlightenment", Embryo Project Encyclopedia. 2008. <http://hdl.handle.net/2286/embryo:125311>

Lewis, E. "Thomas Hunt Morgan and his legacy". Journal of Genetics, Volume 77, Numbers 2-3, 47-53 (199*)

Magner, L. *A History of the Life Sciences, Revised and Expanded*. New York: CRC Press; 2002.

Maienschein, J. "Epigenesis and Preformationism", *The Stanford Encyclopedia of Philosophy* (Fall 2008 Edition), Edward N. Zalta (ed.), <http://plato.stanford.edu/archives/fall2008/entries/epigenesis/>

Marshall, A. "The sorcerer of synthetic genomes." *Nature Biotechnology* 27, 1121 - 1124 (2009)

Mayr, E. *This is biology: the science of the living world*. Cambridge: Harvard University Press; 1997.

Mazzarello, M. A unifying concept: the history of cell theory. *Nature Cell Biology* 1, E13 - E15 (1999)

Mendel, G. *On the Generation of Animals*. Mendel Web. 1865. <http://www.mendelweb.org/Mendel.html>

Pinto-Correia, C. *The Ovary of Eve: Egg and Sperm and Preformation*. Chicago: University Of Chicago Press; 1998.

Plaisance, K. and Reydon, T. *Philosophy of Behavioral Biology*. New York: Springer; 2011.

Preus, A. "Galen's Criticism of Aristotle's Conception Theory". *Journal of the History of Biology* Vol. 10, No. 1, pp. 65-85 (1977)

Reill, PH. *Vitalizing nature in the Enlightenment*. California: University of California Press; 2009.

Rheinberger, H. "A short history of molecular biology." *eolssnet Volume: II*, Pages: 1-31 (1990)

Robertson, K. D. "DNA methylation and chromatin: Unraveling the tangled web." *Oncogene* 21, 5361-5379 (2002)

Roe, S. "The Development of Albrecht Von Haller's Views on Embryology". *Journal of the History of Biology* Vol. 8, No. 2 (Autumn, 1975), pp. 167-190

Roe, Shirley. *Matter, Life, and Generation: Eighteenth Century Embryology and the Haller-Wolff Debate*. Cambridge: Cambridge University Press; 1981.

Ruffenach, S. "Caspar Friedrich Wolff", *Embryo Project Encyclopedia*. 2009. <http://embryo.asu.edu/view/embryo:125309>

Simmons, D. "Epigenetic influence and disease". Nature Education 1(1) (2008)

Sutton, WS. "On the morphology of the chromosome group in *Brachystola magna*". Biol Bull. 4:24-39 (1902)

Venter, C. et al. "Genome Transplantation in Bacteria: Changing One Species to Another" Science 3 Vol. 317 no. 5838 pp. 632-638 (2007)

Windelspecht, M. Groundbreaking Scientific Experiments, Inventions, and Discoveries of the 17th Century. Connecticut: Greenwood; 2001.

DRAFT