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Disciplinary Baptisms: A Comparison of the Naming Stories of Genetics, Molecular Biology, Genomics and Systems Biology

Alexander Powell [1, 3]
Maureen A. O'Malley [1, 3, 4]
Staffan Müller-Wille [1, 3]
Jane Calvert [2, 3]
John Dupré [1]

1. Egenis, University of Exeter, Byrne House, St Germans Road, Exeter EX4 4PJ
2. Innogen, University of Edinburgh, Old Surgeons' Hall, High School Yards, Edinburgh EH1 1LZ
3. These authors contributed equally to this paper.
4. Corresponding author (m.a.o'malley@exeter.ac.uk)

Abstract – Understanding how scientific activities use naming stories to achieve disciplinary status is important not only for insight into the past, but for evaluating current claims that new disciplines are emerging. In order to gain a historical understanding of how new disciplines develop in relation to these baptismal narratives, we compare two recently formed disciplines, systems biology and genomics, with two earlier related life sciences, genetics and molecular biology. These four disciplines span the twentieth century, a period in which the processes of disciplinary demarcation fundamentally changed from those characteristic of the nineteenth century. We outline how the establishment of each discipline relies upon an interplay of factors that include paradigmatic achievements, technological innovation, and social formations. Our focus, however, is the baptism stories that give the new discipline a founding narrative and articulate core problems, general approaches and constitutive methods. The highly plastic process of achieving disciplinary identity is further marked by the openness of disciplinary definition, tension between technological possibilities and the ways in which scientific issues are conceived and approached, synthesis of reductive and integrative strategies, and complex social interactions. The importance – albeit highly variable – of naming stories in these four cases indicates the scope for future studies that focus on failed disciplines or competing names. Further attention to disciplinary histories could, we suggest, give us richer insight into scientific development.

Keywords – Discipline formation, genetics, molecular biology, genomics, systems biology

'Names matter. They are not only labels or reference terms for historical accounts, but strategic tools'

(de Chadarevian 2002, 206)

Introduction

How do scientific endeavours become established as disciplines? Why do some kinds of scientific activities achieve disciplinary status while others fail? More specifically, what role does the naming of a discipline play in its establishment? Questions about disciplinary formation are particularly pertinent in times when new claims to disciplinarity are making themselves heard. Systems biology is an example of such a claimant. Although young and almost untested as a science, the label "systems biology" appears to play an important role in attracting many eminent scientists and a great deal of funding, institutional support, literature, and broader scientific attention. Systems biology's development from a small scientific field will be watched with interest by historians and sociologists of science, as well as scientists and policy makers, because it is much more likely for an aspiring discipline to fail to achieve institutionalized status than to succeed and yet nobody knows what the ingredients of success might be.[1]

In what follows, we compare four scientifically linked disciplines that span the last century to gain a broad understanding of what features lead to their successful establishment. We begin with the emergence of genetics in the early 1900s, then discuss molecular biology from the 1940s onwards, followed by the rise of genomics in the 1980s, and finally return to our contemporary example of systems biology from the late 1990s onwards. We have chosen these examples not only because of their historical links and connections in subject matter, but because the older two disciplines provide a background against which the two newer disciplines can be more effectively investigated. The greater historical detail available on genetics and molecular biology draws attention to aspects of genomics and systems biology that are not yet obvious, and to differences between disciplinary formation in the first and second halves of the twentieth century.

The last century of scientific activity must be seen against the background of the nineteenth century. Early sociologists of science described nineteenth-century disciplinary development as a trend towards increasing specialization, with the subject matter of the discipline–usually reflected in its name–being the key criterion of demarcation (Ben-David and Zloczower 1991 [1962]; Lemaine *et al*. 1976). In biology, therefore, we see disciplines such as botany, zoology, and bacteriology emerging out of natural history, with each of those dividing into further specialties (zoology giving rise to, for example, vertebrate and invertebrate zoology). Accounts of nineteenth-century disciplinary institutionalization have, therefore, been given in terms of the creation of chairs, departments, journals, and societies that supported these specializations (Ben-David and Zloczower 1991, 132-133; Lemaine *et al*. 1976, 2; Kohler 1982, 1-8).

By the beginning of the twentieth century, however, discipline formation began to be driven by something other than specialization, in the form of a trend towards disciplinary definition on the basis of general perspectives and levels of biological process. This trend gave rise to new distinctions that could interact with or become superimposed upon preexisting disciplinary structures. One way of individuating these generalizing disciplines is by what has been called "styles of scientific thought" or reasoning (Harwood 1993; Hacking 2002, 181-192). These loosely defined configurations of commitments to certain objects, technologies, and standards of scientific inquiry are as much about practice as about reasoning. Differences in research style have always coexisted within disciplines, but in the twentieth century different styles began to interact with one another in ways that cut across pre-existing disciplinary boundaries.[2]

So-called "general biology" is one example of this new tendency (Maienschein 1986). A holder of one of the first chairs in this new discipline, Sinai Tschulock, suggested in 1910

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[1] Although some work has focused on the history of particular disciplines, especially those of the nineteenth century, little has been done to find the similarities and differences between a number of disciplines as they develop. In part, this can be attributed to the emphasis given in recent years to studying science in local contexts (see Lenoir 1997; de Chadarevian 2006).

[2] See, for example, Abir-Am's (1980) comparison of emerging molecular biology and Chargaff's practice of cell chemistry.

that biology could be subdivided according to different "ways of thinking" into "biotaxy" and "biophysics". The former would comprise the descriptive disciplines of natural history and the latter would bring together the various specialties (such as developmental mechanics or psychophysics) which in the late-nineteenth century had begun to employ the methods of physics and chemistry in the study of living phenomena (Jahn *et al*. 1982, 453). Biochemistry is another more enduring example of this trend to incorporate distinct styles, research problems, and interdisciplinary relationships into a single domain of inquiry (Kohler 1982). This shift might be characterized as one in which disciplinary demarcation became grounded in epistemological practices, rather than on the earlier basis of ontological categories, in line with some of the demands of medicine and industry of the time (Müller-Wille 2007).

We will use our four examples to explore how twentieth- and early twenty-first-century disciplines were created and institutionalized in relation to disciplinary naming stories. We introduce each case with an account of how the discipline was "baptized", and relate that process to other elements of disciplinary formation such as paradigmatic achievements, defining technologies, and institutional recognition. We are not, however, proposing a general account of disciplinary formation – the historical relationships among the relevant factors are, as we shall show, very different in each case. They demonstrate that twentieth-century disciplines may be individuated variously in terms of specialized tools and methods, overarching approaches and conceptual orientations, or a focus on particular research problems. One critically important role, then, of the varied naming processes encapsulated by baptismal stories is to confer unity on highly diverse scientific activities and aims.

Genetics

The baptism of genetics can be assigned to a precise date. On 18 April 1905, William Bateson, then a fellow at the University of Cambridge, wrote a letter to Alan Sedgwick. The letter dealt with a professorship the university wanted to create from funds donated for the promotion "of the study of vegetable and animal biology" (Bateson 1928, 87-93). Bateson suggested narrowing down this topic to "Heredity & Variation", and proposed "genetics" as the appropriate term.

> If the Quick Fund were used for the foundation of a Professorship relating to Heredity and Variation the best title would, I think, be "The Quick Professorship of the Study of Heredity." No simple word in common use quite gives this meaning. Such a word is badly wanted, and if it were desirable to coin one, 'Genetics' might do. (Bateson 1928, 93)[3]

In the following year, Bateson delivered the presidential address at the *Third International Conference on Hybridisation and Plant Breeding* and used the opportunity to publicize and broaden his advocacy of the name "genetics". "Like other new crafts", he argued,

> we have been compelled to adopt a terminology, which, if somewhat deterrent to the novice, is so necessary a tool to the craftsman that it must be endured. But though these attributes of scientific

[3] A facsimile of the letter can be found at http://www.jic.bbsrc.ac.uk/corporate/images/letter1a.gif.

> activity are in evidence, the science itself is still nameless, and we can only describe our pursuit by cumbrous and often misleading periphrasis. To meet this difficulty I suggest for the consideration of this Congress the term genetics, which sufficiently indicates that our labours are devoted to the elucidation of the phenomena of heredity and variation: in other words, to the physiology of Descent, with implied bearing on the theoretical problems of the evolutionist and the systematist, and application to the practical problems of breeders, whether of animals or plants. After more or less undirected wanderings we have thus a definite aim in view. (Bateson 1907, 91).

Bateson's visionary suggestion met with approval. The proceedings of the conference, including a printed version of Bateson's address, appeared in 1907 under the alternative title *Report on the Third Conference on Genetics* (Olby 1997, sect. ix). In 1908 Bateson was elected Professor of Biology at the University of Cambridge, from money endowed for "the promotion of enquiries into the physiology of heredity and variation". In 1912 another endowment led to the establishment of the first chair in genetics, the Balfour Professorship of Genetics (given to a close collaborator of Bateson), which was dedicated to the "experimental study of heredity and of development by descent".

As we have already noted, a name, along with professional societies, conferences, periodicals, and chairs incorporating this name, were the conventional insignia of a discipline. Genetics acquired these insignia with astonishing rapidity, despite the fact that it met with widespread scepticism, if not outright hostility, from embryologists and systematists. Two factors fuelled its rapid development. First, genetics could claim to address problems that were of interest to practitioners such as animal and plant breeders, physicians, and eugenicists (Paul and Kimmelmann 1988; Allen 1997). Resistance to the new science was as widespread in these communities as in more academic circles (Palladino 1993; Müller- Wille 2005; Harwood 2006), but the promise of novel solutions to old practical problems certainly contributed to the legitimization of early genetics. Secondly, Mendelism came under fierce attack from a rival group studying heredity and variation, the so-called biometric school, and the violent exchanges with this group furthered the consolidation of geneticists as a disciplinary "tribe", complete with a "myth of origin", referring back to Gregor Mendel's 1866 paper on hybridization experiments with peas (MacKenzie and Barnes 1979; Sapp 1990).

But what was genetics actually about? "Genes", one may be tempted to answer. But the term gene was in fact only coined *after* genetics, in 1909, by the Danish botanist Wilhelm Johannsen (Winge 1958). When Bateson suggested a name for the new field, Mendelians were all but united in the theoretical interpretation of the results of their crossing experiments. Bateson's move was therefore a strategic one, not unlike the branding practices that began to be developed for marketing industrial products at the time (Olby 1997). Genetics thus represents a curious case in which a research object was consolidated only after the creation of the discipline that studied the biological problem space already identified by the community.

When suggesting the name for the new discipline, Bateson emphasized that genetics cut across the traditional compartmentalization of biology by subject matter:

> Sciences follow the plan of developing organisms in that they pass through stages of little differentiation, when parts are still doing the work of the whole. In these early stages inquiry must

> be comprehensive. The worker must be wary of narrowness. While he is engrossed and perhaps lost in the idiosyncrasies of orchids a discovery may be made in regard to peas … which is just what the orchidist requires to clear away his obstacles. Not even the time-honoured distinction between things botanical and things zoological is valid in Genetics. (Bateson 1907, 92)[4]

The metaphor of a developing organism used here unites a very broad and a very narrow conception of genetics. On the one hand, genetics is construed as being merely a contributor to the entirety of biology. In fact, genetics amounted to not much more than a certain experimental technology, the isolation of so-called "pure lines" of model-organisms like *Drosophila* and their hybridization (Kohler 1994). On the other hand, genetics was invested from early on with the potential to pervade all of biology from within. Bateson characterised genetics as the "physiology of descent", an apparent oxymoron, since physiology is concerned with the individual organism, while descent has to do with relations between organisms. Taken together they seem to cover all biological phenomena.[5]

This vacillation between a narrow and a broad conception of genetics comes to the fore nicely in a telling detail in Bateson's letter to Sedgwick. His original suggestion as to the precise topic of the Quick Professorship had been the narrow focus of "Experimental Breeding", but he struck out that term to replace it with the much broader area of "Heredity & Variation". Indeed, classical genetics would never come to terms with the precise nature of its narrower subject area, the "gene" (Rheinberger and Müller-Wille 2004). Yet it always retained its distinctive identity by being bound to complex crossing experiments, even when geneticists like Barbara McClintock or Seymour Benzer reached a level of resolution in their experiments that approached that of molecular biology (Comfort 2001; Rheinberger and Gaudillière 2004; Holmes 2006).

Molecular Biology

The disciplinary identity of molecular biology has a complex history, but the origins of the term are uncontroversial enough. William Astbury had used it in papers published in the 1940s, and in his Harvey Lecture of 1950 he suggested a definition:

> The name "molecular biology" seems to be passing now into fairly common use, and I am glad of that because, though it is unlikely I invented it first, I am fond of it and have long tried to propagate it. It implies not so much a technique as an approach, an approach from the viewpoint of the so-called basic sciences with the leading idea of searching below large-scale manifestations of classical biology for the corresponding molecular plan. (Astbury 1952, 3)

Astbury's doubt that he was the inventor of the term was well-founded, for Warren Weaver had used it first in 1938, in his capacity as director of the natural sciences division of the Rockefeller Foundation:

> Among the studies to which the Foundation is giving support is a series in a relatively new field, which may be called molecular biology, in which delicate modern techniques are being used to investigate ever more minute details of certain life processes. (Weaver 1970, 582)

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[4] Bateson mentions orchids and peas to allude to the fact that Mendel's experiments were not noticed by Charles Darwin.

[5] It may well be the case that Bateson constructed his neologism of genetics simply by dropping the prefixes from "phylogenetic" and "ontogenetic".

Consistent with this technological definition, the Rockefeller Foundation played an important role in funding the early development of many of the technologies upon which molecular biology would depend, such as X-ray crystallography, electrophoresis, paper chromatography, and sequencing (Kay 1993). As Astbury's uncertainty indicates, however, Weaver's use of the term was not widely known even among the recipients of Rockefeller funding (de Chadarevian 2002, 207). During the 1940s and early 1950s the term seems to have been applied diversely. In 1941, *Science* announced that Dorothy Wrinch would conduct "seminars in the general field of molecular biology" (Anonymous 1941, 591) and George Baitsell's 1940 use of the term is also broadly consistent with contemporary interpretations (Baitsell 1940). *The Kinetic Basis of Molecular Biology*, however, dealt in 1954 with such topics as reaction kinetics, bioluminescence, ion transport, and muscle and nerve function (Lumry 1955). In these early uses the adjective "molecular" is used to contrast approaches at that level with more traditional biological approaches.

It was probably only when those engaged in unravelling biological mechanisms at the molecular level started to call themselves molecular biologists that "molecular biology" became a compound noun in which meaning is distributed indivisibly over the whole term. The achievement of James Watson and Francis Crick in 1953 stands out as a defining moment. The research programme to which it gave rise focused on a specific set of biological problems: how genetic processes work at the molecular level. Its participants saw themselves as working in a multidisciplinary way and in opposition to established disciplines such as biochemistry (Wolpert and Richards 1988, 101; Mullins 1972). In part it was the *multidisciplinary* character of their activities, however, that provided its practitioners with a sense of disciplinary identity and a basis for constituting themselves along disciplinary lines.

The structural work carried out at the Medical Research Council (MRC) Unit for the Study of the Molecular Structure of Biological Systems had been classified for some time by the MRC as biophysics, but in 1957 Sydney Brenner had joined Crick to investigate the relations between genes and proteins using phage systems, a project they referred to as molecular genetics. Simultaneously, local institutional factors were stimulating the quest for a broader term for the Unit's activities. Molecular biology provided a way of grouping molecular genetics with protein sequencing (primary structure) and the protein crystallography of secondary and tertiary (and sometimes quaternary) structure. In 1958 the Unit was renamed as the MRC Unit for Molecular Biology (Crick 1967; de Chadarevian 2002).

Equally significant was the launch in April 1959 of the *Journal of Molecular Biology*. John Kendrew, as Editor-in-Chief, had been dissuaded by chemist Paul Doty from using the publisher's proposed title, *Journal of Molecular Biophysics*; Doty argued that "molecular biology will take its place between biochemistry and biophysics and I think have the best of both worlds" (de Chadarevian 2002, 208). Even so, molecular biology as a term still had its opponents. In 1961, Conrad Waddington argued against it, advocating instead "ultrastructural biology" (Waddington 1961). By then, however, he had effectively lost the battle.

The early 1960s saw considerable progress by Marshall Nirenberg, Severo Ochoa, and others towards deciphering the genetic code. By 1963 it was possible for a proposal document from what was now called the MRC Laboratory of Molecular Biology (LMB) to report that "the classical problems of Molecular Genetics … are now understood in principle . . ." (Perutz *et al*. 1963, 5). The authors went on:

> … In the long run Molecular Biology is likely to move towards and become part of Cell Biology. …Control mechanisms and cell recognition and communication must have molecular bases; *therefore the proper direction for Molecular Genetics, and probably for Molecular Biology as a whole, to take is towards these more biological problems.* … (Perutz *et al*. 1963, 7-8; emphasis in original)

Joseph Fruton has argued that the award of Nobel prizes in 1962 to Max Perutz, Kendrew, Crick, and Watson "was the most important factor in the general recognition of molecular biology as a distinctive scientific discipline" (Fruton 1992, 210-11). The prestige and authority conferred on the activities of the MRC LMB was such as to ensure that the research carried out there to a considerable extent defined what molecular biology was. That, at any rate, is one reading. Some question whether molecular biology ever was, or still is, a discipline (Gayon 2006). The redirection Max Perutz argued for above represented a substantial broadening of scope and molecular biology then began to struggle to retain its coherence as a discipline. Perhaps we should say that molecular biology achieved a coherent disciplinary identity for a time following the solution of the structure of DNA in 1953. That defining triumph and the working out of the ensuing research programme over the following decade, effected the apparent union of structural and informational (genetic) schools, but they then began to develop independently. Structural work was increasingly referred to as "molecular biophysics" or "structural biology", an indication that molecular biology may have become too broad a term to be useful.

The advent of recombinant DNA techniques and the rise of biotechnology through the 1970s and 1980s further weakened the discipline, as the techniques it spawned were taken up by other disciplines for their own purposes. "Today we are all molecular biologists" is a familiar refrain (Brenner 1989, 131). Recently, an editorial in *EMBO Reports* described the association of molecular biology with cloning and related techniques as a "strangling limitation", and raised doubts about the institutional utility of the name (Gannon 2002). What is not in doubt, however, is the significance of molecular biology's legacy. One of the technologies associated with its achievements, nucleic acid sequencing, would become the basis for a whole new discipline: genomics.

Genomics

The origin of the term "genomics" is frequently recounted. In their editorial to launch a journal, geneticists Victor McKusick and Frank Ruddle (1987) outlined "a new discipline, a new name, a new journal" with the freshly minted word "genomics."[6] They

[6] McKusick and Ruddle would have preferred to title their journal *Genome*, but a Canadian journal was about to relaunch itself with this name (Kuska 1998). It did, and still exists as do a number of other genomics journals established in the 1990s and early 2000s.

assigned credit for its coining to a burst of inspiration from Thomas Roderick in 1986 during a boozy post-conference evening in Bethesda, in which a group of geneticists played with Hans Winkler's 1920 neologism of "genome" (Kuska 1998). McKusick and Ruddle gave genome a *post hoc* etymology from gene and chromosome, but Joshua Lederberg and Alexa McCray (2001) later pointed out that "ome" more generally signifies the collection of all the parts in a unit and that even in the 1920s there were several "ome"-suffixes in common botanical and zoological use. The Lederberg interpretation now dominates, although some dictionaries still prefer the chromosome derivation of "ome" (e.g.: OED Editors 2004). Roderick emphasizes, however, that the main point of the name was that – like genetics – it was about an activity, not a thing: "a new way of thinking about biology" (Kuska 1998, 93).

McKusick and Ruddle elaborated on the sorts of activities entailed by genomics by specifying that it covered the mapping and sequencing of genomes, the full achievement of which would produce "a rosetta stone from which the complexities of gene expression in development can be translated and the genetic mechanisms of disease interpreted" (McKusick and Ruddle 1987, 1). Both sequence analysis and the revelation of its biological significance fit under the general banner of genomics as well, they argued. Many other commentators agreed on this dual-phase characterization. Structural genomics, or sequencing and mapping, would inevitably lead to the much broader project of functional genomics, which involved "the attachment of information about function to knowledge of DNA sequence" (Goodfellow 1997).

While often commonsensically defined as the study of genomes, genomics can in many respects be better understood as a high-throughput reverse form of genetics (looking for function from genes to phenotype), in contrast to the "forward" inferential strategy of standard genetics from phenotype to genotype (Brenner 2000).The "ics" part of genomics no doubt invokes a relationship to genetics, but was also deemed to indicate the field's closeness to "informatics" and computational science at all stages of the genomics research process (McKusick and Ruddle 1987, 2). In fact, the consolidation of bioinformatics occurred simultaneously with the surge of genomic research, gaining additional impetus from the rise of standards-based network infrastructures, data formats and software environments. From being a specialist activity it became a central element of molecular approaches in the life sciences, and an indispensable adjunct of genomics.

Everyone involved in the early naming process emphasized the inclusion of new technologies in whatever was called genomics (McKusick and Ruddle 1987; Kuska 1998). The rapid development of the field – from the sequencing of single genes and viral genomes in the 1970s to huge plant and mammalian genomes in the 2000s – is widely agreed to owe a great deal to continuous technological refinement. Fast, low-cost automated sequencing was combined with optimized algorithms for sequence assembly, huge increases in computational power and database capacity, and new cloning techniques (Venter *et al*. 2003; Shendure *et al*. 2004; Sanger 2001). These technological advances were then enhanced by regulations for the global sharing of data and methods, as well as new strategies for coordinating the many teams of scientists involved in sequencing projects (Lander and Weinberg 2000; Shendure *et al*. 2004; Collins *et al*. 2003).

These factors were nurtured by the combination of political and economic forces existing in the early days of genomics. They included the 1980 Bayh-Dole Act stimulating academia to commercialize its research findings, the 1980 Diamond v. Chakraborty US Supreme Court case that established the patentability of biological material, and the commitment of funding agencies such as the US Department of Energy and National Institutes of Health to genome sequencing projects. Within a decade of McKusick and Ruddle's inauguration of the discipline, another editorial in *Genomics* proclaimed, "Genomics: an established discipline, a commonly used name, a mature journal" (McKusick and Ruddle 1996, 1). The emphasis shifted from structural analyses to functional and comparative ones – the latter "revolutionizing" evolutionary investigation (Lander and Weinberg 2000).

All of these developments and even the very act of naming genomics were achieved within the overarching context of sequencing the human genome, which was preceded by the (lesser) paradigmatic achievements of sequencing a viral genome (1977) and a bacterial genome (1995). Despite the known viability of sequencing simple viral genomes, the human genome project was not universally supported when first advocated in the 1980s. A meeting in 1986 at Cold Spring Harbor concluded that sequencing the human genome would be a waste of scientific time (Cook-Deegan 1994; Lewin 1986). The shift towards the factory-like production of data for its own sake was a radical departure from the more traditional hypothesis- driven approach that had underpinned the successes of molecular biology (Shendure *et al*. 2004; Roberts 2001). Nevertheless, by 1990, the human genome project and its tantalizing goals proved irresistible for funding agencies, politicians and scientists alike. It was even described as the "holy grail" of genetics and molecular biology (Lewin 1986) and it opened the door to a plethora of sequencing projects targeting diverse model organisms (Collins *et al*. 1998; Danchin 2002).

Throughout the 1990s, research projects and publications proliferated (see Figures 1 & 2), and genome databases more than doubled every 18 months (www.ncbi.nim.nih.gov/Genbank/genbankstats.html).[7] Funding came from a variety of government, private non-profit, and commercial sources. Companies with "genomics" in their names multiplied dramatically in the mid- to late-1990s (Cook-Deegan *et al*. 2000). Numerous professorships and departments of genomics were created (see Figures 1a & b), although many of them shared the departmental name with other disciplines and fields (e.g.: Genomics and Proteomics, Genomics and Bioinformatics, Genomics and Computational Biology).

The "glamour" days of genomics did not last much beyond the end of the 1990s, however, and the completion of the first drafts of the human genome in 2001 appeared to

[7] Genbank statistics show that Moore's Law was obeyed in the growth of sequence data only between 1996 and 1998 (roughly). In earlier and later years, and especially in the periods 1993-1995 and 1999-2001, growth was even more rapid than predicted by Moore's Law.

signal that it was time to rethink the scientific aims and future of genomics (Collins *et al*. 2003). Both scientific and commercial payoffs were questioned. Very few drugs were developed from genomic data, due to the limited biological insight accompanying sequence information (Butcher 2005), and genomics-oriented companies began to change their core business from sequence analysis to more traditional pharmaceutical research (Cook-Deegan *et al*. 2000). For scientists, the continual generation of more "parts lists" was increasingly perceived as an inadequate motivation for further research (Bains 2001; Woese 2004).

As one comparative genomicist said, echoing Brenner's effective obituary of molecular biology, "We are all genomicists now. Whether we like it or not, biology has been transformed" by the global approach to molecular data and analysis afforded by genomics (Doolittle 2004, R177; Rossant 2000). The pressing question at the end of the twentieth century became, "transformed into what?" Already in 1997, McKusick had noticed an increasing demand for a systems approach – "more integrated and integrative" – for which DNA would be a "common language." This general shift in scientific and commercial mood prompted a reconceptualization of genomics and the incorporation of its data and technologies into the much broader enterprise of systems biology.

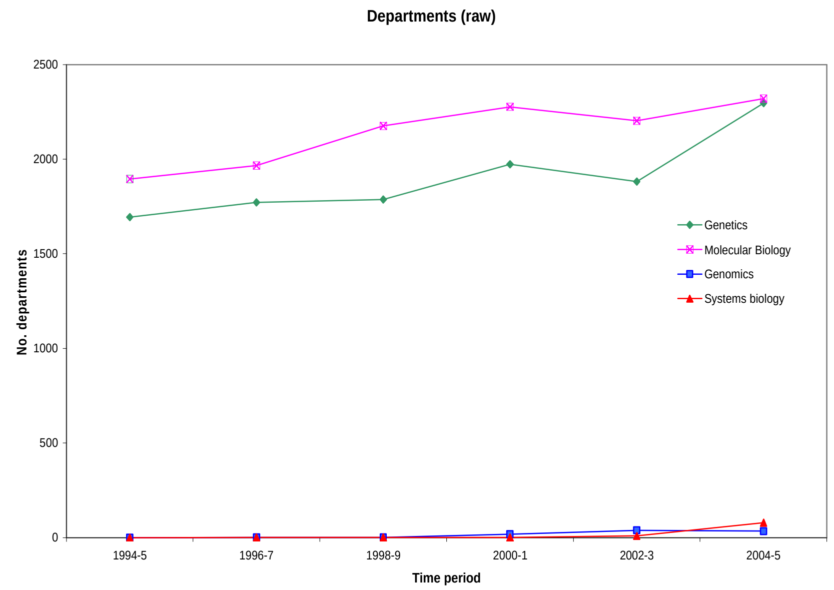
Systems Biology

There is, as yet, no single story of the origin of the term "systems biology", but the application of systems theory to biology has been attempted for several decades. For example, in a 1950 paper Ludwig von Bertalanffy noted that "the characteristic state of the living organism is that of an open system" (1950, 23). Although he did not use the term "systems biology", his focus was on the system-level properties of biological entities. The interaction of systems theory and biology attracted a great deal of attention from other researchers in the 1960s (Wolkenhauer 2001), but interestingly none of their attempts was successful in establishing a new scientific discipline. The mathematical models that were developed were too abstract to be linked to specific biological problems, in part because they had been constructed by theorists who were not particularly interested in tangible biological phenomena (Kitano 2002).

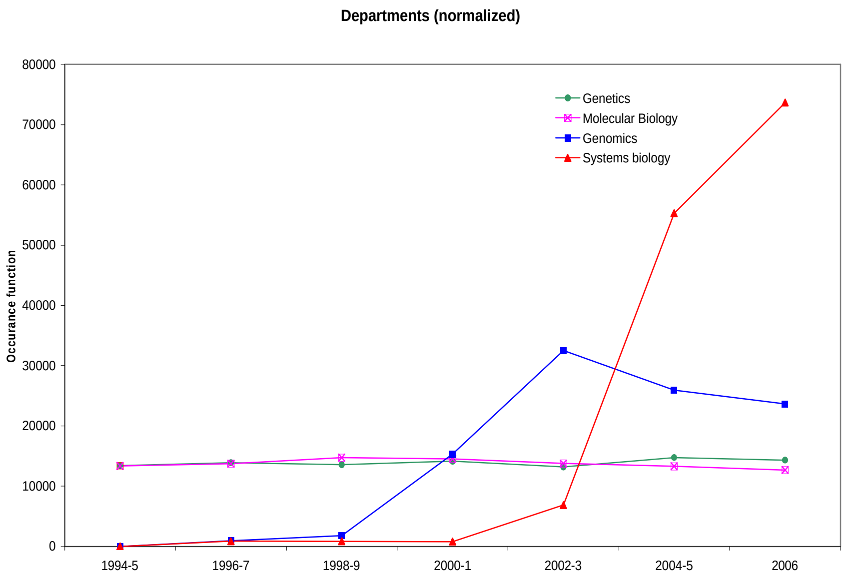
Today there is a rich supply of genome, transcriptome, and proteome data which was not available to these early "systems biologists". There are also new experimental methods which allow the simultaneous measurement of multiple components. Computational processing power has increased exponentially over the last 50 years and this processing power, combined with suitable algorithms and software environments, now makes it possible to apply abstract mathematical models to complex biological systems (Ideker *et al*. 2001a). What is often meant by "systems biology" today is the attempt to make sense of the vast amounts of data that have been accumulated by the genome sequencing projects and other data-gathering exercises. The nascent discipline studies "biological systems as systems" (Kitano 2002,1) and, in common with the other disciplines discussed in this paper, uses a set of tools and techniques that can be applied more broadly. Its distinctive technological character comes from the combination of computer modelling with high-throughput "omics" techniques (e.g.: microarrays, mass spectrometry, sequencing). Both these methods pre-date systems biology, but their combination allows powerful new analyses to be undertaken.

Fig. 1 - **Number of departments.** We searched PubMed for the occurrence of disciplinary terms in the affiliation field. Query terms took the form “Department of X,” where X was genetics, molecular biology, genomics or systems biology. On the assumed basis that Departments are a good indicator of disciplinary consolidation and relative trends, separate searches were not conducted for, say, Centres or Institutes.

(a) Raw data: number of publications returned matching the affiliation query term.



(b) ‘Normalized’ data. The raw data displayed in (a) were normalized with respect to (i) the time period for which the total number of matching publications (summing across all query terms) was greatest (2004-5), and (ii) the query term yielding the highest number of matching publications (molecular biology). This process has the effect of compensating for the overall growth in number of publications with time, and minimizes differences in occurrence frequency between terms so as to show general trends among the terms.



Systems biology is still in its infancy and it is not obvious who is responsible for the name of the discipline. Some sources say that Leroy Hood, a pioneer of systems biology and inventor of the first automated sequencing machine, coined the term in the 1980s (Schaffer 2005). Hood himself says that he was using the name at this time, although he does not think he invented it because it had “been around for a long time” (Hood, personal communication). In a publication in the early 1990s, Hood says “the future of biology will depend upon the analysis of complex systems and networks”, which will require computer modelling (Kevles and Hood 1992, 149). This undoubtedly captures the spirit of today’s systems biology, but although the word “systems” appears, the phrase “systems biology” does not.

Hiroaki Kitano, the leading figure in Japanese systems biology, has a different take on the origin of the term. He says that he decided to use the term in the mid 1990s to put the emphasis on understanding a system as a whole (Kitano, personal communication).[8] Even though there is as yet no consensus about the definition of a biological system (O’Malley and Dupré 2005), the very act of naming the discipline allowed a demarcation of epistemological territory and provided a rallying point for life scientists anticipating a need to go beyond genomics. Kitano says that systems biology is preferable to alternative terms such as “virtual biology” and “computer-aided biology”. His view is that if the name of a discipline is associated only with a particular technology it will not persist. Systems biology is therefore an excellent end-of-the-century illustration of the shift in disciplinary demarcation that began at the end of the nineteenth century. The ontological focus has disappeared (systems can be almost anything) and a broad epistemological approach is generally agreed upon as fuzzily establishing the boundaries of systems biology.

Kitano emphasizes that for a new discipline to be successful it has to have “100 fathers”, by which he means a large group of people who will assume ownership of the field. He also points out that an important step following the naming of a discipline is the lobbying of governments to start funding the research. This lobbying appears to have been successful, for in the last five years there has been a rapid rise in the numbers of international conferences, chairs, departments, institutes, and journals dedicated to systems biology. It must be noted, however, that the number of departments today carrying the name “systems biology” is very small relative to the more established disciplines – an indication that institutionalization is at an early stage (Figures 1a & b). Bibliometric counts of publications with “systems biology” in the title or abstract show very rapid growth since the mid-1990s (Reiss 2005; Bork 2005; see Figures 2a & b).

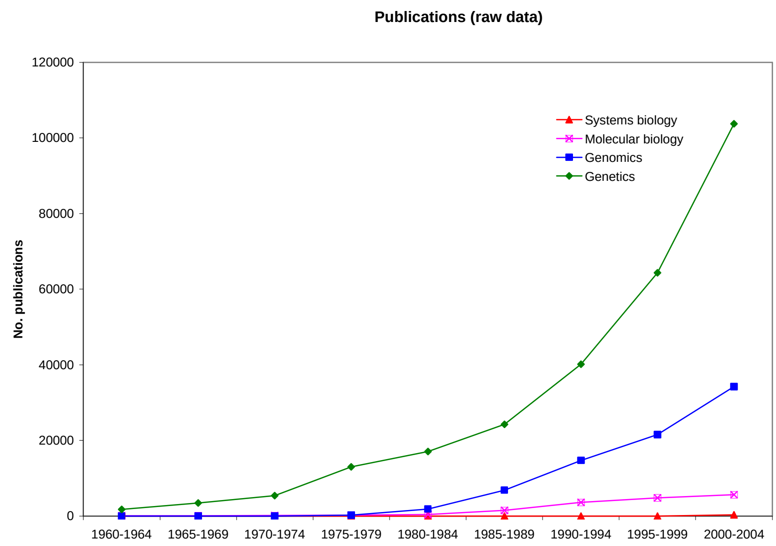
As yet, systems biology can claim no paradigmatic achievement akin to Watson and Crick’s elucidation of the structure of DNA, but the modelling of galactose utilization pathways in yeast (Ideker *et al*. 2001b) could be seen as proto-paradigmatic or a proof-of-principle demonstration that systems biology is viable. Something that would constitute a paradigmatic achievement would be a complete *in silico* model of a cell, although many systems biologists think that this is not something they will see in their lifetimes. As in the case of genetics, systems biology is directed towards a well recognized but broad

[8] There is no agreement amongst leading systems biologists about who should be credited for initiating the development of the field.

scientific problem: specifically to the questions of how to make scientific progress with specialized bodies of data and how to be seen to be doing so even outside the immediately relevant scientific community.

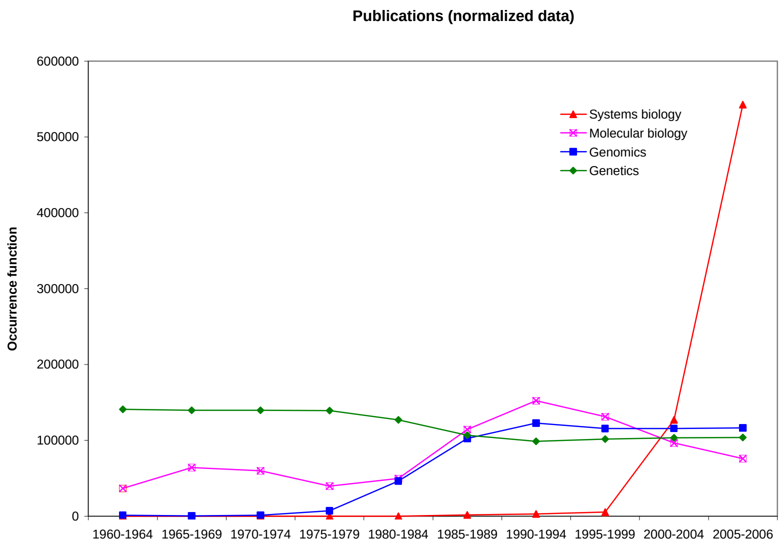
Fig. 2 - **Occurrence of disciplinary terms in PubMed**. Searches were limited to titles and abstracts for each five-year time period. Data have been grouped by discipline: for example, data for "molecular biology" were obtained summing the results of independent searches for "molecular biology" and "molecular biological." (Systems biology = systems biology + systems biological + computational biology; genomics = genomics + genomic; genetics = genetics + genetic.)

(a) Raw data: number of publications matching the query term



(b) Normalized data

The raw data displayed in (a) were normalized in the same way as for Figure 1(b). The total number of term occurrences was greatest for 2000-2004 (data for 2005-6 represents a partial time period) and the most frequently occurring query term group was genetics.



Despite systems biology's recognition and growth, a number of scientists object to the term and have proposed alternatives. A partly successful rival term is "integrative genomics", which has been adopted at Princeton University. The term "integrative biology" is also popular and the UK's Biotechnology and Biological Sciences Research Council (BBSRC) tries to have it both ways by calling their institutes Centres for Integrative Systems Biology (BBSRC 2005). An editorial from *Molecular Systems Biology* suggests "postgenomic biology", "quantitative biology", and "molecular physiology" as candidates (Aebersold 2005). This last term is connected to arguments that systems biology is merely "physiology with advertising" (see Strange 2005). Such objections come from people who are reluctant to introduce new terms for activities that they believe are continuous with previous work. For example, the Norwegian University of the Life Sciences (2006) proposes the label "integrative genetics" in order to "pay due credit to the immense efforts and achievements of the genetics community". Systems biology's success as a coherent discipline is unlikely to depend on whether scientists can agree to unite under a single origin story, but the name itself is certain to be deeply implicated in any coherence that is generated.

Discussion

Do our case studies tell us how disciplines emerge and institutionalize? One of the most obvious characteristics of these disciplinary histories is the seeming plasticity and variability of the process. Some commentators see a clearly defined sequence of stages in the development of "object-oriented" disciplines over the nineteenth and twentieth centuries (Wolf and Hausmann 2001; Guntau and Laitko 1987). They describe early phases which cover the discovery, description, and naming of the discipline's objects, followed by a theoretical phase, after which the more socially defined phases of "constitution," "establishment", and "consolidation" occur (Wolf and Hausmann 2001, 464).[9] This pattern is not reproduced in our four case studies. As origin stories are generated and deployed during the institutionalization of a discipline, the intended scope of the discipline is adjusted in order to facilitate further consolidation and allow integration of nearby fields and techniques. Naming, paradigmatic achievements, definition, and conceptualization of subject matter, methodological precepts, technological dependencies, and social formation are very much contingently related to one another, with disciplinary attributes succeeding one another in no obvious order.

Naming plays a highly variable role in this process. Sometimes the name comes before the object is defined (genetics), the approach and name may precede the social formation of the discipline (molecular biology), the name and social formation may coalesce before major achievements (genomics), or the name may come into being even in the absence of any of these factors (systems biology). Individuals with naming power and audiences for the names vary tremendously, but a critical point seems to be reached in which a name is considered to be central to achieving further scientific coherence. Despite this variability, a number of common themes emerge from the case studies and their discussion may cast light on disciplinary formation in the twentieth century.

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[9] See Lemaine *et al*. (1976) for a much more tentative sequence of events in disciplinary development.

Openness of definition

All of our disciplinary names are marked by the openness and multifunctionality of their definitions. An editorial for the journal *Molecular Systems Biology*, in a reflection on the name "systems biology", points out that "Perhaps surprisingly, a concise definition of systems biology that most of us can agree upon has yet to emerge" (Aebersold 2005,1). However, it is not clear why this should be surprising: as many commentators have pointed out, a vague definition with fuzzy boundaries is capable of including a multiplicity of actors and may in the long run be more successful than a tighter definition of a scientific field. The attractiveness of genomics, for example, lies at least in part in its susceptibility to "definition creep" (Cook-Deegan *et al*. 2000) and its application in numerous scientific and commercial contexts.

As Bowker and Star (1999, 324) point out in respect to classification in general, "Classification schemes always represent multiple constituencies. They can do so most effectively through the incorporation of ambiguity – leaving certain terms open for multiple definitions". It would therefore be counter-productive to attempt to define a discipline too rigidly. To be successful, the name must be flexible in its interpretation by individual actors but must also constitute a common basis of communication both inside and outside of the emerging discipline. Genetics seems to have embodied these qualities very effectively and therefore endures even now, more than a century after its inception. Such "effective ambiguity" creates elastic disciplinary borders which are able to accommodate unexpected research findings and new techniques – at least up until a certain point, where the increasing strain of accommodation leads to the development of new boundaries and labels. Genomics, which might reasonably be thought to be defined by a specific object, the genome, was not so defined and had increasingly to incorporate all manner of high-throughput analyses within its epistemological remit. When that became too encompassing, a new stage of inquiry was sought and possibly found in systems biology.

The import and export of multiple techniques and approaches also has the potential to weaken the identity of a discipline: the later history of molecular biology provides an example of this (in contrast to genetics). And names that are highly polysemous and yet too anchored in a particular technology, such as "computational biology", cannot "fix" a particular research activity as a discipline, no matter how identifiable the approach. There is a balance to be struck, then, between scope and flexibility on the one hand and distinctiveness and coherence of identity on the other.

Interplay of technology and disciplinary approach

We noted in the introduction that many traditionally defined disciplines arose from specialization around the objects of study, whereas twentieth-century disciplines seem to depend much more on particular technologies. Common to our four cases is an emphasis on the technologies introduced, refined, and made centrally important by the new discipline alongside an approach or "mindset" – a new way of conceptualizing and working with the biological subject matter. Neither appears to be sufficient by itself and they are related in complex ways. In genetics, for example, the ongoing interplay between a narrow technique (experimental breeding) and a broad aim (the "physiology of descent", as Bateson put it) informed both the origins and subsequent development of the science. Weaver saw molecular biology primarily in terms of the application of techniques, but Astbury maintained that the new field is "not so much a technique as an approach" (1952, 3). His comment foreshadows Kitano's point that naming a field in terms of a specific technique is not a good strategy for long-term success and that the name should instead draw attention to how the field conceives of its problems.

Some scientists believe that technologies alone are insufficient for forming a new discipline – a position that appears to stem from the belief that technologies are less epistemically "fundamental" than the scientific aims and assumptions they help to articulate. That is, tools do not in themselves elucidate the phenomena to be understood, and hence technologies should be subservient to, rather than determinative of, scientific concerns. Even if technology on its own is not enough, it is clear that technological developments play an essential role in the growth of scientific understanding. The expansion of disciplines such as those explored in this paper tends to be accomplished by specific technologies that can be diffused to, or adopted by, multiple lines of investigation. Their adoption enables different groups of investigators to form self-coordinated social entities. Simultaneously, however, their activities must represent the expression of broader motivations, less constrained by immediate technological possibilities, if a new discipline is to be constituted. In the case of genetics, the overall aim of explicating heredity, variation, and even development was and is the driving force. In molecular biology, the novel thesis was that biological issues would most profitably be addressed and explained at the molecular level. Genomics has a dual-phase approach that sets out sequence structure as the first objective, with the more meaningful function to follow on these earlier (and easier) achievements. The perceived need for the technologically driven acquisition of genomic data to be transformed into proper biological understanding is at least partly behind the push towards systems biology.

Synthesis of reduction and integration

Both genetics and molecular biology have been renowned and criticized for their reductionist stance. Astbury, in his Harvey lecture definition, articulates what are often thought of as the powerfully reductive aims of molecular biology. More recently, however, some authors have put forward strong arguments that molecular biology and genetics never really abandoned a comprehensive biological agenda. "Genetic theories are theories of development", James Griesemer argues, "but they are theories expressed in terms of developmental invariants" (2002, 261). Even the analytic business of molecular biology was never wholly divorced from more synthetic integrated reasoning (Buc 2006; Gannon 2002). Similarly, genomics succeeds as a discipline rather than a technology only to the extent that it does not emphasize sequence structure at the expense of function. And although systems biology is conceived of as being essentially integrative, it too is heavily dependent on the analysis of components and their low-level properties.

This perspective on practice and interpretation suggests that biological understanding always combines analysis and synthesis,[10] and that such combination may be mandated more explicitly for recent biological disciplines. The twentieth-century trend towards discipline formation on the basis of "styles of reasoning" can itself be interpreted as such a synthesizing move on the level of institutions. After a period in which disciplines arose through an analytic process of sub-division and specialization, a phase of synthesis occurred in which new disciplines addressed themes that cut across existing disciplinary divides. It seems likely that some of this "orthogonal" disciplinization can be attributed to the discovery of deep underlying commonalities in organisms, for example regarding cellular mechanisms or biochemical processes. These provide new and shared bases for investigation that become the targets of theoretical and empirical work, as well as of medical and industrial applications. Such investigation builds on or may stimulate the development of particular technologies in ways sometimes capable of stabilizing new disciplinary configurations.

Social connections and interactions

A final and notable feature of our four twentieth-century disciplines is the variety of ways in which they engage with other social institutions. Gibbons and colleagues (1994) have put forward a historical schema in which traditional disciplinary knowledge production, isolated from social influences ("Mode 1"), leads to "Mode 2". In this more recent mode, knowledge production is interdisciplinary and closely connected to wider society. As some critics have noted (Weingart 1997), such a schema misrepresents the highly interactive nature of scientific disciplines throughout their histories.

All four of our disciplines have developed and are developing by establishing strong connections with a range of social institutions including other disciplines and academic specialities (e.g.: genetics with plant breeding and statistics; molecular biology with biochemistry and genetics), non-profit institutions (e.g.: philanthropists funding genetics, non-profit organizations funding genomics and systems biology), commercial interests (e.g.: agricultural firms and plant genetics, biotechnology companies and genomics), and government funding (e.g.: the transformation of genomics into big science by huge amounts of government funding). Although the role of funding agencies in consolidating a discipline around a name is most noticeable in the case of genomics and systems biology (and that increased role may be a key difference between disciplinary formation in the early and later parts of the twentieth century), we think it is clear that social links are important to disciplinary success at any period of scientific history. Individuals may not often say, "I am a genomicist" or "I am a systems biologist," but they will very frequently be referred to as such by general scientific journals, funding agencies, and institutional publicity. These links are enhanced by naming stories that speak generally to broader audiences, including medicine and industry, about the aims of the new discipline.

[10] See O'Malley *et al*. (forthcoming) for a more detailed discussion of this point in relation to synthetic biology.

Conclusion

The key finding of our investigation is the consistent importance but variable role of naming for a discipline and the apparent recognition by scientists of the performative power of such naming. Disciplinary formation is so diverse and ongoing development so variable that names are one of the few factors capable of providing and maintaining disciplinary identity. The need to come up with a name is an indicator of discipline-forming pressures already building up but the way in which that name is conferred and by whom is highly variable. Although names may be coined for personal, professional, economic, political, and intellectual reasons, they must connect effectively with developing research activities and problems, as well as announce some sort of progress to the world outside the pertinent scientific community.

The feasibility of a variety of actors and technologies being named as a discipline depends on a constellation of factors, but once names are given to these constellations, another level of interplay (within and without the new discipline) is introduced. The act of naming is itself a reflection on and articulation of problems in earlier disciplinary structures and implies the vision of a solution and a new aim for the disciplinary area. Techniques, technologies, and methods are given coherence by a broader, more abstract articulation of an overall approach, of which the name provides a constant reminder. Once a name begins to stick, even to a fairly shallow basis, it can have a reifying and cumulative effect. Systems biology, for example, while both the recipient of enormous amounts of funding and the label bestowed on proliferating research institutes, exemplifies how a name unites and gives social strength to a broad array of technologies and intertwined methodological and epistemic practices, even when that array lacks an established paradigmatic core.

Conferring disciplinary status on such a loose basis might seem problematic. It reflects scientific practice, however, in which achieving disciplinary status is a matter of assertive rhetoric, social recognition, and appeal to funders. There certainly needs to be a basis of practice and achievement on which to hang the name, but the name works almost as a marketing tool. The advertising industry operates entirely on the strength of this recognition, but what is a little surprising is that such strategies appear to have developed in the sciences even as early as the first decade of the twentieth century.

A useful way to expand on this finding would be to trace the histories of failed disciplines – the many and varied attempts throughout the history of science to unite combinations of approaches and tools under one banner in order to achieve the greater influence and stability of disciplinary status. We have already mentioned some of these failures: general biology at the end of the nineteenth century and systems biology between 1950 and 1980. Other comparative cases could be apparently successful disciplines (or proto-disciplines) to which alternative names did not adhere. A nice example of this is the defeat of “intentional biology” by synthetic biology (Carlson 2006). Moreover, the “dissolution” of a previously successful name, as in the case of molecular biology, may be as interesting an element of disciplinary history as its creation. There is obviously a great deal more work that could be done in comparative histories of disciplines and, even if no theoretical framework is likely to unite such studies, such research will enrich the history of science and its understanding of how science develops.

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