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Perpetuated Negotiation in the 'Directed Mutation' Debate — Towards an Anatomy of Protracted Scientific Controversy

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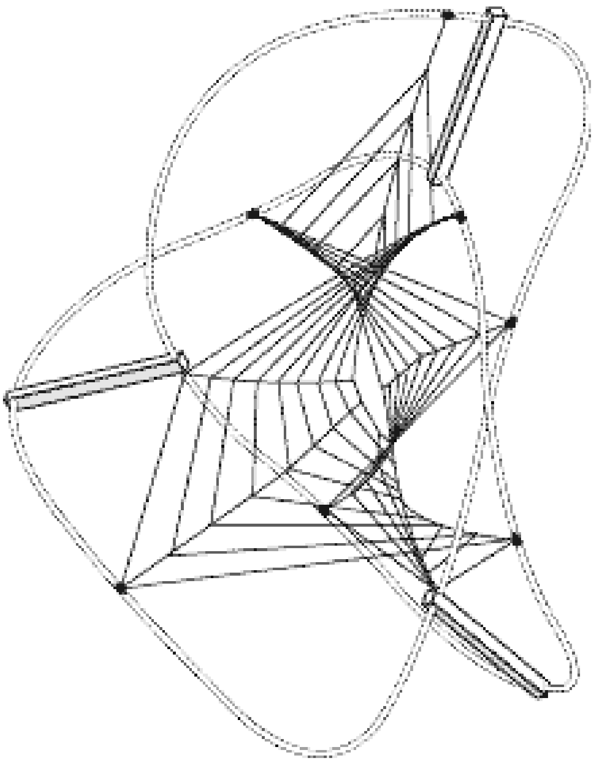

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Perpetuated Negotiation in the 'Directed Mutation' Debate — Towards an Anatomy of Protracted Scientific Controversy*

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Perpetuated negotiation in the 'directed mutation' debate: towards an anatomy of protracted scientific controversy

In this paper I describe the 'directed mutation' debate, a scientific controversy representing the most recent significant attempt to resurrect Lamarckian evolutionary theory. The debate began in the 1980s and is ongoing. The history of the debate is explored in order to offer an insight into the structure and dynamics of protracted scientific controversy. Much of the material here is specific to the directed mutation debate and its late twentieth century context. However, some of the discussion might also relate more generally to scientific controversy.

In my research I use the details of this case study controversy as a way of highlighting possible trends in the structure and dynamics of protracted scientific conflicts. I am not trying to provide generalised statements about controversy from that one case. Rather, I use a detailed and developed narrative of every aspect of this debate to provide pointers as to what might be interesting or revealing controversy dynamics or activities to examine in analogous cases. This method allows the case study to be used as a starting point for the development of some possible categories or themes that might be used more generally to analyse the structure of other protracted scientific controversies.

This paper has three key aims. Firstly, to provide a brief account of the directed mutation debate, highlighting some key participants and events in the controversy. Secondly, to explore the structure and dynamics of the directed mutation debate as a means of illuminating elements that might contribute categories or themes to a 'general anatomy of protracted controversy'. Thirdly, to consider the general adequacy and appropriateness of existing models of scientific conflict in light of the details of this case and the themes and categories that it suggests.

i) Introducing 'directed mutation'

This conflict has been called the 'directed mutation' debate, the 'adaptive mutation' debate and the 'Cairnsian mutation' debate.[1] In this paper I am going to refer to it as the directed mutation debate, since that name gives the best indication of the actual process being contested at the heart of this controversy. Essentially, the directed mutation controversy can be summarised as a conflict between staunch defenders of Darwinian evolutionary theory and a growing contingent of Lamarckian enthusiasts. The major action of this controversy was

[1] For a review of terminology see: Foster, P. L. (1993) Adaptive mutation: the uses of adversity. *Annual Review of Microbiology.* 47: 467-504.

in the last fifteen to twenty years of the twentieth century, although as I describe below the debate is still thriving.

The controversy exists at two principle levels; or rather it exists in the form of two constitutive sub-debates. Firstly, it arose from the observation and publication of an anomaly discovered during microbial molecular genetics research. Specific things were put at stake due to the emergence of this anomalous finding. These included, the stability of the theoretical frameworks and generalised rules of microbial molecular genetics. At this level the debate engages a particular, specialist and comparatively small community and involves all the data, language and practice that supports that sub-discipline. That community is not so much concerned with the implications of the anomaly for evolutionary theory as a whole, but rather is anxious to assimilate this anomaly into the existing theoretical frameworks of their specific specialized subject. The primary concern of that community is the integrity of their specific sub-discipline. Therefore, maintaining that integrity means either assimilating the anomaly or rejecting it, but it need not imply any greater or far-reaching theoretical debate.

The second level of the controversy, and the one that I am most interested in, arose once this bacterial genetics anomaly was used as a tool for perhaps the most significant and protracted attempt to resurrect Lamarckian theory to have been mounted since modern Darwinian theory was established. That aspect of the debate involves conflict between the broad programmes of established and mainstream Darwinian theory versus outmoded and discredited Lamarckian theory.

The community or communities that became engaged as a result of the Darwinism versus Lamarckism aspect of the debate were diverse and composed of many more individuals than were involved in the microbial genetics debate. Other kinds of language, data and modes of practice became involved. At this level there was much more at stake than the very specific challenges of the anomaly in the context of the small disciplinary area from which it had emerged. It is this level of the debate which has chiefly determined the scale, perpetuation, and what one might be tempted to call the 'severity' of this controversy. The combination of this broader debate on alternative evolutionary theories with the specific debate on microbial genetics determined the character of the controversy. I shall return to the details of this conflict below.

ii) Lamarckism Vs. Darwinism

It is useful at this point to establish briefly the significant distinctions between Lamarckian and Darwinian evolutionary theories. Recognition of these differences is an essential prerequisite for understanding why these two theoretical frameworks must necessarily always be in conflict, and cannot possibly co-exist. The incompatibility of the two theories was apparent throughout the twentieth century; Darwinism became established as the principle theoretical

tool for evolutionary work and Lamarckism was more or less abandoned as a valid alternative. Where did the two theories come from and what has their interaction been? For the sake of chronology I will begin with a consideration of the origins of Lamarckism.

Lamarckian evolutionary theory was proposed by French naturalist Jean-Baptiste Lamarck in his 1809 book *Philosophie Zoologique*.[2] The overwhelming majority of people at this time considered species as fixed entities, believing that organisms existed unchanged in the same form in which they had been created. Lamarck, however, promoted a concept of species change or 'transformism'. He argued that over time species change and, in fact, could even change into new species. The means by which Lamarck envisaged that this might happen were complex; importantly, much more complex than they are often given credit for. Lamarck considered that the process of species transformism occurred by two co-acting mechanisms. The principal mechanism was an 'internal force'. Lamarck believed that this was some kind of unknown drive within the organism that caused it to produce offspring slightly different to itself. Lamarck suggested that these differences might accumulate over many generations, perhaps enough to form a new species. Lamarck's second mechanism, interestingly the one for which he is now remembered, was the inheritance of 'acquired characters'. Lamarck suggested that the modifications that an organism acquired during its own lifetime might be inherited by its offspring. He thought that the parent generation acquired these changes by a process of 'striving' and he described animals as 'wishing' to change themselves.[3]

Descriptions of Lamarckian theory produced during the second half of the twentieth century frequently illustrate these processes with the familiar example of the evolution of the giraffe's long neck. In these accounts of Lamarckism the giraffe wilfully stretches its neck generation after generation and passes this acquired trait on to offspring with progressively lengthening necks. That portrayal is of course a gross simplification of Lamarckian theory, although it is a significant example of how certain characterisations of scientific theories can be perpetuated and deployed through education and popular understanding.[4] The significance of this portrayal, and the associated popular understanding of Lamarckism, is discussed below.

Lamarck's theory was influential and enjoyed periods of support throughout the nineteenth and early twentieth centuries, both at a popular and a

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[2] Lamarck, J.B. (1809) *Philosophie Zoologique* trans.H. Elliot (1984) Chicago University Press, Chicago.

[3] For discussion of Lamarck's theory of transformism see: Burkhardt (Jr.), R. W. (1984) The zoological philosophy of J.B. Lamarck. In: Lamarck, J.B. (1809) *Zoological Philosophy* trans. Hugh Elliot (1984) The University of Chicago Press, Chicago.

[4] For further discussion of the 'imaginary' or 'bogus' Lamarck that dominates twentieth century treatments of Lamarckism see: Ghiselin, M. (1994) The Imaginary Lamarck: A look at bogus 'history' in schoolbooks. *The Textbook Letter*, Vol.5, No.4 (view online at: www.textbookleague.org/54marck.htm; Roizen, R. (1971) *The argument of philosophy zoologique.* View online at: www.roizen.com/ron/Lamarck.htm.

professional level.[5] During the early to mid-twentieth century a version of Lamarckism arose which combined the biological principles of Lamarck's theory with the new information on genetics and heredity, and with particular contemporary political and sociological ideologies. That version of the theory became known as Neo-Lamarckism, and is perhaps most widely recognised through association with its prime advocates and architects, for example Paul Kammerer and Tofim Lysenko. Most recently, during the late twentieth century, a new incarnation of Lamarckian theory arose. That version of the theory incorporated advances in molecular biology and genetics and reasserted Lamarckian theory in line with the terms of that 'modern' work. It also lacked the explicit political or ideological elements of Neo-Lamarckism. This version of Lamarckian theory borne out of that revision is termed New Lamarckism.[6] As discussed below, the history of Lamarckism has been characterised by radical fluctuations in the perceptions and support of the theory.

The origins of Darwinian theory, or rather Neo-Darwinian theory as its present incarnation is termed, are more familiar. Several tenets of the theory were memorably outlined in 1859 in Charles Darwin's *The Origin of Species*.[7] Darwin also believed in transformism, which he considered was made possible by the force of natural selection. Darwin did not believe that organisms engaged in a process of striving to achieve better adaptation. Instead, he advocated a view of nature as a culling force; weeding out those organisms that happened to be least adapted, and allowing those that chanced to do better to survive and reproduce. Darwin's original theory enjoyed wide popularity, except perhaps in the period around 1900.[8] During the 1930s and 1940s Darwin's theory was reformulated and combined with genetics and population studies to produce the 'modern synthesis'. The form of the theory that arose from this period was called Neo-Darwinism. Today, this modernised version of the theory represents the primary theoretical tool for evolutionary work.

One of the most fundamental differences between Neo-Darwinism and New Lamarckism relates to the way that each of the theories represents the organism's interaction with the environment. In Neo-Darwinian theory the

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[5] Bowler, P. (1992) *Evolution: The history of an idea*. University of California Press, Berkeley.
[6] See Milner, R. (1990) *The encyclopedia of evolution.* Facts on File Inc. for details of the distinction between 'Lamarckism', 'Neo-Lamarckism' and 'New Lamarckism'.
[7] Darwin, C. (1859) Ed. Burrows, J. W. (1982) Penguin Books, London.
[8] Historian Peter Bowler has termed this period the 'eclipse of Darwinism'. That term reflects the decline in popularity of Darwinism that occurred from the late nineteenth century into the early years of the twentieth century. In that period the theory fell out of favour since it lacked a detailed or demonstrable mechanism for the inheritance of the beneficial types that natural selection favoured. Particulate inheritance based on the gene theory was not yet understood, and it was assumed that natural selection would be undermined because inheritance processes would blend the parent types together and dilute the successful forms. Not until after the 're-discovery' of Mendelian genetics in 1900 did it become possible to envisage how natural selection might be able to drive evolution at the kind of rate necessary to make it functional. See Bowler, P. (1983) *The eclipse of Darwinism: anti-Darwinian evolution theories in the decades around 1900.* John Hopkins University Press, Baltimore; Bowler, P. (1992) *Evolution: The history of an idea.* University of California Press, Berkeley.

organism's genome is a closed system that is placed under environmental pressures. The environment determines the organism's chances of survival, but it does not determine its genetic makeup. Neo-Darwinian theory states that the organism's genetic endowment is determined by the random mutation of its genome at the time of fertilization. During the lifetime of the organism the genetic material cannot be influenced by the quality of the environment; no character that the organism acquires during its lifetime can be passed on to its offspring. Effectively, the state in which the organism is born is the package that its own offspring will be presented with, varying only through the random mutations that will occur in that offspring's genome as it is fertilized.

In Lamarckian theory the organism is able to alter its character throughout its lifetime to improve its chance of survival. According to this theory, any changes in character that have helped the organism enhance its survival can then also be passed to the offspring. That is to say, acquired characters can be inherited. In Lamarckian theory, the quality of the environment determines changes in organisms and thereby in the offspring of those organisms. Implicit in this degree of interaction between the organism and the environment is the idea that the environment must be in contact with the internal machinery of the organism; it must be able to trigger changes and those changes must then be heritable.

Darwinian theory is not burdened by a dependency on any such complex and unknown systems of environment/genome interaction. In Darwinian theory the only influence of the environment on the genome is through the culling effect of natural selection on the less well adapted genetic packages. The implied molecular level complexity in Lamarckism proved impossible to demonstrate over the years and the theory declined in popularity as no mechanism could be found for the inheritance of acquired characters. In fact, during the nineteenth and twentieth centuries, several workers even produced direct evidence that the vital link between the organism and the environment did not exist. Three key instances of such 'disproof' of the Lamarckian mechanism emerged from the late nineteenth century onwards.

1. In the late nineteenth century German biologist August Weismann published a grand and ambitious collection of his works entitled *Essays on Heredity*.[9] In Volume 1 of that collection he described experiments that he had undertaken from 1887-1888 that he claimed demonstrated that modifications to an organism's character during its lifetime could not be passed to subsequent generations by heredity.[10] Weismann's key experimental proof of this impediment to Lamarckian inheritance was based on the amputation of mice's tails over a period of five generations. He concluded from the fact this mutilated state did not

[9] Weismann, A. (1889) *Essays Upon Heredity, Volumes 1 & 2*. Oxford University Clarendon Press, Oxford. View online at: www.esp.org

[10] Weismann, A. (1889) The supposed transmission of mutilations. In *Essays Upon Heredity Vol. 1.* Oxford University Clarendon Press, Oxford.

become heritable during the 18 month study, that the material of heredity was immune to changes in an adult organism. Weismann proposed a generalized rule that stated that the 'germ cells' were inviolate from the 'soma'. This effectively meant that the environment could not get in contact with the material of heredity.

2. Further physical barriers between the environment and the hereditary material were described in the years following Weismann's assertion of the germ/soma divide. In the 1930's and 1940's it was discovered that the material of heredity was confined to the cell nucleus, and that it was composed of DNA.[11] In 1958 Francis Crick extended the description of the interaction between the environment and the genome.[12] He stated that the production of proteins from DNA was *unidirectional* taking only the path DNA $\rightarrow$ RNA $\rightarrow$ Protein. On account of this there was no way that the environment could influence the genetic material. Later, Crick went as far as to term this uni-directionality the 'central dogma of molecular biology'.[13]

3. Meanwhile, on the specific issue of Lamarckian evolution in bacteria (the same organism system that the directed mutation workers later focussed on) a similarly definitive experimental proof had been offered. In 1943 Luria and Delbruck published results of bacterial experiments showing that the kinds of mutations that bacteria underwent bore no relation to the pressures exerted by their environment.[14] That is to say, the bacteria were not 'striving' or 'wishing' to become better suited to their environment, but rather they were at the mercy of random mutational processes for their achievement of adaptive change. I will return to Luria and Delbruck below.

To summarise at this point: ever since the mid nineteenth century the Lamarckian and Darwinian evolutionary theories have co-existed, they have each enjoyed periods of widespread support, and each theory has at some stage lost support in favour of the other. In their modern incarnations Lamarckian and Darwinian theories are intrinsically different and unavoidably incompatible. The history of their interaction and changing fortunes has been protracted. Since the mid-twentieth century Neo-Darwinism has been the preferred theory of the scientific community. Although some small-scale twentieth century revivals of Lamarckism (as Neo-Lamarckism and New Lamarckism) were attempted, after 1950 the theory's status in relation to Neo-Darwinism entered dramatic decline. In the second half of the twentieth century Lamarckism was no longer viewed as a viable alternative theoretical framework for evolutionary work. Key elements of

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[11] See Hammerling, J. (1953) Nucleo-cytoplasmic relationships in the development of *Acetabularia*. *International Review of Cytology*, 2: 475-498; Avery, O. T., MacLeod, C.M. and McCarty, M. (1944) Studies on the chemical nature of the substance inducing transformation of pneumococcal types. *Journal of Experimental Medicine,* 79:137-158.

[12] Crick, F. (1958) On Protein synthesis. In *Symposium of the society for experimental biology XII*. P.153. Academic Press, New York.

[13] Crick, F. (1970) The central dogma of molecular biology. *Nature,*227: 561-563.

[14] Luria, S. E. & Delbruck, M. (1943) Mutations of bacteria from virus sensitivity to virus resistance. *Genetics*, 28:491.

the theory's function at the molecular level had been apparently shown not to operate in nature. Indeed, molecular genetics even appeared to have a 'central dogma' that ruled out Lamarckian evolutionary processes.

The *status quo* had been firmly established around Darwinian principles. It was apparently confirmed that organisms become adapted to their environments through an evolutionary process in which random mutations arise at a constant rate and with no relation to the specific quality of the environment. Those mutations are then subjected to the pressure of natural selection. Organisms experience differential survival depending upon which mutations they happen to have experienced, and adaptation and evolution follow in subsequent generations as a result. The organism has no control; it certainly has no will and it certainly does not 'strive'. Given this context, especially the widespread subscription to Darwinian theory in the second half of the twentieth century, one begins to see the extent to which the material and implication of the directed mutation debate was inflammatory, problematic and predisposed to spark a controversial episode.

iii) The 'directed mutation' debate – A brief history

In 1988 a paper appeared in *Nature*, somewhat out of the blue, which described an observed anomaly in the process of bacterial adaptive change or evolution at times of nutritional stress.[15] Darwinian theory states that organisms placed under stress by their environment are only able to adapt and evolve through the spread of rare beneficial, and most importantly, chance mutations, that happen to suit them to the challenge. However, the 1988 paper in *Nature* reported that bacteria challenged by changes in their environment were in fact able to adapt in a much less haphazard way to the new conditions.

In that paper three experiments were reported in support of the thesis that bacteria can control the course of their adaptation. The first experiment used non-lactose digesting *Escherichia coli* bacteria. It showed that these bacteria, which are normally unable to use lactose as a nutritional substrate, underwent high levels of mutation to a lactose digesting character when they were provided with no other source of food than lactose in their medium. It appeared that the selective pressure to utilise lactose for nutrition led to increased levels of mutation with that specific outcome. However, this lactose reversion mutation is comparatively common, so a second experiment was needed to show that similarly high levels of this apparently directed mutation also occur when the mutation required is of a more complex or rare type. To demonstrate this, the researchers tested the bacteria's ability to undergo double mutation to the arabinose *and* lactose digesting form in media where only those two substrates were available as a food source. Two simultaneous mutations are required to achieve this adaptive change. The 1988 paper reports that this more complex double adaptive mutation also occurred at a much higher rate than anticipated

[15] Cairns, J. Overbaugh, J. & Miller, S. (1988) The Origin of Mutants. *Nature*, 335: 142-145.

from chance alone. Finally, the paper describes adaptive mutation in the cryptic 'ebg' gene of *E.coli.* In its active form the ebg gene allows bacteria to digest lactose even if their specific gene for lactose digestion is not functional. In order to become active the ebg gene must undergo two mutations. The coincidence of those two mutations in a bacterial cell normally only arises roughly one in every 10 million billion generations. The 1988 paper reported that several bacteria using the activated ebg gene to digest lactose appeared in the media within just two weeks.

Instead of having to depend on the emergence of a rare beneficial mutation for adaptation, it seemed that these bacteria were able to undergo a non-random mutational process that allowed them to achieve exactly those kinds of mutations that would render them adapted. They did not have to wait for a beneficial chance mutation to pop up, instead they seemed to be able to achieve just the right genetic changes to fast track their evolution to suit the environment. Their mutation was not random with respect to environmental quality as Darwinism demands, but rather it appeared determined by the quality of the environment. Hence the observed anomaly was termed 'directed mutation'.

The paper's authors were a team of microbial molecular biologists from the School of Public Health at Harvard University. The research team was led by Professor John Cairns, and thus directed mutations also became known as Cairnsian mutations. So how did the authors present this anomaly? And how did they handle or frame the challenge that it represented to molecular microbial genetics and to established Neo-Darwinian evolutionary theory?

A first point of interest for these questions is that the Harvard team entitled their 1988 paper *'The Origin of Mutants'*. That act of naming presented an indication of the approach and the attitude the team intended to adopt. If the audience wondered whether this small group of specialist workers would shy away from the broader and more profound implications of their observations, avoiding a conflict that might go beyond their specific area of speciality into the realm of evolutionary debate, then here is the first sign that they planned no such subtlety. This rather inflammatory and somewhat sarcastic title plays on Darwin's '*The Origin of Species*' and indicates the position that the proponents of directed mutation would adopt in the controversy that followed. Without having to read further the title has primed the reader for the kind of commentary on evolutionary theory that the authors are willing to offer. The advocates of directed mutation used a strong and unapologetic voice in their discussions of the implications of their bacterial research for the broader debate on the relative merits of Lamarckian and Darwinian theories.

In the abstract to this first paper we see more evidence of the researchers' lack of apology for their non-Darwinian observations. The abstract includes a significant Lamarckian reference, and the researchers choice of language frames the observed anomaly not only as an issue for bacterial researchers, but also as

a challenge to evolutionary and genetics theorists more generally. It states that: '…cells may have mechanisms for choosing which mutations will occur'.[16] In that one statement we see a couple of interesting choices being made by the authors. Firstly, the use of the word 'choosing' gives a sense that there is some kind of active, deliberate and even conscious participation of the bacteria in their adaptive process. That fits with the Lamarckian concepts of 'wishing' and 'striving' that were a principle force of transformism in the original theory. Secondly, the Harvard team choose here to suggest that this process of directed mutation might be a phenomenon in 'cells'. Although they had only made a study of some common bacterial species, they were keen to suggest that what they had observed might be a normal and widespread cellular and genetic process.

Several implications arise from the abstract alone. Firstly, the notion of cell 'choice' undermines a fundamental tenet of Darwinian theory, which demands that mutational processes be random with respect to the quality of the environment. Secondly, the existence of a directed mutation mechanism in 'cells' implies that some path of communication is in fact open between the environment and the hereditary material. For directed mutation to occur there must be some means by which the cell can perceive the quality of its environment and then undertake mutation to fast track it, and its subsequent offspring, to a state of adaptation. Of course, allowing for the presence of such an open system of communication between the material of heredity and the environment would mean abandoning Crick's 'central dogma', which as I explained above describes the unidirectional path between DNA and proteins and renders the cell nucleus closed to influence from outside.

So, the debate began with the publication of a provocative paper that framed the bacterial anomaly in a certain way and prepared the scene for conflict. The authors presented the anomaly as a microbial genetics problem, while also asserting a broader challenge to established theoretical descriptions of the processes of adaptation and evolution. The researchers indicated that they were prepared to use the results of their bacterial experiments as a means by which to challenge the overwhelming attachment of the scientific community to Darwinian theory.

Considering the tone of their presentation, and the implied assault on established evolutionary theory, the rapidity and extent of response that followed is not surprising. Response to the paper was in fact immediate; a review article on directed mutation by renowned American geneticist Franklin Stahl appeared in the same issue of *Nature* as 'the origin of mutants'.[17] In that article Stahl suggested that 'readers will find it good exercise to try to build more highly specified schemes' than Cairns *et al* for the molecular action of directed mutation, but adds that 'top marks will go to those who can build their model solely from familiar elements.' Stahl was in effect appealing to the mainstream

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[16] Cairns, J., Overbaugh, J. & Miller, S. (1988) The Origin of Mutants. *Nature*, 335: 142.
[17] Stahl, F. (1988) A Unicorn in the garden. *Nature*, 335: 112-113.

community to muster a defence of orthodoxy in the light of these anomalous findings. His recommendation being that the best way to deal with the findings was to reinterpret them within the terms of established Darwinian theory. So in just one issue of *Nature* the gauntlet had been laid by the Harvard team and had been taken up by a key representative of the orthodox community. In the coming months further contributions to the debate followed in the form of letters to the editor, other commentaries and reports of additional experiments, and a range journals became host to the debate.

There are two key points to note from this early phase of the debate. Firstly, it soon became apparent that the Harvard experiments were repeatable and consistently generated the appearance of directed mutation.[18] In fact, it seemed that the phenomenon occurred in several species of bacteria and that adaptive mutations occurred in relation to a range of nutritional stresses. As a result, critics were really only able to disagree with the analysis of the phenomena, they could not disagree that the phenomenon existed. Generally, the maximum concession critics would make was that directed mutation might well exist, but could only do so as a bacteria-specific anomaly.

The second point to note from this period of the debate is the rapidity with which the sharp polarization between the protagonists and antagonists of directed mutation developed. From the outset, University of California evolutionary biologist Richard Lenski and microbiologist John Mittler established themselves as the Harvard team's key adversaries.[19] They claimed that Cairns and his team had misinterpreted their results and had failed to account for the fact that in 1943 Luria and Delbruck had shown categorically that bacterial adaptation was random. Lenski and Mittler produced a series of articles during the 1990s that called for further evidence of directed mutation and for details of a mechanism of the proposed adaptive process.

The precedent of Luria and Delbruck's work was in fact the major focus for critics of directed mutation. Interestingly, the Harvard team had anticipated this and had dedicated much of their 1988 paper to a description of the essential differences between their experimental design and that of Luria and Delbruck. As they explained, Luria and Delbruck had used a lethal bacteriophage virus to exert environmental pressure upon the bacteria that they wanted to encourage to adapt. The problem with the use of that agent is that, as soon as the bacteria are

[18] For example, repetitions, modification and extensions to the original directed mutation assays were reported in: Hall, B. G. (1990) Spontaneous point mutations that occur more often when advantageous than when neutral. *Genetics*, 126, 5-16; Cairns, J. & Foster, P. (1991) Adaptive reversion of a frameshift mutation in *Escherichia coli. Genetics,* 128, 695-701; Foster, P. & Cairns, J. (1992) Mechanisms of directed mutation. *Genetics*, 131, 783-789.

[19] Some key examples of Lenski and Mittler's co-authored contributions to the directed mutation debate include: Mittler, J. & Lenski, R. E. (1990) New data on excisions of Mu from E.coli MCS2 cast doubt on directed mutation hypothesis. *Nature*, 344, 173-175.; Mittler, J. & Lenski, R. E. (1992) Experimental evidence for an alternative to directed mutation in the bg1 operon. *Nature*, 356: 446-448.; Lenski, R.E. & Mittler, J. (1993) The directed mutation controversy and Neo-Darwinism. *Science*, 259:188-194.

subjected to it they are killed. The only bacteria that survive are those that happen to have a mutation conferring resistance to the virus. Under these experimental conditions there is no time for any process to occur in which the cells might perceive the challenge and have an opportunity to acquire an adaptive solution to it. In the view of the Harvard team Luria and Delbruck's experimental design meant that they had not provided the opportunity for adaptive mutation to occur, and so they had not in fact tested the system they had set out to investigate. Their conclusions on the randomness of bacterial mutation were therefore bogus.

To avoid the problem of immediate lethality the Harvard researchers chose nutritional stress as their way of exerting pressure on the bacteria. In the directed mutation experiments the bacteria were denied their accustomed food but were provided with plenty of other nutritional substrates that they would be able to use if they made small adaptive genetic changes. This short-term starvation did not kill the bacteria, but rather forced them into a state called 'stationary phase'. During stationary phase bacteria do not reproduce, but DNA mutation and replication can continue. The presence of alternative foodstuffs in their environment meant that the bacteria stood to benefit in terms of growth and reproduction rates if they did adapt to use these other sources of nutrition. Any individual bacterium that achieved a successful mutation during stationary phase would become capable of feeding itself, would exit stationary phase, reproduce and give rise to a population of cells adapted to use the new nutritional substrate.

On account of this considerable difference in experimental design Luria and Delbruck's 1943 conclusions were actually relatively irrelevant to the directed mutation debate. Luria and Delbruck had investigated environment directed adaptive change through a series of experiments that, by their lethal nature, in fact precluded the study of any such adaptive phase. In contrast, the Harvard team's choice of nutritional stress as the environmental pressure to exert on the bacteria took advantage of the natural 'stationary phase' in bacterial reproduction to allow the perfect opportunity for a phase of adaptation to occur subsequent to the introduction of an environmental challenge. Interestingly, in spite of these differences, and in spite of the fact that Cairns repeatedly reiterated these distinctions, Luria and Delbruck's 1943 work remained a popular source for Cairns' opponents over the next five to ten years.

During the 1990s John Cairns, and a growing community of directed mutation advocates, published repetitions of the original experiments, descriptions of directed mutation in a wider range of bacterial species and even reports of directed mutation in another uni-cell, yeast.[20] They also answered their critics and pressed forward with attempts to hypothesize a molecular process for

[20] For discussion of directed mutation in yeast see: Hall, B. G. (1992) Selection-induced mutations occur in yeast. *Proc. Natl. Acad. Sci. USA*, 89: 4300-4303; Steele, D. F. & Jinks-Robertson, S. (1992) An examination of adaptive reversion in *Saccharomyces cerevisiae. Genetics*, 132: 9-21.

directed mutation. Both supporters and critics of directed mutation continued to publish commentaries and further research in key scientific journals.

The advocates of directed mutation provided various suggestions concerning the mechanisms that might underlie the directed mutation process. These suggested mechanisms took several forms. Some proposals represented 'strong' versions of directed mutation. These relied heavily on the notion of bacteria perceiving the quality of their environment and determining their mutations, and therefore adaptations, as a direct response to it.[21] There were also 'weak' versions, which suggested that directed mutation might be somewhat less specific, being caused by a stress induced hypermutation strategy specific to bacteria, rather than by any more directed strategy for mutation.[22]

By the late 1990s, the journal-based debate had reached a stalemate. The advocates of directed mutation could not proceed beyond their speculative discussions of potential mechanisms for the phenomenon. They had not found evidence of directed mutation in any multi-cellular organisms, nor had they been able to demonstrate the existence of any molecular systems that might permit environment to DNA communication. Meanwhile, critics of the theory seemed unwilling to abandon the comparison of directed mutation with Luria and Delbruck's findings. The structure of the conflict began to change. The debate was pursued in short treatments in numerous books, through attempts by some textbook editors to include directed mutation as a bacterial evolutionary anomaly, and, most importantly, on a wealth of professional and popular websites. ,

Although the journal-based debate had a high profile during the 90s, and has maintained a persistent presence ever since, that was nothing compared to the enormous extension of scale and enthusiasm associated with the move to the Internet forum. On the Internet a huge and diverse audience has become engaged in the debate, while many of the original advocates and adversaries in this conflict now also use this medium to continue their discussions. In that forum the concept of directed mutation has been adopted in the service of many and diverse agendas, and the level of the conflict concerned with the clash of Darwinism and Lamarckism has flourished and gained momentum.

This brings the history of the directed mutation debate more or less up to the present day. To summarise, the debate has exhibited different phases, and has witnessed the involvement of a large and ever-changing debating

[21] See for example: Cairns, J., Overbaugh, J. & Miller, S. (1988) The origin of mutants. *Nature*, 335: 142-145; Cairns, J. & Foster, P. (1991) Adaptive reversion of a frameshift mutation in *E.coli*. *Genetics*, 128: 695-701; Foster, P. & Cairns, J. (1992) Mechanisms of directed mutation. *Science*, 260: 1221.

[22] See for example: Hall, B.G. (1990) Spontaneous point mutations that occur more often when advantageous than when neutral. *Genetics*, 126: 5-16; Bridges, B.A. (1997) Hypermutation under stress. *Nature*, 387, 557-558; Torkelson, J., Harris, R., Lombardo, M., Nagendran, J., Thulin, C. & Rosenberg, S. (1997) Genome-wide hypermutation in a subpopulation of stationary-phase cells underlies recombination-dependent adaptive mutation. *The EMBO Journal.* Vol. 16, No.11, 3303-3311.

community. The debate has been protracted, is ongoing, and shows no sign of approaching resolution. In fact, in the Internet forum the process of recruitment to the debate continues, and directed mutation now engages a vastly expanded community.

iv) The neglected anatomy of protracted controversy and the action of perpetuating forces

In this section I explore how issues arising from this case study might contribute to a more general consideration of dissent. There are two key issues that I want to discuss in more detail. Firstly, I consider how the material of the case study facilitates reflection upon the nature and usefulness of existing tools for the description and understanding of the structure and dynamics of scientific controversy. The fact that this debate has been so protracted, has included many phases, and remains unresolved, gives us the opportunity to assay existing tools and models against its history as a way of evaluating their effectiveness and appropriateness. Secondly, I consider how a developed account of the history of the directed mutation debate aids in understanding the means by which this debate has been protracted. This section seeks to identify some general categories of activity and influence that have acted to perpetuate this conflict.

- How effective are existing theoretical tools in the analysis of protracted scientific controversy?

Case studies of protracted and unresolved scientific conflicts highlight a common problem inherent in many theoretical models of scientific controversy. At their foundation the majority of models assume that a three-part structure underlies controversy. In spite of the specific terminology or depth of focus that these models use, what each effectively describes is the process by which an **anomaly arises**, is **negotiated** and is **resolved**. In general, these descriptions and analyses, whether they are predominantly sociological, historical or philosophical, are invariably focussed upon the achievement of resolution and closure. Even where description of the exact means of anomaly resolution is not the prime emphasis, still theoretical tools assume closure as the ultimate goal or end point of scientific conflict; they focus on the processes by which anomalies are rendered unproblematic. Even many of the sociological models concerned with the activity of controversy participants remain directed towards the means by which these participants resolve their differences.[23]

[23] A notable exception is sociologist Thomas Gieryn's study of 'boundary work'. Gieryn suggests that during conflicts, or contests for epistemic authority as he sees them, the process of negotiation is all important. Through negotiation the boundaries are draw between the orthodox/unorthdox, mainstream/marginal, rational/non-rational etc. Gieryn is interested in how these authority contests are played out, which leads to a focus on the negotiation phase more in line with that recommended in this paper. For a detailed outline of boundary work see: Gieryn, T. (1995) Boundaries of science. In: *Handbook of Science and Technology Studies.* Ed. S. Jasanoff *et al*, 393-443. Sage Publications, Thousand Oaks, California.

The closure of the controversy is all-important in these theoretical frameworks. Closure appears to be the goal of scientific activity – it is the motivation for those involved in a controversial episode. There is a simple enough reason for this clear enthusiasm for the 'ends' of conflicts in the analytical literature. Controversy is often viewed as an undesirable kind of activity in science. In fact, it even represents a kind of failure of the scientific process. Three philosophers of science, Peter Machamer, Marcello Pera and Aristides Baltas explain this aversion to conflict, stating that: '…the absence or resolution of disputes has been taken as the hallmark of scientific knowledge as compared to other disciplines or fields of experience'.[24] They also point out that, the 'view that science should be ultimately uncontroversial flourished at the time of the founders of modern science' and has been perpetuated by scientists and philosophers ever since.[25]

It seems that protracted debates in science undermine the 'special' or dignified nature of the scientific enterprise and the knowledge that it generates. Karl Popper has stated that: 'Science is one of the very few human activities- perhaps, the only one, in which errors are systematically criticised and fairly often in time, corrected'.[26] Machamer, Pera and Baltas add that it is that conception of the process of science that leads to the state in which: '…it is typical of scientists and others to believe that any dispute or controversy is resolvable given further information or data, which, in their turn, necessarily will be forthcoming given enough time and money.'[27] Theoretical tools that describe the process of anomaly negotiation in science have been formulated in the context of these perceptions. The inherent belief that science should be, and invariably will be, defined by the resolution of conflicts results in the production of descriptive tools that often betray that optimism and reinforce those goals.

In the context of these perceptions, protracted and apparently irresolvable controversies seem to defy explanation. They apparently reveal a breakdown in the process of the acquisition of scientific knowledge, they imply that existing theoretical frameworks are weak and cannot withstand anomaly, and they threaten to undermine the special nature of scientific activity. Protracted controversies appear as aberrations, or at best perhaps as 'unfinished' conflicts that given time will eventually fall within the descriptive power of end-directed modelling tools.

This common perception of sustained periods of conflict in science has resulted in there being little theoretical attention focussed specifically on the

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[24] Machamer, P., Pera, M. & Baltas, A. (2000) *Scientific Controversies: Philosophical and Historical Perspectives.* Oxford University Press, New York. p.4.
[25] Ibid.
[26] Popper, K. (1963) *Conjectures and Refutations.* Routledge and Kegan Paul, London. p.216
[27] Machamer, P., Pera, M. & Baltas, A. (2000) *Scientific Controversies: Philosophical and Historical Perspectives.* Oxford University Press, New York. p.4

character or dynamics of protracted phases of negotiation or conflict. In particular, theoretical works often overlook the specific *causes* of controversy perpetuation. These forces of perpetuation are held to exist, in the majority of models, in what we might think of as an interruption phase; these debates are considered suspended in the negotiation phase. Models generally predict that an anomaly will arise, that it will be perceived by the appropriate community, that a phase of negotiation will be undertaken, and that, finally, the anomaly will be resolved by any number of processes such as assimilation, abandonment or redefinition.[28] In a protracted controversy, this process stalls in the negotiation phase — that is to say, there is an interruption at that point in the process through which it is imagined that scientific activity should proceed.

To consider protracted phases of negotiation as a passive phenomenon, or as part of a process *en route* to inevitable closure, results in the unfortunate side effect of overlooking the very features that characterise and determine the protraction of these long running conflicts. It is during that period of interruption and drawn out negotiation that various features specific to the conflict, and the community involved in it, can actively contribute to the perpetuation of the controversy and its failure to reach closure.[29]

➢ Perpetuating forces and impediments to closure during conflict negotiation

In the case of directed mutation, in which the negotiation phase has been very drawn out, we can quite easily identify what some of these active perpetuating forces might be. Having identified these it might be possible to establish some categories of perpetuation force that might have contributed to the prolonged negotiation phases of some other scientific controversies.

Examples of perpetuating forces in the directed mutation debate:

1. **A Many-levelled Debate**

[28] For a detailed discussion of the various modes of closure see: Eds. Engelhardt, H. T. & Caplan, A. L. (1987) *Scientific Contorversies: Case studies in the resolution and closure of disputes in science and technology.*Cambridge University Press, New York.

[29] In Eds. Engelhardt, H. T. & Caplan, A. L. (1987) *Scientific Controversies*. Cambridge University Press, New York, the contributing authors explore the influence of political and ethical content and connatation on the structure and dynamics of scientific disputes. They effectively identify such content as a perpetuating force of controversy negotiation, although they express that perpetuation of negotiation instead as impediment to closure; as such they render the perpetuation of negotiation passive and assert closure as the inevitable goal of the conflict activity. It is worth noting that distinction of expression, since it illustrates again the general tendency of theorists to focus on the end directed achievement of controversy closure rather than on the structure of the negotiation phase in its own right. In spite of this distinction it is clear from that text that political and ethical content would qualify as a perpetuating force of the kind being described here. That category is not significant to the case of the directed mutation debate, although it would contribute a category of perpetuation to the 'general anatomy' of protracted controversies that is discussed at the end of this paper.

I have shown above that the directed mutation debate involved conflict at the level of microbial genetics specifically, but also at the level of evolutionary theory more generally. The clash of these two levels of debate impeded the achievement of closure. Many of the critics' key publications explicitly and expressly focussed on the genetics anomaly represented by directed mutation. For instance, some authors queried aspects of methodology and took issue with the legitimacy of certain counting techniques and apparatus. However, in almost all of those papers the critics would take the opportunity to also express their disdain for non-Darwinian work and their objection to Lamarckian associations. The proponents of directed mutation would then issue papers in response to the methodological queries, in which they would also restate their view that directed mutation was a non-Darwinian process.[30] Effectively, attention to the microbial genetics problem was being used as a way of legitimising, especially in journals like *Nature* and *Science*, continued publication on this issue. As a result, although it looked as if the directed mutation anomaly was being negotiated, it was in fact only being restated and re-challenged. The broader evolutionary issues at stake, which were being presented as a secondary strand of discussion in the published material, were in fact driving the debate. It was largely the opponents and proponents views on the broader evolutionary conflict that maintained their engagement. However, it was the mask of the molecular genetics debate that meant they could continue to air their conflict in the key journals. Efforts towards closure were thereby misdirected and negotiation was focussed on the molecular genetics problem, rather than on the evolutionary problems that had precipitated and perpetuated the core of the conflict.

2. A Well-established Establishment

The component of this conflict that focussed on evolutionary theory was undertaken in the context of pre-existing and well-established positions on these issues. In the 1980s Darwinism was absolutely established as the primary theoretical tool for evolutionary work. A long history — too long to go into here — involving the formulation of the modern synthesis, the adoption of Charles Darwin as an iconic figure in science and popular culture, and the rise of molecular genetics had contributed to a singular professional allegiance to Darwinian theory in the late twentieth century. Not only had Darwinism been significantly promoted, but also Lamarckism had suffered serious defamation and stigmatisation by association during the twentieth century.[31] Therefore, when in 1988 John Cairns proposed a Lamarckian

[30] These two levels of argument are best exemplified in the exchanges between John Cairns (and his various co-authors) and co-authors Richard Lenski and John Mittler in the period roughly 1988-1995. See references above.

[31] During the twentieth century Lamarckism became associated with fraudulent practice after Austrian biologist Paul Kammerer was accused of doctoring specimens to give the appearance of acquired characters. Kammerer committed suicide shortly after the accusations were made which appeared to confirm his adversaries' suspicions. For details of Kammerer's story see: Koestler, A. (1971) *The case of the midwife toad.* Random House, New York. Also, between the 1930's and 1960's the Lysenkoist

theory of adaptation in bacteria he did so in the context of extremely well defined and widespread preconceptions of Darwinism and Lamarckism. The individuals engaged in this debate all had pre-conceived ideas about the relative merits of Lamarckism and Darwinism. Their preconceptions, informed by their educational, intellectual, and cultural context, necessarily influenced their reaction to non-Darwinian work. The well-developed allegiance of evolutionists to Darwinism and their often unconcealed contempt for Lamarckian theories certainly determined some of the tone of the debate. Feelings ran high on the issue of conflict between Lamarckian and Darwinian theories. Many of these biases were the subconscious effects of engagement within certain professional and social cultures, and so it was difficult for participants to concede on matters of their allegiance during the negotiation.

The advocates of directed mutation perceived this settled orthodoxy with frustration.[32] It appeared to them that however repeatable and legitimate their observations might be, that they would prove controversial so long as they required the scientific community to abandon absolute attachment to Darwinism. These facts prolonged the debate, since negotiation of the material of the conflict, however effective, could not resolve the simple fact that the Darwinian defenders would not accept a non-Darwinian phenomenon, even as a bacteria specific anomaly. While negotiation of a molecular genetics anomaly might achieve closure, negotiation concerning attachment to certain evolutionary frameworks is underpinned with irreconcilable differences that debate cannot relieve.

3. A Meeting of Disciplines

The fact that the debate chiefly involved two quite different communities was a further reason why closure was difficult to achieve in the case of directed mutation. The directed mutation research emerged from a community of molecular biologists, however, the research was received by an audience with much broader professional composition and interests. That audience included a number of evolutionary biologists. This fact prolonged the debate on account of the different styles of science determining practice and negotiation in these sub-disciplines. At a basic level the approach of

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movement arose and fell in Russia. This movement advocated national agricultural practice based on Lamarckian theory and was heavily underpinned with Marxist ideology. Lysenkoism eventually emerged as an untenable state policy for agriculture and evidence for the action of Lysenko's principles was not forthcoming from further research. Subsequently, Lamarckism was tainted with that practical failure as well as with the stigma of attachment to radical politics. For details of Lysenkoism and its political context see: Lewontin, R. & Levins, R. (1976) 'The problem of Lysenkoism'. In: Eds. Rose, H. & Rose, S. (1976) *The radicalisation of science.* Macmillan, London.

[32] The advocates of directed mutation often likened their critics' defence of Darwinism to the defence of religious conviction. They thought that the challenge to Darwinism that their research implied placed an unfair burden upon their work in the context of defence of dogma by the scientific mainstream. These issues are discussed in Foster, P. L. (1993) Adaptive mutation: the uses of adversity. *Annual Review of Microbiology*, 47: 467-504.

molecular biologists and evolutionary biologists to controversy within their respective fields is quite different.

Molecular biologists are chiefly engaged in adding details of form and function to their body of knowledge. Molecular biology has a theoretical framework at its base, but it is composed of many theories that interact. In molecular biology an anomaly of molecular activity in one species of organism can be relatively unproblematic and can be assimilated as part of a flexible and varied knowledge base, provided that it is assimilated as being specific to that system. On the other hand, in the case of evolutionary biology, there is a much more apparent governing theory that determines the approach of researchers within the subject. Adherence to the tenets of Darwinian theory pervades every aspect of research within the sub-discipline. There cannot be anomalies in this field that conflict with that theory at any fundamental level. Since Darwinism is supposed to be an all-embracing description of organic evolution, even system specific anomalies can serve to undermine the theory as a whole.

We can employ some well-known theoretical tools to illuminate the conflict in styles between molecular biologists and evolutionary biologists. For example, in simple terms, we might think of evolutionary biologists' adherence to Darwinian theory as an example of a Kuhnian 'paradigm' in operation. From that point of view, anomalies that challenge the legitimacy of Darwinian theory (the paradigm) cannot be assimilated. An anomaly must be rejected (disproved) or, if the paradigm cannot withstand the assault of the anomaly, a 'revolution' must occur and the paradigm must be abandoned.[33] In that context, if directed mutation was to be accepted at all it would need to represent a significant enough challenge to force a revision of the Darwinian paradigm. The evolutionary biologists engaged in the debate did not consider that the directed mutation anomaly represented a serious enough challenge to the paradigm to precipitate any such 'revolution'. Therefore, in that disciplinary context the only available option was to reject the anomaly since it was incompatible with the paradigm.

On the other hand, Kuhn's 'paradigm' concept appears to relate less well to the practice of molecular biology. That discipline's body of knowledge, and the theories that attempt to order it, are subject to more subtle and constant amendment. That community operates a complex system of scientific activity that might be better described with reference to Lakatosian 'research programmes'.[34] In the language of research programmes we might think of molecular biology as having a 'hard core' of irrefutable 'negative heuristics' that include cell theory, Mendelian genetics and other basic precepts of the

[33] Kuhn, T. (1962) *The Structure of Scientific Revolutions*. University of Chicago Press, Chicago.
[34] Lakatos, I. (1976) *Proofs and refutations*. Cambridge University Press; Lakatos, I. (1970) 'Falsification and the methodology of research programmes' In: *Criticism and the growth of knowledge*. Ed. Lakatos & Musgrave (1970) Cambridge University Press.

discipline. The hard core is surrounded by the 'protective belt' of positive heuristics that constantly undergo investigation and reassessment. That protective belt expands as new data is accumulated. New findings can be added to this body of theory since there is no burden of irrefutability placed on the protective belt. Since, in this case, the 'protective belt' is growing the research programme qualifies in Lakatos' terms as 'progressive'. In this context the molecular biologists engaged in the directed mutation debate are happy to assimilate bacteria specific directed mutation into their set of positive heuristics, at least for the time being. This is in contrast to the paradigm serving activity in evolutionary biology, which made no such assimilation possible even in the short term.

The debate was protracted because to each community the challenge appeared to have a different form and severity. The very notions in each of these communities of what might constitute appropriate resolution were significantly different. Whereas molecular biologists thought the anomaly was sustainable, evolutionary biologists were under pressure to reject or redefine the anomaly, or else undergo a major revolution of their discipline. Although the goal of both communities may have been the resolution of this conflict, their different approaches meant they did not share a view of what resolution might entail, and how it might be achieved. As a result, the efforts towards closure were diffused and the debate was prolonged.

4. Strong Advocacy by a Key Individual

The directed mutation debate was sustained during the 1990s in part due to Professor John Cairns' persistent advocacy. He consistently published extensions and defence of his research. He dedicated considerable effort to describing a mechanism for directed mutation, and he consistently produced direct responses to critics' comments. He co-authored with numerous others, and thereby recruited supporters from many different institutions. He has continued to contribute to the debate until the present day, although he is in his mid eighties.[35]

This type of activity is not particularly unusual. Often we can link a particular controversy with the name of one, or perhaps a couple, of its long-term active advocates. For example, in relation to 'the memory of water' we think of Jacques Benveniste, for 'punctuated equilibria' we remember Niles

[35] Key examples of Cairns' contribution to the debate between 1990 and 2000: Cairns, J. & Foster, P. (1991) Adaptive reversion of a frameshift mutation in *E.coli*. *Genetics*, 128: 695-701; Foster, P. & Cairns, J. (1992) Mechanisms of directed mutation. *Genetics*, 131: 783-789; Cairns, J. (1993) Directed mutation. *Science*, 260: 1221; Foster, P. & Cairns, J. (1994) The occurrence of heritable Mu excisions in starving cells of *E.coli*. *EMBO*, 13: 5240-5244; Cairns, J. (1995) Adaptive mutation and sex. *Science*, 269: 289; Cairns, J. (1998) Mutation and cancer: the antecedents of our studies of adaptive mutation. *Genetics*, 148(4): 1433-1440; Foster, P. & Cairns, J. (1998) Adaptive mutation of a lacZ amber allele. *Genetics*, 150(3): 1329-1330; Cairns, J. (2000) The contribution of bacterial hypermutators to mutation in stationary phase. *Genetics*, 156(2): 923-926.

Eldridge and Steven J Gould, we think of 'jumping genes' and Barbara McClintock, or of 'Steady State' cosmology and link it to Fred Hoyle.[36] These kinds of dedicated individual advocates actively keep their controversies open. They are reluctant to give in to mainstream views, and often express disdain for what they perceive as a restrictive or closed-minded establishment. They generally plough significant energy into reformulating, re-describing and re-proposing their theories as part of their dedicated ongoing attempts to have their work accepted. A key characteristic of these individuals is often their personal dedication to their theories. They have often staked reputation, finance, pride and career on the success of their advocacy.[37] The individuals actively prolong negotiation and attempt to block closure attempts made by their opponents.

5. Change of Forum

I mention above that a significant phase of extension and protraction of the directed mutation debate began when the discourse moved from majority presentation in journals to majority presentation on the Internet. For this case at least, that shift represented a significant force of negotiation perpetuation and impediment to closure. Once the debate shifted to the Internet forum, closure became almost daily a more and more remote possibility. Recruitment of new supporters, critics and commentators increased enormously, and directed mutation engaged the attention of individuals with diverse backgrounds. In addition, some of the contributors to the journal-based debate selected this medium to extend their contributions away from the strictures of journal publication.

In the Internet forum the strand of the debate concerning the general conflict between Darwinism and Lamarckism became much more explicit. Discourse on that issue was also promoted by popular engagement with that aspect of the debate above and beyond the degree of popular engagement with the molecular biological problem of directed mutation.[38] In addition, there has been significant attention from those involved in the creation versus evolution debate. They have interpreted the directed mutation phenomenon in many ways; some as a sign of weakness/refutability in established

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[36] Advocates' key primary sources for these controversies:
Davenas, E., Benveniste, J. *et al* (1988) Human basophil degranulation triggered by very dilute antiserum against IgE. *Nature*, 333:816.
Eldredge, N. & Gould, S. J. (1972) 'Punctuated equilibria: an alternative to phyletic gradualism' In: Ed. Schopf, T (1972) *Models in paleobiology*. Freeman Cooper, San Francisco.
McClintock, B. (1951) Chromosome organisation and genic expression. *Cold Spring Harbour Symposium Quant. Biol.* 16: 13-47.
Hoyle, F. (1948) A new model for the expanding universe. *Monthly Notices of the Royal Astronomical Society.* 108: 372-382.
[37] These issues are discussed in detail in relation to Jacques Benveniste and his advocacy of water's memory in Schiff, M. (1995) *The memory of water*. Harper Collins, London.
[38] See: www.science-frontiers.com/sf075/sf075b06.htm

evolutionary theory and others as evidence of 'design' in the natural world.[39] Also, directed mutation has been absorbed and translated in service to several non-scientific agendas. For example one website hosts discussion of the links between a process of directed mutation and the achievement of spiritual enlightenment and the development of consciousness.[40] This diversification of the meanings and implications of the debate has lead to a proliferation of forms of negotiation and a diffusion of options for closure. This change of forum and thus of scale has acted to perpetuate the debate. In more general terms, this phase of the directed mutation debate might also highlight the potentially widespread importance of Internet based discourse to the analysis of modern scientific controversies.[41]

6. Good fit with Popular Culture

Popular interest in directed mutation was encouraged by the broader cultural context that underlay the debate. During the late 1980s and throughout the 1990s British and American publics in particular became enthused by ideas about the repression of maverick science, the fate of non-mainstream intellectual developments, the restrictive powers of the scientific mainstream generally, and the concealment of radical intellectual ideas. Programmes like Fox television's *The X Files* were generated as part of this culture and fed into it. *The Fortean Times*, the journal of the paranormal, reported elevated levels of subscription.[42] In such a context it was easy for the directed mutation research to be seen as a stunning and revolutionary intellectual development that had been stifled by the conspiracy of a repressive establishment. Sources available on the Internet show just how many people took an interest in directed mutation on that kind of basis.[43] The result was that directed mutation had a larger and more supportive popular audience than might have been expected for a molecular biological phenomenon. The debate was perpetuated by these interested parties as they translated the conflict to suit their own agendas and diversified the kinds of negotiation being undertaken. They also represented enthusiastic consumers of the primary scientific materials produced from this debate.

7. Debates on Evolutionary Theory

[39] For examples see: www.prophecyinstitute.com/science/update/up-32b.html; www.grisda.org/origins/20060.htm; www.talkorigins.org
[40] www.swcp.com/swc/Essays/bio.html
[41] There are of course epistemological issues surrounding the question of whether Internet discourse represents a form of scientific debate at all. Those general issues are too thorny to debate here. However, in the case of the directed mutation debate specifically the engagement of many of the original journal article authors in the Internet-based discussions means that it can be argued that legitimate scientific debate is still ongoing in at least some areas of this larger forum.
[42] www.forteantimes.com
[43] For examples see: www.science-frontiers.com/sf075/sf075b06.htm; www.geocities.com/jorolat/.direct.html; www.alternativescience.com/censorship.htm

I have mentioned the different views of the molecular biologists and the evolutionary biologists concerning what was at stake in this particular debate. Added complexity is derived from the additional factors that are put at stake in any discussion of evolutionary theory. Evolutionary theory is the means by which many people attempt to understand man's place in nature and describe the human condition. When evolutionary problems are at the heart of a debate there is significantly more at stake than data, or the relation of that data to a knowledge base. Tied up in the conflict are far more pressing and emotive issues such as religion, ideology, our existing perceptions of man's place in nature, and our aspirations concerning how we prefer to tell the story of human origins and existence.

Lamarckian resurrections have been traditionally tied up with radical left wing politics during the twentieth century.[44] In particular, the very marked association between Lamarckism and communist ideologies associated with Lysenkoism in 1930's Russia has in many ways added an indelible political strand to Lamarckian sympathy. Although these issues are not addressed explicitly in the journal publications on directed mutation, the tacit preconceptions derived from them underlie the debate. Also, Darwinian theory has come under increasing attack from creationists in recent years. The legacy of those attacks has necessarily been a more vigorous defence of Darwinian theory. It has been more vital that evolutionary theory and Darwinism appear immune to debate. In the climate of Darwinian opposition any threat to Darwinian theory represents a threat to evolutionary theory as a whole, since academic conflict surrounding these issues can be taken to betray weakness in the theoretical frameworks.

With so much of such a serious nature at stake, we cannot expect individuals on either side of the debate to give ground easily. Whereas in a debate about data people can be persuaded with evidence, where ideologies are concerned convincing an opponent becomes far more difficult. The opponents and proponents of directed mutation were conflicted on all these issues. The achievement of a resolution would therefore have required an enormous persuasive achievement by one side or the other concerning not only data but perceptions and ideologies.

We have examined a few of the forces that appear to perpetuate the conflict in this case study. How might these translate as categories for thinking about perpetuating forces in controversies more generally? Firstly, even from this short list it is possible to discern two main categories of perpetuating force. There are those that are internal to scientific practice and those that act from outside the immediate community involved in the conflict. The latter might stem from the broad context of the period or the historical precedents there underlie the

[44] For discussion of these links see: Lewontin, R. & Levins, R. (1976) 'The problem of Lysenkoism'. In: Eds. Rose, H. & Rose, S. (1976) *The radicalisation of science.* Macmillan, London;

material of the conflict. We might think therefore of perpetuating forces existing in intrinsic and extrinsic forms. In terms of categories, there appear to be a number of general conditions that might relate to the perpetuation of negotiation and which might contribute to a possible general anatomy of protracted controversies.

For example:

a) A controversy might be perpetuated where it encompasses debate on several levels or of several problems.
b) A debate might be perpetuated where there is a very established and stable mainstream view under attack.
c) A debate might be perpetuated when it involves two or more communities that do not share a common approach to the management of anomalies and their resolution.
d) A debate might be perpetuated by the advocacy of one or a few dedicated individuals.
e) A debate might be perpetuated when it is reinvigorated or reinvented by translation to a different publication forum.
f) A debate might be perpetuated when it arises within an enthusiastic and/or sympathetic cultural context.
g) A debate might be perpetuated if it involves a challenge to evolutionary theory.

Conclusion

This discussion highlights the complexity of conflict negotiation phases in science. Many existing theoretical tools largely neglect that internal complexity and the heterogeneity of negotiation phases between instances of conflict. Models tend to be end directed towards the achievement of closure, and closure is identified tacitly or explicitly as the goal in scientific conflict. When a controversy is prolonged during the negotiation phase the usual expectation is that resolution must be pending. Attention to the details of the negotiation phase and its protraction are limited because the conflict appears ‘incomplete’. This theoretical approach is perpetuated by a widespread and overwhelming attachment to the perception of science itself as inherently immune to protracted debate, and predisposed and purposed to conflict resolution.

However, an unresolved controversy is not necessarily just a controversy awaiting resolution. Rather, the negotiation phase is an active process, and likewise the protraction of that negotiation is also active. If negotiation is prolonged it may be because specific forces are actively perpetuating it and also actively preventing closure. In that context, conflict perpetuation is equally as active a phenomenon as we already consider controversy closure to be. The structure and dynamics of scientific controversies, as historians, philosophers and sociologists are becoming increasingly aware, are inextricably linked with the motivations, aspirations and biases of their advocates and their adversaries. In

the case of the directed mutation debate we can see how these features and many others come to actively shape the negotiation of this anomaly.

There is more to controversies than the means by which they come to an end. The traditional view of controversies as a process of anomaly identification, negotiation and resolution need not be challenged, but rather our view of the activities in each of these phases might benefit from a move away from the notion of goal direction towards closure. The structure and dynamics of scientific controversies might be illuminated by closer theoretical analysis of the diversity of negotiation phases that seem to exist.