CHANCE AND NECESSITY IN ARTHUR PEACOCKE'S SCIENTIFIC WORK

by Gayle E. Woloschak

Abstract. Arthur Peacocke was one of the most important scholars to contribute to the modern dialogue on science and religion, and for this he is remembered in the science-religion community. Many people, however, are unaware of his exceptional career as a biochemist prior to his decision to pursue a life working as a clergyman in the Church of England. His contributions to studies of deoxyribonucleic acid (DNA) structure, effects of radiation damage on DNA, and on the interactions of DNA and proteins are among the most important in the field at the time and have had a lasting scientific impact that is still felt today. Peacocke's arguments with Jacques Monod over stochastic (chance) and deterministic (necessity) processes driving evolution became important independently for both the science and the religion communities and appear to have contributed significantly to his decision to become involved in science-religion dialogue rather than continuing his work exclusively in the field of science. Nevertheless, although Peacocke took on an active church life and ceased his experimental work, he never left science but continued to read the scientific literature and published a scientific review on different approaches in defining DNA structure as recently as 2005.

Keywords: deterministic processes; DNA—deoxyribonucleic acid; evolution; RNA—ribonucleic acid; stochastic processes

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The goal of this essay is to demonstrate how Arthur Peacocke's early career in science shaped his later contributions to the science-religion dialogue, predominantly through his discussions about the relative importance of chance and necessity in biological systems in general and in evolution in particular.

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Peacocke was trained initially in chemistry and then biochemistry at Oxford University, and at that time he studied a variety of biochemical pathways that were important for biological systems including the kinetics of bacterial growth and theoretical studies of pathways that might be important in biological systems. He then took a position at Birmingham University where he rose to the rank of Senior Lecturer in Biophysical Chemistry. In 1959 he became a Lecturer in Biochemistry at St. Peter's College and later also at Mansfield College, both at Oxford. His research expertise in experimental and theoretical biochemical/biophysical systems provided him with a background that would be important in his later arguments about evolution.

Peacocke's Studies of DNA Structure

Peacocke's early scientific research focused on the effects of different treatments on nucleic acids: ribonucleic and deoxyribonucleic acids (RNA and DNA). He investigated effects of high temperature, different pH conditions, and salt concentrations on the structure of these molecules (Laland, Lee, et al. 1954; Peacocke 1954; Peacocke and Schachman 1954; Peacocke and Walker 1962a, b, c). However, he soon moved on to studies of effects of gamma-radiation on DNA structure. Around this time it had just been determined that DNA was the hereditary (genetic) material, and the fact that DNA is the molecular basis of heredity piqued Peacocke's interest in this molecule (Drysdale and Peacocke 1961), although exactly how DNA gave rise to proteins in the cell, how DNA was structured and ordered, and how it functioned as the key element of heredity were not understood until at least ten years later. Radiation had been discovered in 1895 by Wilhelm Conrad Roentgen, and by the late 1950s radiation was being used as a major approach for treatment of cancer. It also was known that radiation might be associated with the induction of growth malformations and cancer both from the studies of the Hiroshima and Nagasaki bomb survivors and from ongoing clinical studies. In hindsight, it seems reasonable to presume that this effect of ionizing radiation might be the consequence of damage to the hereditary material. At the time, however, this was a very bold assumption upon which to base one's research. Considering the very limited knowledge of the structure of DNA at that time, one cannot but be impressed with Peacocke's courage and vision at taking this research direction. Results of these studies were published in journals that are to this day considered to be among the most prestigious. From that time until the end of his research career Peacocke's manuscripts continued to appear regularly in such high-impact publications as he continued to investigate DNA always from new and exciting angles.

Peacocke's lab undertook studies of the effects of radiation directly on the DNA itself (Cox, Overend, et al. 1955; 1958; Peacocke and Preston

1961) rather than examining the effects of radiation damage on DNA within cells, which would have been very difficult if not impossible with the technology of the time. Moreover, studies with whole cells would have been insufficiently controlled to establish that the damage to DNA was directly caused by radiation. These studies by necessity examined very high doses of radiation, because smaller doses would not have created an amount of damage that would have been detectable with the existing equipment.

Looking back, we can see that this was the first encounter that Peacocke had with random damage to DNA as the hereditary material caused by influences from the environment. This was perhaps the first time anybody could have perceived that the hereditary material of living cells absorbs random damage mediated by the environment. This entirely new concept had far-reaching implications for the understanding of biological evolution, and very few scientists at that time understood it. Such thoughts must have started to form in Peacocke's mind and to lead him to ponder the interaction of living matter with the nonliving world and the communion of the whole of creation. At the root of his subsequent deep thoughts on the nature of the universe and laws of creation lay these first experiments. For someone else, these could have been just data, but for Peacocke they germinated into something more metaphysical.

The results of Peacocke's studies were among the first to demonstrate that ionizing radiations such as gamma-rays induce single- and double-strand breaks in the DNA—that is, breaks in either one or both strands of the DNA double helix. These results are still accurate, and it has since been shown in cells that the DNA double-strand breaks are the most important lesion when considering cell killing induced following radiation exposure. This is the mechanistic basis for the use of radiation for cancer treatment, but it also is the basis for the harmful side-effects of radiation exposure. It also has been shown in cells that double-strand breaks can be repaired in an error-free and error-prone fashion and that error-prone repair often leads to mutations associated with cancer induction. Therefore, Peacocke's experiments were the first step in understanding how radiation can be used both as a cure for and a cause of cancer. Peacocke's early work set the stage for continued analyses of mechanisms of radiation-mediated injury that have led to the modern complex fractionated regimens that are used today so successfully for treatment of cancer. The work led to understanding the risks to DNA of radiation exposure, resulting in the concept of normal tissue toxicity, which is the treatment-limiting factor in treatment of cancer with radiation; it is easy to kill the cancer with radiation but much more difficult to not destroy the surrounding normal tissue, thereby killing the patient. Studies of radiation-induced DNA damage like those Peacocke and his colleagues carried out were precursors of the complex tissue-specific studies that are ongoing today.

Another very important set of studies published by Peacocke's lab examined proteins in bone that bound to radioactive elements such as Yttrium and Thorium (Williams and Peacocke 1965; Peacocke and Williams 1966; Williams and Peacocke 1967). This work was an important precursor to the present understanding of how particular radioactive materials that home to bone tissue induced bone cancers (osteosarcomas) in people who had been exposed to these materials. It is likely that these early studies of random DNA damage induced by radiation, either from internal emitters or from external beam irradiation, helped to shape Peacocke's later ideas about stochastic (random) versus deterministic events in creative processes in nature. Peacocke's later books that are often quoted in the science-religion community frequently used the example of radioactive decay of radionuclides as a stochastic process that is by nature unpredictable and yet represents an important force in nature (Peacocke 1986; 1993). These early studies led Peacocke to a clear understanding not only of stochastic processes in nature but also of how they affected biological systems.

Peacocke's move back to Oxford, where he taught and did research at two different colleges (St. Peter's and Mansfield), was accompanied by adding several new directions to his work. He continued to study the structure of "naked" DNA but also started to work on DNA isolated from cells still wrapped in proteins that normally accompany it inside cells. Among the studies on "naked" DNA was the work that resulted in a long series of highly noted publications on the binding of various dyes to RNA and DNA, and the effects of such molecules on the structure, and in later works the function, of nucleic acids (Drummond, Simpson, et al. 1965; Blake and Peacocke 1966; Drummond, Pritchard, et al. 1966; Nicholson and Peacocke 1966; Pritchard, Blake, et al. 1966; Blake and Peacocke 1967a, b; Blake and Peacocke 1968; Lloyd, Prutton, et al. 1968; Peacocke 1968; 1969). Most of the dyes that Peacocke studied fit into the category known as DNA intercalating agents; such molecules bind specifically to DNA by fitting into the inner structure of the DNA double helix and find their way to fit into a space between DNA bases. They "intercalate" or squeeze their way between two bases that are next to each other on the DNA helix. When this occurs throughout the entire DNA strand, it can be detected because the dye accumulates in the DNA in high quantity. These dyes were interesting to Peacocke for a number of reasons. Their effect on DNA is very similar to the effect of radiation, because these dyes are known to induce mutations in the DNA, so this clearly was a continuation of his previous interest in DNA damage. More important, these dyes and how they bind to DNA gave important clues about the actual structure-function relationship of the DNA molecule.

As an aside, it is interesting to note that the very dyes that were used in Peacocke's pioneering studies with DNA structure are still used in most molecular biology laboratories today as dyes to detect DNA and RNA when they have been separated into different size fragments using a technique called gel electrophoresis. As Peacocke had noted, they are powerful mutagenic chemicals and must be handled with care in any lab situation.

Peacocke's work with DNA intercalating agents was being done at the time when Watson and Crick had just defined the crystal structure of the DNA molecule demonstrating that it was double-stranded and that the bases were located in the center in a protected region of the molecule. Nevertheless, very little about the final structure of DNA inside cells was known—whether it existed in a cell in double-stranded form only or whether triple helices were also found, whether it was branched or forked or just a single helix, whether once disassociated (denatured) DNA strands would reassociate (renature), and other similar questions. Peacocke's studies with intercalating dyes set the stage for his own discoveries in this area. Furthermore, Peacocke investigated the denaturation and renaturation of "naked" DNA and RNA (Cox, Jones, et al. 1956; Lifson and Peacocke 1956; Thrower and Peacocke 1966; 1968); he also extended these studies into the area of deoxyribonucleoproteins—combinations of DNA and protein isolated from cells as complex molecular assemblies and closer to the natural state of DNA in living cells than the pure DNA he studied in his prior work. Again, he investigated denaturation and renaturation under different conditions (Peacocke 1960; Bayley, Preston, et al. 1962; Murray and Peacocke 1962; Giannoni and Peacocke 1963; Giannoni, Peacocke, et al. 1963; Lee, Walker, et al. 1963; Lloyd and Peacocke 1965; Leveson and Peacocke 1966; 1967; Diggle and Peacocke 1968; 1971; Haydon and Peacocke 1968; Murray, Bradbury, et al. 1970; Diggle, McVittie, et al. 1975), and widened the spectra of possible causes of lesions resulting from exposure to gamma-ray irradiation (Peacocke and Preston 1961; Lloyd and Peacocke 1963; 1966; 1968; Lloyd, Nicholson, et al. 1967) to ultrasound. Peacocke and his colleagues examined how ultrasound degrades DNA and other biomolecules (Pritchard, Hughes, et al. 1966; Peacocke and Pritchard 1968a, b). The result was very similar to that done with radiation except that ultrasound was much more powerful at inducing breakage of DNA strands. Like radiation, the DNA breaks appeared to be induced in a random fashion in the solution, and it was proposed that a similar random cleavage of DNA would occur if cells were exposed to ultrasound. The approach of breaking DNA into small fragments with ultrasound is used in many molecular biology laboratories today as a method for creating small random fragments of DNA from very large DNA molecules (such as DNA from mammalian cells).

While the studies with the intercalating dyes were going on in his laboratory, Peacocke's group also was using the technique known as circular dichroism to attempt to answer the same questions about DNA structure that were tantalizing the biophysical chemistry community at the time (Blake and Peacocke 1965a, b; Dalgleish, Fujita, et al. 1969; Dalgleish and

Peacocke 1971a, b; Dalgleish, Feil, et al. 1972; Dalgleish, Peacocke, et al. 1972). Circular dichroism is a type of spectroscopy technique that measures differences in the absorption of left-handed compared to right-handed polarized light that are caused by differences in structural asymmetries. This technique is used today to examine how proteins fold, how stable a protein is when heated, and other similar questions. Because DNA has a regular structure to it, circular dichroism can be used to determine whether materials, such as for example intercalating dyes, disrupt the structure and how the actual disruption is configured. Peacocke's group combined their skills with intercalating dyes with the techniques applied in circular dichroism and used this to attempt to tease out answers to questions about the nature of the DNA double-strand helix.

Together, Peacocke and his colleagues demonstrated that the structure of DNA is a double-stranded helix that is not branched or forked. These studies drew a great deal of attention from Watson and Crick and many others in the DNA structural biology–biophysical community. Peacocke's work was highly cited in the literature, and he was invited to speak at many prominent conferences to present his work. He published in the most important peer-reviewed journals of his day and became well known for this work, and his findings have proven to be seminal in the field and accurate to this day. Most of modern molecular biology is based on this knowledge about the structure of DNA as defined by Watson and Crick and refined by Peacocke and his colleagues. Peacocke's publications in the field of molecular biology and DNA structure rank among the most important of the past century.

OTHER STUDIES

This essay is not intended to be a complete review of Peacocke's scientific work but rather is an attempt to present the most important studies, particularly those that would later prove to be the most influential for his work in the science-religion dialogue.

For example, his experiments with various proteins (Williams and Peacocke 1965; Foord, Jakeman, et al. 1970; Lloyd and Peacocke 1970; Ashton and Peacocke 1971; Oliver, Pike, et al. 1971; Cleave, Kent, et al. 1972; Fell, Liddle, et al. 1974; McVittie, Esnouf, et al. 1977) that were of biological significance provided important contributions to the field. Of particular interest were studies on some proteins that bound to nucleic acids (Diggle and Peacocke 1968; 1971; Haydon and Peacocke 1968; Diggle, McVittie, et al. 1975). Now it is known that hundreds, perhaps thousands, of proteins in the body bind to nucleic acids. In Peacocke's day it was known that specific proteins called histones bound to DNA and that many proteins involved in the synthesis of proteins composed the ribosome, which was a large complex of RNA and proteins. Peacocke's studies used the methods he had developed in his early studies to examine protein assembly onto DNA and RNA. His published papers toward the end of his term at Oxford and following his ordination as a pastor in the Church of England focused on these protein-nucleic acid interactions, and it is clear that this would have been the direction of his continued research had he not stepped out of the realm of the active scientific research laboratory and into the science-religion sphere.

Chance and Necessity in Peacocke

In 1977 Peacocke perhaps best articulated the question of chance and necessity in biological systems in a short review paper he published in *Trends in Biological Sciences* (Peacocke 1977). The article was a tribute to and a continued argument with Jacques Monod, who had expressed the view that all of life was based on a series of chance events. Based on this article and later books by Peacocke, it is likely that his change in focus from active research scientist to advocate for the development of a synergy between science and religion was largely shaped by Peacocke's discussions (and arguments) with Monod as well as Peacocke's concern for potential misunderstandings that could develop from an understanding of a natural world driven exclusively by chance (or stochastic processes).

As was mentioned earlier, at the beginning of Peacocke's career little was known about DNA beyond its structure. The way in which DNA fulfilled its role as the hereditary material became understood only in the 1960s. It was found that DNA codes for all cellular proteins through a process where triplets of successive bases in DNA code a single amino acid of the protein or, in three cases, signal a stop for protein production. Because there are sixty-four combinations of four nucleotides (DNA is made of only four nucleotides) and there are only twenty amino acids, it became obvious that changes in DNA (mutations) can often be "silent" and produce no change in the protein.

To a large group of scientists, best represented by Monod, this meant that changes in DNA not only are random by their origin but are in most cases neutral with respect to the destiny of the organism. Out of this possibility that mutations may be neutral came a view that both creation and (for the most part) the effect of mutations are random processes and that therefore blind chance is the most important driving force of evolution. In the early 1970s this became a popular and common view of evolution.

According to most scientists today, this idea of evolution is erroneous because it is incomplete. Although mutations do occur in a random fashion, their outcome on the destiny of the organism can range from unnoticeable (neutral) in some cases to lethal in other cases; however, this effect can be predicted, and it is deterministic for the organism. (A predicted lack of effect is no less deterministic than an effect that is lethal.) Of course, these effects are additionally molded by the environment that the organism lives in, creating an opportunity for natural selection to play its role. Therefore, while stochastic forces can be associated with the induction of mutations, their effects on the organism that expresses these mutations are deterministic (large or insignificant, the effect of the mutation is predictable). This fact is undisputed today, but during the 1970s an overwhelming emphasis was made on "neutral" mutations, the randomness of their origin, and a view that evolution largely amounts to blind chance.

What happened was that many in the scientific community of that time became overwhelmed with those recent realizations about nature and mechanistic action of mutations. We can liken this period in evolutionary biology to many situations in other sciences when a new discovery illuminates old knowledge with a new understanding. Almost always at such times balanced views are temporarily lost, and everything old is explained anew in the attempt to employ only the newly discovered idea. It takes great presence of mind and courage to stand up to such a tide of opinions and voice the need to preserve a balanced view—and even to recognize such a need—and it is of great credit to Peacocke that he was such a lone voice at this time. His work on DNA damage by ultrasound, gamma irradiation, and intercalating dyes coupled with the knowledge that these treatments have profound influence on the fate of organisms exposed to them (developmental malformations, cancer, and so on) prepared Peacocke to have a clearer view of mutations than his contemporaries had. He was able to see the deterministic nature of mutations in the future life of the organisms that sustained them, while others focused wholly on the fact that many mutations do not have to have any effect on the fate of the organism. Many of Peacocke's contemporaries failed to see that the lack of effect of mutations in such cases is also deterministic.

In his arguments and discussions, Peacocke upheld the correct view on mutations and a correct view on evolution. It is very likely that this fight to uphold a scientific truth in the world of science pushed Peacocke to try to connect scientific truth with religious truth and enrich both fields by emphasizing the need for an honest and balanced science-religion dialogue. He perceived that the religious arena would be made stronger the better it was able to absorb and embrace scientific truth, while honesty in science takes courage of individual scientists that could be empowered by their religious beliefs. It is possible that he perceived that his own religious attitudes helped him in his battles for truth in science, and wished to help others to reach the same place that he himself had reached.

In discussions with scientists believing in evolution driven by neutral mutations and in his books for the general public, Peacocke argued that nature and life processes involve a combination of chance occurrences and processes that are mediated by necessity (or are deterministic in nature). He argued that there are many random processes in nature, such as the decay of a radioactive material (as described above) or mutation induction (thus agreeing with Monod on this point). At the same time, nature also is full of processes driven by necessity—that is, they are predictable and deterministic in nature. For example, although there are stochastic and deterministic processes that occur following exposure of cells and tissues to radiation, cancer, which is mediated by mutation induction in cells, is a random process, not predictable in advance, that can occur at any dose (including background doses that we receive from our environment) and often evades predictive capabilities of people who make risk estimates of radiation effects on human populations. In common terminology, mutation induction following radiation exposure would be considered to be a chance occurrence. However, some radiation effects are also deterministic in nature: late tissue toxicities (occurring months to years after radiation exposure) and acute radiation syndrome, which are non-cancer complications of radiation exposure, have dose-limit thresholds, are predictable, and can easily be regulated by establishing dose limits. An example of this type of deterministic exposure is cataract induction, which scientists know will not occur in individuals unless they have an eye exposure above a certain threshold dose. By Peacocke's definition, these deterministic effects would be those of necessity—if the dose is high enough, then of necessity the end result will occur.

Peacocke applied these concepts of chance and necessity to his arguments with Monod on evolution as well. He agreed with Monod that evolution is driven by random events such as mutation; when in time and where in the genome a particular mutation would occur was random, not predictable, and occurred by chance. Peacocke stressed, however, in contrast to Monod, that other processes in evolution were driven by necessity. He used as his example natural selection, which by definition selects for those processes (mutations) that allow for the population best suited for certain conditions (niche) to survive. By necessity, a change in climate to a colder environment will select for certain survival features that are predictable: thicker fur over thinner hair, longer sleep cycle over shorter sleep cycle, slower metabolism over faster metabolism, and so on. Because these features can be predicted from a set of known parameters, they are deterministic, or driven by necessity. Peacocke successfully argued against "blind chance" as the only driver of evolution, and today the view put forth by Peacocke is generally accepted by the evolutionary biology community. Peacocke was not the first to articulate it, but he was among the first to successfully and publicly argue the point not only in the scientific community but in the broad public forum as well.

Based on discussion with Monod and others who supported the concept that blind chance was the main driver of evolution, Peacocke came to view this issue as one of major concern for the religious community. It is very likely that this issue, which became the focus of so much of his later writing in the science-religion arena, was among the major influences in Peacocke's decision to follow a religious calling and to eventually become an important leader in the science-religion dialogue. Peacocke's background in DNA structure-function studies and his experience with protein interactions provided him with a good preparation for consideration of evolutionary biology and facilitated his clear statements about the role of chance and necessity in evolution. He articulated this not only in a scientifically sound way but also in language that was accessible to nonscientists.

Peacocke never stopped being a scientist, even when he took on other mantles in his life. He continued to keep up with scientific discoveries in his field and even published a historical review of the area in a *Trends in Biochemical Sciences* paper in 2005 (Peacocke 2005). The fact that he continued to keep abreast of the latest science and at the same time pursued his interests in science and religion kept his writings fresh and accurate. Peacocke firmly established that any science-religion dialogue must include scientists and must be not only exact from a religious view but also have scientific accuracy and timeliness.

Peacocke made a tremendous mark on the science-religion community and left a legacy for those who continue in this dialogue. He foresaw that science could have a negative impact on the religious community if some attempt was not made to provide a bridge between the two communities, and he did this in several very important ways. As an outstanding world-renowned scientist, he was well aware of the scientific approach to problems and the limitations of the questions that science could address. He was an advocate for a religion that was not hampered by false thinking and at the same time was not afraid of tackling scientific issues. He did this through the evolution debate, which was a central focus of his time and continues to be a major matter for concern even now. Peacocke's clear religious thinking, his fearlessness in tackling difficult issues, and his keen scientific intellect all made him a gift to the science-religion community who will leave a mark for decades to come.

NOTE

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