

A Comment on the Symposium Papers on “The Tools of the Discipline: Biochemists and Molecular Biologists (1945-1975)”^{*}

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Introduction

I am grateful to Soraya de Chadarevian and Jean-Paul Gaudillière for the invitation to comment on the papers in this special section of the *Journal of the History of Biology* and to the authors for providing such rich and richly interlocking papers. The symposium, building on recent traditions of examining “the right tools for the job”¹ and studying local cultures in science,² opens up a number of lines of work particularly worthy of pursuit over the next few years. Accordingly, I will concentrate on some larger themes deserving further exploration rather than the details of the papers.

It may help to highlight some the threads woven into the rich tapestry of case studies presented above. I hope these serve as Ariadne’s threads, encouraging readers of *JHB* to address some larger issues raised by the work done in this symposium. Some of the issues are, of course, specific to post-war biochemistry and molecular biology, but others, I will suggest, are of quite general interest and transcend the specificities of these particular disciplines. [‘Disciplines’? That, itself, raises one of the questions that we must face.]

Commonalities

All four papers focus on the development of ‘local cultures’, on the roles that those cultures play in channeling scientific work, and on exchanges between local cultures. Typically, the local cultures are at the level of a department, a laboratory, or a working group, sometimes a larger institution, but always units within which multiple tools and approaches are employed and within which tensions exist between workers with different backgrounds, training, or disciplinary allegiances. The exchanges between local cultures are multi-leveled. They include circulation and improvement of techniques and equipment; employment of common tools such as ultracentrifuges, radioisotopes, and

* Submission version of Burian, Richard M. 1996. “The tools of the discipline: biochemists and molecular biologists’: A comment.” *Journal of the History of Biology* 29: 451-462.

¹See, for example, *The Right Tools for the Job: At Work in Twentieth-Century Life Science*, ed. A. E. Clarke and J. H. Fujimura (Princeton: Princeton University Press, 1992), and the special section on “The Right Organism for the Job,” *J. Hist. Biol.* 26 (2) (Summer, 1993), 235-367, ed. M. Lederman and R. Burian.

²See, e.g., the papers by Gaudillière, Kevles, Rheinberger, Uchida, and Burian in *J. Hist. Biol.* 26 (3) (Fall, 1993). The topic is a rich one with a rapidly growing literature.

sequencing techniques; exchange of organisms; and circulation of personnel among virtually all of the institutions studied in the foregoing papers. Important exchanges occur between bench workers who employ similar or overlapping techniques or the same or similar organisms, working groups, laboratories, people who have formulated conflicting hypotheses, people from competing or cooperating units or who attend the same meetings, workers from different ‘subdisciplines’, workers from different disciplines whose views about some problem(s) or hypotheses are in fundamental conflict, heads of laboratories and their institutional superiors or external sponsors, etc. The complex issue of delimiting the ‘networks’ involved here, but also of developing, defining, and delimiting the ‘problems’, ‘experimental systems’, ‘reliable methods’ ‘disciplines’ ‘issues’ and ‘aims’ at stake are key aspects of the study of ‘local [scientific] cultures’.

Local cultures, of course, must be placed within larger cultural contexts. These are even more heterogeneous than the above lists suggest. They may be institutional cultures (very different at, say, the California Institute of Technology, the Massachusetts General Hospital, the Cavendish Laboratory, the *Institut Pasteur*, and the *Université de Strasbourg*). They include disciplinary cultures. They surely include the cultures of sponsoring agencies or within which those agencies are embedded. Thus, the fact that a particular line of work was supported by the Rockefeller Foundation in the 1940s already tells us something about how it was articulated and evaluated as compared with work sponsored by, say, the NIH or the MRC in the 1960s. And there are national cultures. The authors of our four papers contextualize local cultures differently (some of the differences will be explored below). But they are all agreed, I believe, that proper understanding of a local culture requires proper contextualizing of that culture within some set of larger cultures. The word ‘proper’ in the previous sentence points to one of the problems on which we will focus: like delimiting ‘disciplines’, the attempt to find the ‘appropriate’ or ‘proper’ means of contextualizing a local culture to assist us in understanding the work done by those who worked within it raises difficult, ill-understood, and consequential problems.

Differences

There are, of course, major differences among our authors and their cases. These concern more than the details of the case studies; they go to the ‘stories’, the implicit analyses of historical causation or historical importance, and the broader morals to draw from those cases. Angela Creager, in her study of the attempt to establish a biochemistry department freed from a predominantly service mission under Wendell Stanley at the University of California, Berkeley, focuses on choices regarding central problems, methodologies, and subjects of investigation (e.g., macromolecules and viruses rather than bioenergetics and cell metabolism) and on the institutional issues at UC Berkeley associated with developing an institutional base for the would-be or forming discipline of molecular biology. She articulates the issues regarding choices and institutionalization primarily in terms of differences *among biochemists* (i.e., people who called themselves *biochemists* and who belonged to departments or professional societies of biochemistry). Creager discusses the elaborate institutional structure of the relevant sciences at UC

Berkeley and the strong bases already established for outstanding biochemists in quite different units, with all of the corresponding perquisites, allegiances, jealousies, commitments, and so on, all of which served as obstacles to the formation of a unified or umbrella-style free-standing biochemistry department including all of the major players involved (both institutional and individual). In addition, she examines the important role of patronage and sponsorship — including the Rockefeller Foundation, the State of California, and various federal and private agencies — in providing the enormous physical and material resources which Stanley was able to mobilize by means of which to reshape various aspects of the mission of his department and the virus laboratory.

In this complex setting, it eventually became necessary to establish a firm institutional differentiation between the virus-centered, macro-molecule centered, research mission-centered Virus Laboratory (later Department of Virology), allied to Stanley, and the Department of Biochemistry (which he founded) and other biochemical units and enclaves at Berkeley. All this greatly influenced the local institutional definition of molecular biology, as opposed to biochemistry. During the early 1960s, when the institutional differentiation between biochemistry and molecular biology took shape at UC, Berkeley, many of the elaborate and expensive tools that had earlier been the special property of Stanley and his group became relatively widely available in ‘black box’ form from commercial and federal sources and were widely used in biochemistry and (would-be?) molecular biology laboratories all over campus. The new availability of instrumentation appropriate to the study of proteins and amino acids, of nucleic acids and nucleotides, altered the local context in such a way that differentiation among groups with access to the tools for such work became even more pressing than it already was. Together with other aspects of Creager’s account, I take her to hold that local institutional politics and allegiances played at least as important a role in delimiting the differences between biochemistry and molecular biology at UC Berkeley as methodologies, problem choices, and pre-existing disciplinary allegiances. Perhaps the best shorthand for this claim is that local institutional factors were dominant in demarcating the differences between biochemistry and molecular biology at Berkeley.

In contrast, despite many important parallels between Creager’s account and Soraya de Chadarevian’s account of developments at the Cavendish and various MRC-sponsored units, I take de Chadarevian to place greater stress than Creager on *interactions between “‘political’ negotiations [with sponsors and at the institutional and disciplinary levels] and those on the bench level”* [MS p. 2, my emphasis]. In other words, for her (or for the Cavendish as opposed to Berkeley?), what is critical is the connection between what happened at the bench in intra-institutional collaborative networks and the “institutional and disciplinary developments propelled by the same people” [MS p. 2]. Thus, in the British setting (which traditionally placed less emphasis on collaboration than the American one), the formal assignment of a worker engaged in collaborative work within the MRC Unit for the Molecular Study of Biological Systems presented an interesting political problem in 1962, when the unit moved to from the Cavendish to the new Laboratory of Molecular Biology.

As de Chadarevian points out [n. 46], after some negotiations Edmundson, who had come to work with Kendrew on the sequencing of myoglobin in 1960, was not placed in the division of protein chemistry under Sanger, the sequencer *par excellence*. (Although he joined the MRC lab in 1962, Sanger, of course, had been based in the

Department of Biochemistry, not the Cavendish or the MRC Unit, though he was also funded by the MRC.) Even though Edmunson’s research problem was appropriate to the division of protein chemistry, he was eventually assigned to Kendrew’s new division of molecular genetics, partly because of the importance of the particular project to Kendrew’s division. Part of the problem may be that a project that would formerly have required inter-institutional collaboration (between Biochemistry and the Cavendish) could not yet be handled comfortably as an intra-institutional collaboration. Be this as it may, on the accounts we have been offered in Creager’s and Chadarevian’s papers, such an issue concerning intra-institutional collaboration appears less likely to have been critical at Berkeley. For present purposes, it is particularly important to note that, as de Chadarevian shows, problems of this sort in the MRC unit were closely connected to issues ‘on the bench level’ — e.g., disagreements over the value and appropriate use of automated sequencing instrumentation and the integration of such work with x-ray crystallography. It appears that such issues were reflected in differences between the divisions in question.

In spite of the obstacles to cross-unit collaboration, de Chadarevian’s account suggests that (as it happened) the MRC Laboratory of Molecular Biology had done much more preliminary work in the 1950s suited to foster the development of interactions between genetic and [sequencing-related] biochemistry in the early 1960s than, on Creager’s account, had been done in Berkeley. De Chadarevian connects this consequential preadaptation to a complicated politics of funding, naming, and neighboring,³ a politics of both networks and disciplines [MS pp. 19 ff.] favoring the outcome of closer intra-institutional cooperation between units (built up slowly on the basis of specific collaborations) in the new MRC Laboratory of Molecular Biology, opened in 1962, than occurred in the Berkeley Biochemistry and Virology Departments. If this characterization is fair, the question of why and how the ‘federation’ (de Chadarevian’s word for the new MRC laboratory) came to forge new cross-disciplinary and cross-unit bench networks among crystallographers, sequencers, and geneticists, albeit slowly, in ways that Stanley’s Department of Biochemistry and Virus Laboratory did not [in spite of his attempt to employ viruses as the central organisms and to focus on macromolecules] is precisely the sort of puzzle, rooted in the particularities of the cases, that calls for general examination. We should seek to go beyond mere particularities to understand how such an outcome was achieved, though this search may prove fruitless.

The differences flagged in the last two paragraphs are all the more striking in light of the closeness in time between the formation of the MRC’s and Berkeley’s Department of Molecular Biology (for which the planning committee was formed in 1962) and the extent to which parallel institutional issues affected the planning of these two units. In contrast, Hans-Jörg Rheinberger’s comparative study of work on protein synthesis in the laboratories of Ernest Gale and Paul Zamecnik terminates in the early 1960s, before the sorts of institutionalization of molecular biology just discussed were achieved. Rheinberger’s paper is less concerned with institutional settings than the previous two studies; rather, it concentrates on what he calls ‘experimental systems’. Together with

³Supplemented by a tendency in the culture of the Cavendish that she mentions, but does not discuss explicitly, to hold informal seminars and discussions on particular problems of interest to a given group outside the normal work schedule and ignoring the boundaries between units.

many other aspects of local cultures, including bench practices, access to instruments and funding, institutional settings, and disciplinary politics, Rheinberger highlights the importance of differences between experimental systems. Such systems are, of course, the product of many years’ labor and must be built in stages with no clear assurance whether they will peter out, lead into blind alleys, or pay off handsomely, whether they will answer the questions for which they were designed or transform the work from one orientation to another. One reason that work on protein synthesis in the early 1950s appeared to be a “maze [from] which there seems to be no easy way out” [MS p. 2] was the inadequacy of the experimental systems then available to handle the specific tasks required. Of course this inadequacy is closely allied to conceptual problems — no one had an adequate account of precisely what tasks *were* required! — but it is crucial to Rheinberger’s argument that the open-ended character of experimental systems is intimately tied to the openness of the problems that they are used to address. Equally crucial is his claim that the development of the system forces reconceptualization of the problems it can face — that the very regularities of a well developed system, combined with the particularities of what it is and is not sensitive to, constrain and alter the tasks it can and it cannot perform. Thus, experimental systems acquire features that play an enormous role in shaping the conceptual as well as the technical articulation of the problems dealt with, thus affecting the powers and limitations of the people working with those systems to deal with problems of certain classes.

Interestingly features of different systems, some of which have come to be understood in hindsight, sometimes allow us to understand, after the fact, why or how they could aid in the generation or resolution of certain questions and not others. This is not only because they bring with them and require certain technical practices (though that is always important), but also because of various features of the experimental systems not recognized *ab initio*, features sometimes uncovered by the investigators who developed the system and sometimes not. Often key features (or key sensitivities to disturbance) of an experimental system are not recognized for many years and then only in the light of findings in an unexpectedly cognate area.

For example, in his conclusion, Rheinberger points out that the high rate of metabolic turnover in Gale’s system, based on *Staphylococcus aureus* unexpectedly made it enormously difficult to develop *in vitro* (as opposed to *in vivo*) assays of the sort technically required at the time in order to reconstruct the steps in protein synthesis and that this particular disadvantage was (in a sense fortuitously) escaped by those who employed Zamecnik’s rat liver cell-based system.⁴ In this study and in much other recent work, Rheinberger emphasizes the extent to which scientists and sponsors must invest in experimental systems when they attempt to address large-scale problems (such as that of protein synthesis or the genetic code) and that such systems typically lead scientists into uncharted territories. This perspective surely deserves greater exploration in studies of the institutionalization of research and of disciplines, of the relationship between sponsors, patrons, granting agencies and the scientists whom they fund. Thus,

⁴Other features of this sort (e.g., the presence of much more RNase in bacterial than in rat liver cells) are highlighted by Rheinberger in various places. These points will be amplified in his *Experimental Systems, Difference, and Writing. Towards a History of Epistemic Things. The in vitro synthesis of Proteins* (Stanford: Stanford University Press, in press).

experimental systems should be included in the list of factors that interact with the larger context. They must be taken into account in our effort to understand how local scientific cultures mesh with larger cultures and gain support. Beyond this, since there are many ways in which experimental systems exhibit ‘a life of their own’ and force scientists to alter their practices and commitments, they must be seen as having sufficient independence to alter the culture into which they enter. This need not, I claim, make them agents (or even *actants* in Latour’s and Callon’s terminology). In any event, we have here a nice illustration of the difficulty in delimiting the heterogeneous list of contextual factors that bear on, and alter, the shape of local cultures. The recognition that experimental systems have autonomous properties that must be uncovered, and that they significantly affect prospects for sponsorship, and lead laboratory groups to important shifts in practice is thus consequential far beyond the confines of these case studies.

To close this section, consider briefly some general points from Jean-Paul Gaudillière’s treatment of the formation of a multi-institutional network of scientists working on various properties and functions of RNA, especially mRNA, in France in the late 1950s and early 1960s. Like de Chadarevian, Gaudillière traces the interactions between “changes of practices and their relation to the formation of disciplinary commitments” [MS p. 3]. The network of RNA workers he examines is more inter-institutional and more explicitly caught up in negotiations over government funding than the networks at the focus of de Chadarevian’s attention. Here too, we see the definition of ‘molecular biology’ adapted to the particular strengths available locally (in the Pasteur Institute, and various institutions connected informally with it) and the attractiveness of particular lines of work to particular sponsors (including the Rockefeller Foundation, the NSF and the NIH) — but also, thanks to the high degree of state management of science in France, nationally. As in Berkeley, the attempt to establish autonomy for RNA research and the would-be discipline of molecular biology (to ‘demedicalize’ them [MS p. 8]) also played an important role in the politics of the planning for work on RNA. But, far more than the other studies, Gaudillière’s concerns the circulation of analytical tools among individuals and laboratories in different institutions, groups engaged on distinctive programs of research of their own. This sharing of materials, methods, and instrumentalities helped bind together a network of workers with rather divergent interests, a network whose organization he analyzes elegantly.

Partly because of the larger French cultural setting this network worked differently than it might have in England or America. The obverse of the central control of scientific research in France is the autonomy of laboratory directors and research programs, once funded. This heightens what Gaudillière calls “the continuity of local practices” [MS pp. 24 ff.]. Thus the research programs of Jean-Pierre Ebel (organic chemistry of tRNA), François Gros (‘short pulse’ experiments as an extension of metabolic studies of nucleic acids, sucrose gradient separation of RNAs, role of magnesium in stabilizing mRNA, etc.), Marianne Grunberg-Manago (enzymology and biochemistry of RNA reactions, including production of synthetic polynucleotides), and Jacques Kruh (biosynthesis of hemoglobin), to pick four examples from his paper, all were built on, or resumed work on, projects started earlier, but employing the tools for analyzing RNA that had been circulated in forming the network characterized by Gaudillière. If Gaudillière is right, what linked this network together was the strongly structured practices that allowed the same materials and techniques to be used in different

local settings, for only partly overlapping purposes. Correspondingly, the ‘ideology’ [my term] and political-disciplinary structure of molecular biology, built around the RNA network was loose and would not yield easily to a conceptual definition as opposed to one in terms of (loose) political and funding alliances.

Granting this, the binding together of this network *was* specifically fostered by the DGRST and reflects the proposals of the *Colloque de Caen* of 1956. And it reflects the ideology of working in “teams”, fostered not only by the DGRST and the groups around Ephrussi and Monod, but also by the American model and Rockefeller funding in the formative period after WW II.⁵ What it does *not* reflect, I suggest, is a coherent account or understanding of what is distinctive of molecular biology or a clear basis for forming a discipline organized around a moderately well defined set of problems or techniques. It is against this background that Gaudillière emphasizes the “nexus or practices” that helped bind these different programs together, that helped turn these otherwise independent groups and strands of work into a self-conscious collaborative network. He emphasizes the role of mRNA [I think he should include tRNA as well] as a ‘boundary object’, crucial to the formation and maintenance of the network.

Conclusion and Issues for Further Investigation

This last result leads, rather naturally, to some concluding observations and a series of questions for further investigation. These case studies show that in all of the sites examined the institutionalization of molecular biology as a ‘discipline’ was primarily driven by the need to separate groups of practitioners with divergent but overlapping interests within the local context. Thus molecular biology was contingently separated from agricultural or medical biochemistry, virology, work on the physiology of nucleic acids, etc. for contingent *local* institutional reasons. This makes it even more pressing than it already was to try to understand how molecular biology came to be delimited on a larger scale. How did it come to be a discipline with specific intellectual content [or did it?], including some problems, tools, and practices and excluding others; how did it gain authority as *the* forefront biological science by the mid-1960s? We need to understand the ways in which the tensions between different practices, projects, aims, understandings of the goals of molecular biology, etc. were resolved, on what scale and in what venues, so that something approximating the political character of a discipline, rather than a federation was achieved. If these case studies provide a sound starting point, it will prove difficult to answer the interconnected questions implicit here satisfactorily.

One means of getting at such questions that should prove of considerable interest is to examine carefully the work of those who were widely cited in the papers of the late fifties through the mid seventies by the people now considered major founders of molecular biology. By studying the contributions of those who are now omitted in the standard histories and recollections we will gain a clearer sense of the possibilities that were open as molecular biology took shape. It is already widely recognized that the

⁵See, e.g., D. Zallen “The Rockefeller Foundation and French Research,” *Cahiers pour l’histoire du CNRS* 5 (1989): 35-58.

contributions of a number of biochemists have been given short shrift, but (as the example of Ernest Gale in Rheinberger’s study illustrates⁶) there are a great many more figures whose lines of work were then crucial but who are now lost sight of. To understand both what molecular biology was at the time of its early institutionalization and what it has become, it will be enormously helpful to understand at what point the definition or ideology “hardened” and the grounds for inclusion and exclusion of individuals and lines of work. Studies of this sort are appropriate in many other areas as well, of course; in general they should reveal a great deal about the intellectual, practical, and political character of disciplines.

Since the laboratory practices of molecular biology required the contributions of a vast number of individuals whose work is not treated in the standard histories (including unsung technicians as well as laboratory leaders and publishing scientists) and since there were more dead ends in the choice of techniques and experimental systems than successes, another important direction of research concerns the establishment of the practices around which networks were built. This will require studies of lines of work that were abandoned, the dead ends and near misses in various settings. It is always a harder task to trace such ‘failures’ than to trace ‘successes’, knowledge of which has been kept alive by their role in ensuring the reputations of the ‘victors’ in the ‘competition’ for fame and glory and their subsequent perpetuation because of the successes in which they played a key role. But studies of dead ends are especially important since, as Rheinberger’s studies in particular have shown, the unknown features of experimental systems, especially when they are being developed and are employed to attack problems whose definition is not yet clear, reshape the very possibilities that scientists recognize and can cope with. It is clear that during the formative period of molecular biology (but not just molecular biology!) large-scale reshaping took place and the accounts of the field (discipline?) were re-formed a number of times before it more-or-less stabilized. To this extent, there was something like a struggle over the proper boundaries and account of the field — to what extent should it be understood in terms of information, of molecular structure, as including traditional enzymology, as limited to studies of nucleic acids and proteins, as replacing traditional studies in virology, physiology, and other disciplines, as ...? There was also a parallel struggle for preeminence and authority both within the nascent discipline and in contention with the established disciplines and departments. Only by understanding the field of contrasting open-ended possibilities will we truly understand the process by which molecular biology took shape and how it became what it has become. Similar claims clearly apply equally to other disciplines.

All of this, of course, also connects to issues about funding, support, and institutionalization. And it heightens the problem of setting the contexts within which to examine local laboratory cultures. To illustrate: Following Gaudillière, I suggested that certain features of centralized French administrative culture greatly influenced the

⁶My own list of candidates is already too large to write out here, but it might help to cite another example of a different sort — Henry Quastler, who tried to apply Shannon-Weaver information theory literally to the analysis of genetic information and whose work will be analyzed usefully in Lily Kay, *Who wrote the Book of Life? A History of the Genetic Code* (Chicago University Press, forthcoming, 1997).

character of the collaborative networks that could be formed there, in contrast with what could be done in Britain and the United States. Similarly, the relationship between molecular biology and biochemistry was different in each of these three countries in virtue of the different histories, political standing, and institutional bases of that discipline in their national cultures. It is likely (but a matter for investigation!) that such differences influenced the opportunities for introducing new bench practices, if in no other way, then by delimiting the niches within which certain practices could be initiated.⁷ And since new practices can fail to achieve their objectives, can transform the direction of work and disciplinary allegiances of their practitioners, can lead only to routine results, or can open up important new vistas, the character of the available niches from which to work can prove to have a strong influence on the direction that new work takes if and when it starts to flourish. A key aspect of this problematic, not yet adequately studied I believe, is the problem of drawing boundaries between different kinds of work and determining where it should fit among established disciplines and/or within some new construct. To the extent that an ‘international’ solution is ultimately achieved to such problems, it must surely be achieved in light of initially different ways of dealing with it in different countries.

Underlying work of the sort we have been exploring is the thorny problem of how best to contextualize the work being studied. This is, I believe, one of the major historiographical problems that we must face in the history of science. It is, of course, by no means a new problem, but a particularization of the age-old problem of the (seeming) overdetermination of historical events. If we deal with local cultures, to understand how they develop and their fate we need to understand their location within larger cultures. But it is utterly unclear how to draw appropriate boundaries on the relevant larger culture(s). As even this brief discussion has shown, institutional cultures, the cultures of sponsoring agencies, ‘the’ culture of science (or of biological science, physical science, etc. as appropriate), and national cultures all *can* provide relevant contexts, all can occasionally determine the fate of work undertaken in a particular local context. The potentially intractable problem of delimiting the boundaries of investigation looms large here, but it is one that must be faced explicitly to profit fully from the enormously stimulating investigations of local cultures exemplified in the four papers published in this symposium. My own view is that we have no abstract standard available for determining which boundaries are appropriate to a given study and, indeed, that no single contextualization is adequate to the examination of any given case, but that, nonetheless, we can (at least sometimes) distinguish useful and explanatory delimitations of the larger context from others that prove to be misleading.

⁷The situation in France is particularly interesting in this regard. As my colleagues and I have argued [but also Gaudillière and many others], fundamental work in Mendelian, physiological, and molecular genetics had to be initiated outside of the university system, by ‘outsiders’ within the system of research laboratories. See R.M. Burian, J. Gayon, and D. Zallen, “The Singular Fate of Genetics in the History of French Biology, 1900–1940,” *J. Hist. Biol.* 21 (1988): 357–402. This had as one consequence the necessity for international collaborations after WW II in order to bring various techniques into the relevant laboratories, acquire crucial funding and sponsorship, and to forge a sufficiently robust network to gain a full hearing for the work that would not otherwise been likely to gain a secure foothold in France.

Comments on “The Tools of the Discipline”

Against this background, I hope that the four papers published in this special section will stimulate the readers of *JHB* to carry out similar studies — i.e., studies that seek to characterize and contextualize local experimental cultures — over a wide range of cases. I also hope that some of those who take up this challenge will deal with the larger questions raised by the need to find a way of balancing different, sometimes competing, contextualizations of such studies. The fact that any given case requires multiple contextualizations, resulting in multifaceted representations no one of which is alone adequate, will surely land us in fascinating, hopefully fruitful and productive, controversies.