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# Social epistemology of scientific inquiry: beyond historical *vs*. philosophical case studies

*Introduction*.

I will discuss moving beyond case studies as a strategy for dealing with the problem of normative/descriptive dualism. This is of course a quite general philosophical issue. I am concerned specifically with the way normative/descriptive dualism polarizes the study of scientific inquiry into two mutually exclusive, yet co-dependent, projects: description of our actual scientific practices and their results, or abstract examination of epistemic ideals detached from our practices. The split is most striking, and has occasioned the most controversy, with respect to *social* aspects of our knowledge-generating practices.[1] With respect to this issue, history and philosophy of science seem starkly opposed. It seems we must choose between describing the historical unfolding of our scientific practices, or elaborating abstract epistemic ideals, when what is wanted is an account that includes both: epistemic ideals that apply to our practices. I propose to resolve this dilemma, by explicating a conception of the epistemic ideal of scientific objectivity from the social aspects of our scientific practices. This ideal of objectivity is both normative and engaged with the historical unfolding of experimental inquiry. It thus bridges the gap between history and philosophy of science in the notoriously controversial field of social epistemology. The way in which this solution moves beyond case studies may shed light on the relation between history and philosophy of science in other areas as well.

*The problem*.

The problem should first be set out a bit more precisely. I presuppose that (1) the distinction between knowledge and opinion is a *sine qua non* of epistemology; (2) any adequate epistemology of scientific inquiry must explicate the distinction between scientific knowledge and opinion in a way that relates to our scientific practices; and (3) any adequate *social* epistemology of scientific inquiry must do so in a way that engages

[1] For a range of perspectives, see Hollis and Lukes 1982, Labinger and Collins 2001.

significant social aspects of those practices.[2] Normative and descriptive approaches to the social epistemology of scientific inquiry are *prima facie* incompatible. On a thoroughly descriptive view, epistemic standards distinguishing knowledge from opinion are of a piece with our scientific practices. There is no 'absolute' standard outside the historical contexts in which they emerge and (for a time) persist.[3] Knowledge is distinguished from opinion in virtue of satisfying epistemic standards resulting from complex and highly contingent social negotiations. As social structures, values and interests change over time, epistemic standards for scientific knowledge change in correlated ways. Although they may be described, these changes cannot be epistemically evaluated. Any standard for such evaluation would transcend the variable socio-historical contexts in which our scientific practices occur. But, on this view, there are none. In contrast, normative epistemology (in the Anglophone analytic tradition) requires such standards: epistemic ideals that prescribe our practices independently of the historical course of scientific inquiry.[4]

Normative/descriptive dualism effectively segregates history and philosophy of science, with respect to the social aspects of scientific inquiry. On the descriptive approach, social epistemology of scientific inquiry is a form of historical investigation. On the normative approach, it is continuous with epistemology in the analytic tradition. So normative/descriptive dualism has significant consequences for the relation of history and philosophy of science in the emerging and contentious field of social epistemology, and in science studies more generally.

Yet an adequate social epistemology of scientific inquiry needs both. On a thoroughly descriptive approach, the distinction between scientific knowledge and what

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[2] If an account fails to coherently explicate the distinction then it is outside the scope of epistemology, falling instead into another domain (*e.g.*, psychology, philosophy of mind). If an account fails to engage our scientific practices, then it does not concern scientific inquiry, though it may address other epistemological issues (*e.g.*, analysis of knowledge, dynamics of epistemic authority). This is, evidently, a minimal adequacy condition.

[3] See, *e.g.*, Barnes and Bloor 1982, Fleck 1979[1935], Fuller 1988, Rouse 1996, Kusch 2002. Of course, there may be invariant epistemic standards, common to all or most scientific contexts. It is somewhat doubtful that such general invariant standards for scientific inquiry exist, since all proposals to date, from Mertonian 'disinterestedness' to Kuhnian empirical accuracy, are evidently false. But invariance merely partitions epistemic standards into 'same' and 'different' relative to contexts being compared. This distinction does not provide a basis for epistemic evaluation across socio-historical contexts. Generality as such does not clarify the distinction between knowledge and opinion.

[4] See, *e.g.*, Goldman 1999, Kitcher 2001.

is accepted as such within a particular socio-historical context collapses (*cf*. Barnes and Bloor 1982, 27). Scientific knowledge is thus identified with beliefs accepted as knowledge at a particular time/interval by the scientific community (or an authoritative portion thereof) – that is, opinion accepted as authoritative. The distinction between knowledge and opinion is just the difference between authoritative and non-authoritative opinion. Such a distinction can be drawn for any cognitive enterprise: law, religion, government, philosophy, art, *etc*. So there is nothing, on a descriptive view, to distinguish scientific inquiry from other social practices that involve belief and opinion - that is, most human activities. The descriptive approach therefore fails to explicate the distinction between knowledge and opinion in a way that engages our scientific practices. It engages, instead, a much broader domain of human social action, within which our scientific practices recede into the broader social fabric. Thoroughgoing descriptivism effaces the epistemic significance of scientific inquiry.[5] This approach, on its own, is therefore inadequate for social epistemology of scientific inquiry (though it might be defended on its own terms as epistemology of human social endeavor).

The normative approach is vitiated in a complementary way. Though epistemic ideals such as rationality and objectivity have long been considered characteristic of scientific inquiry, their relationship to our actual practices is difficult to specify. Social constructivist critiques of normative epistemology highlight this difficulty. How can epistemic standards distinct from our practices nonetheless exert 'prescriptive grip' on them? Is it not less mysterious to dismiss them as pretty fictions to dazzle the uninitiated and inspire novices? This would make normative epistemology "no more than an empty play on words or an epistemology of the imagination" (Fleck 1979[1935], 21). In response, normative epistemologists offer case studies of epistemic ideals in scientific practice: intuitively clear cases of epistemic success and failure in historical or contemporary scientific inquiry are shown to conform to some idealized epistemic standard (*e.g.*, Kitcher 1993, 2001). But such case studies are not a satisfactory rebuttal.

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[5] This is not a merely theoretical worry. In recent sociology of science, attention has in fact shifted to science as policy, as regulation, as a strand of political economy, or as the epistemic face of the modern state (*e.g.*, Knorr Cetina 1999, Drori et al 2003, Jasanoff 2005; Frickel and Moore 2006). The work of scientists themselves – the painstaking pursuit and articulation of justificatory evidence for scientific knowledge - has largely vanished from sociological discussion. Ironically, fine-grained descriptive study of our scientific practices seems to have undercut their further study.

Scientific inquiry is not 'pre-packaged' into cases for philosophical consumption. 'Exogenous' epistemic ideals engage our actual practices only in conjunction with further assumptions specifying which aspects of scientific episodes are epistemically relevant. So case studies in normative epistemology show (at best) that an epistemic ideal applies to our scientific practices relative to a partition of those practices into epistemically relevant and irrelevant aspects. But this is question-begging. Normative social epistemologists have themselves persuasively argued against the individualistic assumption that social aspects of scientific inquiry are epistemically irrelevant (*e.g.*, Longino 1990, Kitcher 1993, Kornblith 1994, Goldman 1999, Solomon 2001). Parallel arguments can be made for the social interactions and negotiations that establish epistemic standards in actual practice.

The descriptive approach presents an incisive challenge for normative epistemology of science – not by proving that epistemic standards must be socially constructed (as noted above, this is not even an adequate alternative), but by highlighting the arbitrary and *ad hoc* nature of the epistemic relevance relations that underwrite the application of ideal epistemic standards to our scientific practices. Many different specifications of epistemic relevance are possible, and absent a principled rationale for selecting among them the associated epistemic ideals lack normative force for our practices.[6] Application to our scientific practices thus relativizes epistemic ideals to one partition among many. A 'relevance partitioning principle' would of course underwrite application of ideal epistemic standards to our practices. But it does not seem that any such is available. Any attempt to identify such a principle will face the same difficulties as epistemic ideals themselves. *A priori* arguments in support of one partition over another cannot settle the matter, since what is at issue is the application of epistemic ideals to our practices, not the cogency of those ideals as such. On the other hand, appeal to contemporary acceptance of certain aspects of certain episodes as exemplary concedes to descriptivism. If epistemic ideals apply to our scientific practices only in virtue of our acceptance of certain exemplars, then the distinction between epistemic standards and local criteria of acceptance collapses in practice. So, despite the availability of

[6] Recognition of this arbitrariness is one plausible motivation for endorsements of pluralism in social epistemology and philosophy of science (*e.g.*, Goldman 2002, Kitcher 2004, Kellert *et al* 2006). However, the challenge it poses for normative epistemology of scientific inquiry has been insufficiently appreciated.

philosophical case studies, ‘exogenous’ epistemic ideals fail to prescribe our scientific practices, being relative to an arbitrary distinction, or collapsing into descriptivism.

Normative/descriptive dualism thus poses a dilemma for epistemology of scientific inquiry: either epistemic standards distinguishing scientific knowledge from opinion are dependent on social structures, values or interests, or they are not. If they are, then epistemology collapses into description of socio-historical facts, and scientific inquiry recedes into the complex and dynamic pattern of the broader social and cultural fabric. If epistemic standards are independent of social structures, values or interests, then epistemology proposes abstract ideals with no clear prescriptive relation to our actual practices of scientific inquiry. What is needed is an epistemic standard that can bridge the gap between abstract ideals and our pervasively social scientific practices, to yield an adequate epistemology of scientific inquiry.

Neither historical nor philosophical case studies (as discussed above) can be of help here. In fact, the dilemma for social epistemology of scientific inquiry is posed by these two kinds of case studies. The descriptive approach is underwritten by studies of many different disciplines and historical contexts, which robustly indicate that our scientific practices are suffused with social interactions and sociological influences.[7] Selection of topics for inquiry, development and implementation of methods and evidential standards, and acceptance of scientific claims are all social practices, involving multiple individuals and (unavoidably) their various interests. Further historical case studies demonstrating this familiar empirical result are otiose, and (as noted above) unmotivated. Philosophical case studies showing that ‘exogenous’ epistemic ideals apply to our scientific practices are vitiated by question-begging assumptions as to which aspects of our practice are epistemically relevant. Another illustration that selected aspects of a selected scientific episode conform to an independently-obtaining epistemic ideal will not help matters. Resolving the dilemma requires moving beyond both sorts of case study, into a new framework for examining scientific inquiry.

[7] For example: Collins (1975), Knorr-Cetina (1981), Latour and Woolgar (1979), Shapin and Schaffer (1985), Pickering (1995), Collins (1998), Knorr Cetina (1999). See Shapin (1982) and Golinski (1998) for detailed surveys of the relevant literature; Knorr Cetina (1999, 263 note 1) and Bloor (2004, 919-920) for citation lists.

*Social action framework.*

Philosophy of social action provides a framework that is compatible with both normative and descriptive approaches to scientific inquiry, and so of accommodating their diverse case studies to one another. Its core is a thin but robust consensus concerning practical reasoning and action, deeply entrenched in everyday and technical explanations of human activity, and explicit in recent philosophical accounts of social action. This is simply that human action can be understood and explained in terms of 'fit' between goals and means, that is, in terms of instrumental rationality. Appeal to inquirers' goals and means is explicit in Latour's actor-network theory (1987) and Pickering's mangle of practice (1995). In Shapin's interest model (1975), the tie between broad socio-cultural interests and inquirers' goals and means remains partly implicit, yet underwrites the explanatory force of these accounts. Several influential sociological accounts discuss the goals and means of individual inquirers in light of 'the end of science' conceived as the *telos* of a social structure (Merton, 1973) or the expression of a mood characteristic of a 'thought-style' (Fleck, 1979[1935]). Others (Collins 1975, Knorr Cetina 1981) focus on the social organizations and epistemic practices that structure scientists' means-end reasoning; the latter provides the starting point for such laboratory studies, and is presupposed by them. Means-end reasoning underpins the philosophy of political naturalists like Rouse (1996) and Fuller (2002), as well as their accounts of scientific inquiry. The same goes for naturalistic epistemologists, such as Hull (1988), Goldman (1999), Kitcher (2001). The goals and means of scientific communities also figure in Solomon's (2001) and Longino's (2002) social accounts of scientific rationality and knowledge (respectively).

This widespread commitment to means-end reasoning in explanation and understanding of human action entails two constraints on agents' goals and means so understood. A goal must, at minimum, engage an agent's motivation such that her intentional action may ensue, the latter being subject to assessment in terms of instrumental rationality. To take an action to be a means to a goal is to include it in a plan for achieving that goal. This is not to stipulate that intentions or actions must be instrumentally rational, only that they fall within the scope of instrumental rationality, to be understood and explained in terms of 'fit' between goal and means. This is a weak constraint, but it does rule out: (1) having a goal which cannot be achieved no matter what one does; and (2) taking as means actions that could not be included in a coherent plan specifying how one's goal might be achieved. These constraints impose two necessary (though insufficient) conditions for instrumentally rational action: achievability (for goals) and coherence (for means).

Recent philosophical accounts of social action extend these minimal preconditions for instrumental rationality to activities involving multiple interacting participants (Gilbert 1989, Searle 1990, Bratman 1999, Kutz 2000, Miller 2001, Tuomela 2005). Though there are deep differences among them, all these accounts endorse the idea of a shared goal achieved by multiple participants acting according to their parts.[8] For practical reasoning in social action, what is at issue is not what an individual can do, but what multiple individuals can accomplish together: a shared goal. In social as well as individual action, an agent is committed to a plan that includes her intended action as a part. What distinguishes participant means from means taken in individual action is that the plan necessarily involves others' actions as well. This entails an additional requirement of coherence: that one's means be coordinated with those of other participants. Social action is understood and explained in terms of the connection between shared goals that participants hope to accomplish together, and the coordinated means by which they try to do so. This entails two requirements: that the shared goal of a given social action be achievable, and the means taken to it coordinated among participants. These minimal preconditions for instrumental rationality therefore provide a minimal consensus framework, compatible with both normative and descriptive perspectives on scientific inquiry.

Of course, there is nothing about goal-oriented social action subject to constraints of instrumental rationality, peculiar to scientific inquiry. Fleshing out this minimal framework requires empirical study of scientific episodes. I shall focus here on one in

[8] For example, if my climbing partner and I share the goal of climbing Half Dome, then we are each committed to trying to get to the top as a duo. Accordingly, we plan and execute our climb by coordinating actions, *e.g.*, taking turns to lead and belay. Each of us participates in social action aimed at the shared goal of reaching the top together. In contrast, everyone who plans to climb Half Dome has the *same* goal, in the sense that all plan to do the same thing. But this goal is not shared by all would-be climbers. We are not all trying to reach the top together. My partner and I aim to reach the top together, but whether or not any of the others also do so is not our concern. If their goals figure at all in our plans, it is only as a background condition, like inanimate objects or weather.

particular: the effort to isolate and characterize blood stem cells, an episode of recent cellular immunology (Fagan 2007).

*Preliminaries*

The search for the blood stem cell (HSC) emerged from the confluence of cell biology, genetics and radiation research in the mid-20th century, and coalesced in the early 1960s around a new experimental approach: the spleen colony assay. A notable result in 1988 led to a developmental turn, with important ramifications for stem cell and cancer biology. Historical study of this episode, focused on shared goals and coordinated means of participants, fleshes out the minimal social action framework for a representative experimental success. This is not a philosophical case study illustrating the application of an exogenous epistemic ideal for scientific knowledge; I have not proposed any such ideal. Nor is it an historical case study illustrating that epistemic standards change in response to changing social structures, interests or values; clearly the evidential standards we use do vary and change, but I have not supposed that these are identical to that which distinguishes scientific knowledge from opinion. So my narrative description of this episode is not a case study reinforcing the normative/descriptive divide and associated dilemma. It is a case study, if you like, of scientific inquiry in the social action framework, but the latter is sufficiently thin to make that a rather trivial point. It is the empirical study within this minimal that yields a substantive result.

I focus on the HSC episode for three reasons. First, it is well-suited to examining the relation of epistemic standards for scientific knowledge and social aspects of scientific practice within a framework of shared goals and coordinated means. The search for HSC exhibits a complex social structure, is explicitly goal-oriented, and is recognized by practicing scientists as including several important successes. In all three respects it is typical of contemporary experimental biomedicine.[9] So the search for HSC is a representative episode in which the features of interest for social epistemology of scientific inquiry in a social action framework are evident, but not peculiarly exaggerated.

[9] For example, this episode is one of nineteen singled out by the editors of *Immunological Reviews* as "turning points in modern immunology" (Koretzky and Monroe 2002); the 1988 *Science* paper is cited frequently but not astronomically (~1300 according to 'Web of Science').

My second reason for selecting the HSC episode is methodological. The following descriptive account is based on the published record, interviews with participating researchers, and my own experience as a graduate student in the Weissman lab (1994-1997). The last familiarized me with this episode of immunology research, and provided access to many of the social interactions involved. However, I was not directly involved in the search for HSC and did not participate in the episode described here. My personal experience with the episode allowed me to use published sources and to obtain interviews with participants more efficiently than would have been possible otherwise. The account below (a fragment of the entire study) is based on these two sources (see *Appendix* for details).

Finally, the HSC episode is significant for understanding the history of immunology and stem cell research. Blood-making ('hematopoietic') stem cells occupy a distinctive role in the immune system and in our understanding of it. Though diverse cells are involved in immune function, all develop from a common precursor type, localized (in adults) to bone marrow.[10] Most blood and immune cells live only a few days or weeks, and do not divide with sufficient rapidity to replenish themselves. But one or a few blood stem cells can completely reconstitute an immune system that functions over the long-term, continuously dividing into progeny that differentiate into all the cells of the immune system.[11] As the beginning of the developmental history of the immune system, HSC provide an inclusive starting point for explaining and understanding its diverse mechanisms and our experimental manipulations thereof.[12] Examining the epistemic history of HSC research provides an illuminating view of immunology more generally. Furthermore, HSC are the best understood and most facilely manipulated of all stem cell types, providing a standard for characterizing other stem cells (embryonic, neurogenic, tumorigenic) in clinical and laboratory settings.

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[10] In mammalian development, HSC arise from anterior mesoderm. Embryonic hematopoiesis is first localized to yolk sac blood islands, then fetal liver, and finally to bone marrow.

[11] This is why bone marrow transplants are clinically effective: to treat leukemias (for example), the entire immune system is ablated with radiation or chemotherapy, and then completely reconstituted by a bone marrow transplant containing a few HSC.

[12] Embryonic stem cells play an analogous role in understanding and explaining organismal development. This is not to say that HSC are foundational for immunology in the sense of providing first principles for theories (modern immunology arguably has no such principles), nor that HSC encapsulate the whole of the subject in a kind of 'meta-preformation.'

Tracing the development of evidential standards for isolating HSC and other stem cell types thus sheds light on the epistemology of stem cell research more generally. So my criteria for selecting the search for HSC as a representative episode of recent experimental science, do not reinforce the dilemma framed by socio-historical and philosophical case studies.

*Search for HSC*

Though the existence of HSC was inferred in Owen's 1945 study of blood group genetics in bovine twins, the search for these elusive cells began over a decade later.[13] A key interim discovery occurred in 1951, when radiation biologists observed that lethally-irradiated mice could be 'rescued' by bone marrow transplantation.[14] High levels of γ-radiation destroy the immune system, which is ordinarily fatal. But mice given lethal doses survive if later injected with bone marrow cells from a 'donor' of the same inbred strain. Transplanting bone marrow cells effectively transplanted a functioning immune system. Biomedical researchers noticed the clinical applications, and began to systematically investigate 'radiation rescue' in mice. The search for HSC coalesced out of this international research program, beginning with a new experimental system: the spleen colony assay.

The spleen colony assay was invented by medical biophysicists at the Ontario Cancer Institute, who noticed that, after about two weeks, 'rescued' mice developed nodules on their spleens.[15] Each nodule was found to be a colony or clone descended from a single donor bone marrow cell, containing all the known hematopoietic cell types. Cells taken from a spleen colony could rescue lethally irradiated mice and produce splenic colonies in their turn. These three capacities of colony-forming cells were taken

[13] Owen observed that many bovine fraternal twins had identical blood types, though 'untwinned' full siblings rarely did. He explained these curious results as due to exchange of blood cells between fraternal twins by vascular fusions *in utero*. Since blood samples were taken from adults, Owen's explanation implied that embryonic events influence the phenotypes of blood cells circulating years later. However, cell physiologists had shown that cell lineages founded by "formed erythrocytes" had short life spans of days or weeks (Jordan 1942). Owen concluded that "embryonal cells ancestral to the erythrocytes of the adult animal… are apparently capable of becoming established in the hemapoietic tissues of their co-twin hosts and continuing to provide a source of blood cells distinct from those of the host, presumably throughout his life" (401). He did not, however, pursue this hypothesis.

[14] Lorenz *et al* (1951).

[15] Till and McCulloch (1961), Becker *et al* (1963), Siminovitch *et al* (1963).

to define HSC: (1) radiation rescue by reconstituting the immune system; (2) multipotency, differentiation into multiple blood cell types; and (3) self-renewal, maintaining these capacities far longer than the life span of a single blood cell. HSC so defined could be detected only in retrospect, after these capacities had been realized. They were rare cells; less than 0.1% of bone marrow in adult mice. At this point the experimental goal became clear: prospectively enrich bone marrow cell preparations for HSC, using the spleen colony assay to measure enrichment.

This goal was shared mainly by hematologists, medically-trained experts on blood cells. About a dozen research groups took up the project in the mid-1960s (including the inventors of the spleen colony assay). Though in competition, these groups met regularly to share results and methods. The social structure of this stage of the search for HSC is concisely represented in a participant summary from one such meeting (in 1968, Figure 1). The different groups shared a core experimental method, a standard for measuring HSC enrichment (top). Representatives of the main groups are associated with diverse variations on this core method (below). The aim of the meeting, and others like it, was to pool and compare the results of different variations on the spleen colony assay. Through such interactions, the different lab groups formed a more inclusive group, with the shared goal of prospectively isolating HSC. The search for HSC proceeded by division of labor: each group used a somewhat different method, and results were pooled and compared at regular meetings to assemble a comprehensive consensus.[16] Experimental protocols lengthened, as methods of enrichment were concatenated.[17] By the mid-1980s, the community had made considerable progress – up to 200-fold enrichment of HSC from mouse bone marrow (Visser *et al* 1984). This was the state of play when the search was abruptly transformed.

The transformative event was a widely-publicized announcement by the Weissman lab at Stanford University in 1988 that the search for HSC in mice was over –

[16] *E.g.*, annual meetings of the Midwest and Southern "Blood Clubs" (mid-1980s); annual symposia on Molecular Biology of Hematopoiesis (1985-1989). The main groups seeking HSC were in Toronto (James Till, Ernest McCulloch, Norman Iscove), Manchester (T. Michael Dexter, Elaine Spooncer, Brian Lord), Melbourne (T. R. Bradley, Dean Metcalf), and distributed throughout the Netherlands (Jan Visser, D.W. van Bekkum, John Dicke) and the Eastern USA (Malcolm Moore, Peter Quesenberry).

[17] Based on cell size, density, rate of division, and surface phenotype. See reviews in Watt *et al* (1987), Spangrude (1989), Visser and van Bekkum (1990).

murine HSC had been purified and characterized (Spangrude *et al* 1988).[18] This result (two decades in the making) emerged from a distinct line of research that differed in three important ways from the hematological search for HSC. First, the shared core of the Weissman group's search was not an experimental system, but the shared goal of characterizing mechanisms of immune cell development in terms of surface phenotype, movement and function of single cells. Second, being uncommitted to any particular experimental method, the Weissman group made opportunistic use of whatever new techniques were available. In particular, they enjoyed early access to fluorescence-activated cell sorting technology (developed at Stanford in the Herzenberg laboratory) as paying members of a 'shared FACS users group.'[19] Third, instead of dispersed division of labor, the lab served as a center for continuous and cumulative collaboration in the search for HSC. Research interests within the lab were diverse, and its shifting membership was free to pursue whatever project they chose. The result was a loose and shifting assemblage of lines of inquiry, many of which concerned blood cell development.

In the early 1980s, three such projects were coordinated into a focused search for HSC. Three kinds of interaction were crucial for this search: multiple collaborations within the Weissman lab, participation in Stanford's shared FACS users' group, and a collaboration with a West German laboratory. The upshot was a cell labeling and tracking experiment that characterized and isolated a cell population 2,000-fold enriched for HSC function. This was the result announced in 1988, published in *Science* (Spangrude et al 1988). Though the paper had only three authors, the result depended on decades of sustained collaboration involving dozens of researchers, in and outside the Weissman lab. Initially controversial, the Weissman group's result is now recognized as a significant contribution to modern immunology; a representative biomedical success.

[18] See Fagan (2007) for further details on the Weissman group's search and the 1988 result.

[19] FACS is a method for rapidly sorting cell populations, one cell at a time, according to level of surface expression of particular molecules, which are detected by specific binding of antibodies conjugated with fluorescent tags. The aim is to separate functionally distinct but morphologically similar cells without killing them, so purified cell populations can be used in further experiments. The first FACS apparatus was developed at Stanford University in collaboration with Becton Dickinson. For more on FACS, see Bonner *et al* (1972); Herzenberg *et al* (1976); Keating and Cambrosio (1994, 2003), Herzenberg and Herzenberg (2004).

However, their success did *not* consist of isolation of HSC, nor even greater enrichment of HSC from mouse bone marrow. Methodological diversity among the hematologists yielded divergent assessments of how the Weissman group's result compared to earlier work, preventing clear consensus among those most concerned with this issue.[20] Arguably, the Weissman group did not improve on extant HSC purification protocols. Divergent assessments of the issue persist today. Moreover, within a year all interested parties had agreed that the Weissman group's cell population was heterogeneous, and various groups (including Weissman's) began working to characterize more finely-grained cell populations.[21] So the success of 1988 certainly did not consist in the isolation of a pure blood stem cell, and arguably, not even of HSC enrichment relative to other available methods.

What it did consist of was, first, articulation of a new model of blood cell development coordinating HSC capacities with cell phenotype; and second, a new direction and impetus for the search for HSC as a project of cellular immunology. Both resulted from distinctive features of the Weissman group's search for HSC. As noted above, the hematological HSC research community proceeded by aggregating the results of different groups working to isolate it. Their methods were diverse, not coordinated by a single model of cell development or physiology. In contrast, the Weissman group coordinated the defining capacities of HSC with cell surface characteristics at the single-cell level, in a way that readily extended to humans and to other developmental stages. This amounted to an improved model of the development and function of the immune system, and (via developmental analogy) gestured toward future clinical applications.[22] This result fit with the biomedical goal of immumology: knowledge of the immune

[20] Though all agreed that HSC are pluripotent, self-renewing and responsible for radiation rescue, different groups took different aspects of HSC as primary. Responses to the 1988 result thus discriminated between experimental methods and emphases. Many hematologists conceived of HSC primarily in terms of spleen or *in vitro* colony formation, while the Weissman group defined HSC in terms of the correlation between *in vitro* colony formation and *in vivo* immune reconstitution. The resulting divergent assessments of the 1988 result persist today. Within the Weissman lab, the 10-fold greater enrichment was and is recognized as success.

[21] Lemischka *et al* (1986); Visser, in Radetsky (1995, 91); Spangrude (1989, interview of 12/4/2006); Müller-Sieburg (interview of 4/6/2007).

[22] 'Model' is the term used by HSC researchers, and, increasingly, by philosophers of science as a generalization of 'theory,' which admits non-linguistic representations as well as more traditional theories amenable to axiomatic presentation (*e.g.*, Giere 1988, Longino 2002). Models in this sense are representations of subjects of inquiry, in which mathematical laws or idealized causal or formal relations are satisfied. Theories may be thought of as 'families' of models and associated similarity claims.

system and treatment of infectious disease, autoimmune disorders, and cancers (Paul 1983, Kuby 1995, Paul 2003). The tie to cellular developmental immunology gave new direction and impetus to the field of HSC research. The widely-publicized *Science* paper created a new interface between previously distinct lines of inquiry. Controversy then ensued over their different methods and standards for isolating HSC. Yet the occasion of this controversy became the most enduring aspect of the Weissman group's success. The 1988 model itself was superseded within a year, but the Weissman group's distinctive method (coordinating surface phenotype with developmental potential and immune function at the single-cell level) was emulated and modified by many other groups, and the search for HSC drew on rapid advances in cellular immunology throughout the 1990s. The two aspects of success were interdependent: announcement of the coordinated model precipitated the interface of experimental hematology and developmental immunology, and the standards according to which that model counted as improved emerged from that interface, endorsed by the more inclusive HSC community.

Other successes followed: further refinement of bone marrow cells by self-renewal capacity (Morrison and Weissman 1994), reconciling apparently incompatible models of blood cell development (Kawamoto *et al* 1997, Kondo *et al* 1997), and ramifications of HSC research for stem cell and cancer biology, realized in new interfaces between these fields (Dontu *et al* 2003). Continued pursuit of HSC led in turn to further new interfaces with neurobiology, developmental biology, evolutionary biology, and cancer research. Concomitantly, models of blood cell development became increasingly robust and detailed (Figure 2). In these various ramifications of the search for HSC, two aspects of success are robustly recognized by participating researchers: improved models of cell development, and coordination of groups or individuals with different goals. This pattern recurs at different levels of social organization: within a single lab, among different lab groups, and across fields and disciplines.

*Scientific success*.

Two aspects of the 1988 success can be distinguished: construction of an improved model of blood cell development, and formation of fruitful new interfaces between distinct lines of inquiry. Both are *coordinations*: of HSC function and cell phenotype in an improved model of blood cell development, and, at the social level, of the search for HSC with other successful lines of inquiry. As noted above, this pattern of recognized success recurs throughout the episode, at different levels of social organization. This recurring pattern is also seen in other episodes of experimental inquiry, including those described in influential science studies texts: Boyle's experiments with the air-pump, isolation and characterization of thyrotropin releasing factor (hormone) at the Salk Institute, gravitational wave research in Italy and the US, Pasteur's anthrax vaccine, the Wassermann test for syphilis.[23] So diverse socio-historical case studies indicate that this pattern of recognized scientific success (improved models, and new interfaces) is robust across various disciplines and historical contexts. This is, of course, a robust empirical result, not a normative thesis about scientific success.

Yet this descriptive schema also displays some kinship with normative epistemic ideals. Models[24] are recognized as improved when they increase the scope, consistency, precision or accuracy of scientific accounts of the empirical world. Coordination of diverse lines of inquiry via new interfaces similarly recalls epistemic virtues long identified with scientific knowledge: consistency, coherence and unification.[25] However, it will not do to simply identify epistemic ideals with the two aspects of success. Models are improved relative to epistemic standards of groups, which vary widely over time and across fields, and in response to social interactions and structures. Formation of new interfaces is a highly contingent matter, influenced by available technology, world events,

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[23] Shapin and Shaffer (1985, 3-7, 30-31), Shapin (1996, 96); Latour and Woolgar (1979, 106); Collins (1998, 299), Latour (1983, 260-264), Fleck (1979[1935], 14-19).

[24] Models in science represent parts of the world under investigation in particular respects and degrees, which vary depending on available techniques and the purposes for which those models are constructed. Techniques and purposes, in turn, vary widely across disciplines, fields, and socio-historical contexts. Improvements to a model strengthen or extend the similarity claims associated with it, according to the standards of the relevant research community.

[25] New interfaces between distinct lines of inquiry can arise in three ways: a single line of inquiry divides into two (or more) distinct branches; two distinct lines of inquiry merge to become one; and two distinct lines of inquiry remain distinct, but alter their relation to one another. All three are a means to (though not a guarantee of) greater consistency, coherence or unification of scientific knowledge. Division of a single line of inquiry into two disambiguates the goals and means at work within a line of inquiry, reconciling inconsistencies between apparently incompatible models and thereby organizing inquiry more efficiently. Merging of two distinct lines of inquiry to form a new, more inclusive group is, roughly speaking, the converse of division of labor. The subject matter of distinct lines of inquiry is seen to connect, such that models previously thought unrelated are seen as relevant to one another. Conflict and controversy ensue, precisely because of the new connection; coordination is achieved (at least in some cases) via these apparently antagonistic social interactions. Lines of inquiry are then seen as more coherently organized, contributing via different roles to a larger project with a more inclusive shared goal.

and mere coincidences as well as the (often unexpected) results of lines of inquiry themselves. So the way in which epistemic ideals of consistency, coherence and unification are cashed out in any particular new interface depends on many contingencies, as well as the standards for evaluation of models accepted by the groups in question.

The social action framework captures this indirect relation: the two aspects of success are participant means to the shared epistemic goal of scientific inquiry, scientific knowledge. That is, recognized successes (improved models and new interfaces) are seen as contributions to scientific knowledge: provisional, partial, and unavoidably enmeshed in human social interactions, yet all directed toward a further end. The social action framework accommodates normative and descriptive approaches to social epistemology of scientific inquiry without identifying scientific knowledge with the outcome of successful scientific episodes, nor dismissing as irrelevant the socially-enmeshed epistemic standards used in actual scientific episodes. The task now is to specify this end or shared goal, using the results of empirical study of our scientific practices. One such result (generalizing from the HSC episode) is that the two aspects of success are coordinated in our scientific practice. Models count as improved according to the epistemic standards of some particular group pursuing a line of inquiry. These standards are unavoidably enmeshed in that group's socio-cultural context. Models meeting the standards of different lines of inquiry are brought into critical contact by formation of new interfaces between research groups. New epistemic goals and standards for their achievement are then negotiated. Models that satisfy standards of improvement in one context are thus given critical scrutiny from a new (though not wholly unrelated) perspective. And so on, as inquiry continues. The two aspects of success are thus coordinated means for ongoing successful inquiry – iterations of model-construction and interface-formation.

*Scientific objectivity*.

Having characterized these means by socio-historical study of scientific practice, we can now ask: what must the shared goal of our scientific practices be like, given the means taken to it? Here the minimal requirements for social action come into play. Recall that these are preconditions for conceiving scientific inquiry in terms of instrumental rationality.[26] If scientific practices can be understood and evaluated in terms of instrumental rationality, then they have a shared goal that is achievable by coordinated participant means: construction of improved models and coordination of lines of inquiry via new interfaces. Historians, sociologists and philosophers of science, as well as scientists themselves, do try to understand scientific inquiry in this way (as well as others). So these requirements, though minimal, have quite broad prescriptive force. Applied to the descriptive account of scientific success in the social action framework, these minimal constraints on social action explicate the distinction between scientific knowledge and opinion.

Scientific knowledge, the shared goal of our scientific practices, must be achievable by the coordinated means taken to it. There is of course no guarantee of success, nor can a comprehensive plan be detailed. One reason for this is that formation of new interfaces between distinct lines of inquiry is highly contingent, as is the negotiation of new epistemic standards brought into critical contact thereby. A consequence of this socially-enmeshed contingency is that the pattern of formation of new interfaces cannot be specified in advance. If formation of new interfaces is unpredictable in advance, then the epistemic standards resulting from such new interfaces are likewise unpredictable. So the standards to which a successful model will be held accountable cannot be specified in advance.

The minimal constraints on instrumentally rational social action require that shared epistemic goal of scientific inquiry be achievable by the interplay of construction of improved models and formation of new interfaces, where the epistemic standards successful models must satisfy cannot be specified in advance. That is, scientific knowledge (conceived as the aim of inquiry) must be such as to possibly result from the coordinated means taken to it. So scientific knowledge must be such as to possibly satisfy epistemic standards not specifiable in advance. This is, admittedly, a very thin characterization of scientific knowledge, but it suffices to rule out 'knowledge by agreement' as the goal of scientific inquiry.

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[26] This is not to say that scientific inquiry is instrumentally rational; only that it may be understood and evaluated in these terms (*i.e.*, the fit between goals and means). This account is neutral as to further requirements for instrumental rationality and epistemic variants of same.

Knowledge that is so only in virtue of the epistemic standards of specifiable groups in particular socio-historical contexts, is not an achievable shared goal of our scientific practices. So the epistemic standards distinguishing scientific knowledge from opinion are not identical to the epistemic standards accepted within particular socio-historical contexts (if we suppose that our scientific practices can be understood in terms of fit between goals and means). This is an important (negative) result. One can grant that our scientific practices are pervasively social, and indeed that social interactions are necessary for epistemic success in all but the most fragmentary and circumscribed episodes of scientific inquiry, without identifying scientific knowledge with authoritative opinion in particular contexts.

Put more positively, this result specifies the ideal of scientific objectivity in relation to our scientific practices. Our scientific practices, conceived as social action satisfying prerequisites for instrumental rationality, aim at knowledge that is so in virtue of satisfying epistemic standards that are not limited to any specifiable group. Such knowledge is 'objective' in a sense long associated with the epistemic distinctiveness of scientific inquiry, but hotly contested in recent studies of science (*e.g.*, Longino 1990, Daston and Galison 1992, Boghossian 2006). Objective knowledge, in this sense, is knowledge independent of the opinions of any single individual or group of individuals. In the terminology used here, that anyone (or any specifiable group) accepts a model as scientific knowledge does not make it so. The relevant epistemic standard does not depend on features specific or idiosyncratic to particular groups of inquirers (and, *a fortiori*, individual inquirers).

This result is not to be confused with an analysis of the concept of objectivity. It is, rather, an explication of an epistemic ideal implicit in our scientific practices, brought out by framing descriptive socio-historical narratives of scientific inquiry in terms of social action theory. This conception of scientific objectivity is normative, in two senses. First, it is required for understanding scientific inquiry in terms of means-end reasoning. Second, it specifies an epistemic ideal that allows for principled epistemic evaluation of our scientific practices. To be sure, this thin conception of scientific objectivity does not allow for all the epistemological critique of science one might want.[27] It is, rather, a starting point from which more substantive epistemic ideals could be elaborated.[28]

*Conclusion*.

This account of scientific objectivity bridges the gap between social aspects of scientific practice, on the one hand, and epistemic ideals of scientific knowledge, on the other. It does so by moving beyond the historical and philosophical case studies that frame the original dilemma. My account moves beyond historical case studies of the social aspects of scientific inquiry by embedding them in a social action framework that entails minimal normative requirements. Descriptive socio-historical accounts in turn yield a robust two-part account of scientific success that approximates traditional epistemic ideals of scientific knowledge. This two-part account of scientific success unifies diverse socio-historical case studies of scientific inquiry and so characterizes participant means to the shared epistemic goal of these practices. The minimal constraints for social action then specify the epistemic ideal of scientific objectivity. So my account also goes beyond philosophical case studies illustrating the application of an 'exogenous' epistemic ideal. Here the problem of principled application to our scientific practices simply does not arise. Instead, the distinction between scientific knowledge and opinion is explicated by engaging with the social aspects of our scientific practices from the outset. The resulting epistemic ideal of scientific objectivity validates normative epistemology of scientific inquiry and provides a starting point for elaborating further social epistemic norms. So it may play a grounding and framing role for philosophical case studies of scientific inquiry as well. I have not attempted such an expansion here, however. I have, instead, focused on the dilemma for social epistemology of scientific inquiry posed by

[27] It is not, however, toothless. For example: Intelligent Design; the entanglement of science and business interests; and 'imperialism' among the sciences. The Intelligent Design movement (considered as a line of inquiry rather than an educational policy) is not science because its proponents fail to participate in scientific inquiry (new interfaces with evolutionary research do not form) and do not share its goal (the knowledge ID aims at conforms to the convictions of a specifiable, idiosyncratic group). Associations between scientific inquiry and business interests raise epistemological concerns; my account provides a principled way of sorting problematic from unproblematic entanglements (emphasizing constraints on formation of new interfaces). Finally, among the sciences, attempts at 'disciplinary takeover' or sweeping assertions of hegemony are diagnosed as epistemically problematic (impeding formation of new interfaces).

[28] For example, Longino's social epistemic norms for reliable empirical knowledge (or something very like them) could be grounded by this minimal account (1990, 2002).

normative/descriptive dualism: epistemic standards distinguishing scientific knowledge from mere opinion either fail to engage our actual social practices, or collapse into description of socio-historical facts. I have outlined a way out of this dilemma that integrates history and philosophy of science. It is through understanding our scientific practices as social action that we gain purchase on epistemic ideals of *our* scientific inquiry, rather than idealized abstractions.

*Appendix: Interview methods*

Interviews aimed to identify and characterize social interactions recognized by participants as crucial in the search for HSC; and to reveal participants' attitudes toward these interactions (see below for details). Specifically, I sought to understand how interviewees conceived of their research activities in relation to those of other scientific inquirers, within and among laboratories and research communities, and the impact of these interactions (if any) on achievement of research goals. The inteviewees were: Laurie Ailles (Institute for Stem Cell Biology and Regenerative Medicine, Stanford); Robert Coffman (Dynavax Technologies, Berkeley); George Gutman (University of California, Irvine); Leonore Herzenberg (Stanford University); Libuse Jerabek (Stanford University); Motonari Kondo (Duke University); Sean Morrison (University of Michigan); Jerry Spangrude (University of Utah); Christa Müller-Sieburg (Sidney Kimmel Cancer Institute, La Jolla); and Irving Weissman (Stanford University). Interviewees were selected to provide a range of perspectives on the search for HSC. All but one (Herzenberg) are or were at one time members of the Weissman lab. Their periods of involvement with the search for HSC range from 2-3 years to more than three decades, and from the late 1960s to the present day. Interviewees' scientific roles in the episode include: graduate student, laboratory manager, medical student, post-doctoral fellow, principal investigator, and technician. Their subsequent career trajectories also vary widely, and include academic research, clinical research, and industry. The description emerging from these multiple interviews is therefore robust to these different participants' perspectives and roles.

To allow participants' attitudes to emerge, rather than imposing my own assumptions in the form of leading questions, I used the methodology of qualitative research interviewing. See Merton *et al* (1956), Briggs (1986), Seidman (1998); Zuckerman (1977) and Gerson (1998) on strategies for interviewing scientists in particular. Interviews focused on the search for HSC, and tended to proceed chronologically; otherwise discussion was unstructured, and ranged in duration from 75 minutes to two hours. Interview guides and biographies were prepared in advance for each subject. During interviews, "probe notes" were taken as reference points to facilitate returning to key events and attitudes (Gorden 1980). Interviews took place during visits to subjects' laboratories, and were supplemented by one or more of the following: a tour of laboratory facilities, further informal discussions with lab personnel, and attendance of the weekly lab meeting. These laboratory visits contextualized the taped interviews in two ways. First, they provided information about interviewees' current setting and style of working, and framed their attitudes toward past interactions in terms of contemporary roles and projects. Second, these engagements with interviewees' current working environment provided an opportunity to discuss the relation between the search for HSC and their current projects, eliciting interviewees' attitudes toward scientific success over time. Both were important for framing and interpreting the taped interviews.

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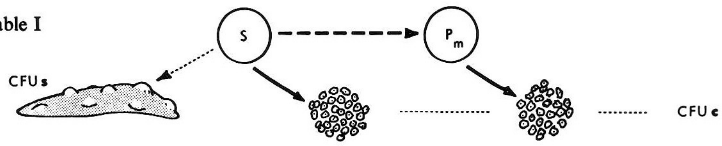
Figure 1

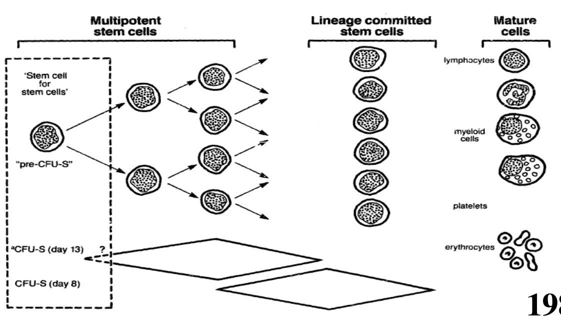
**Table I**



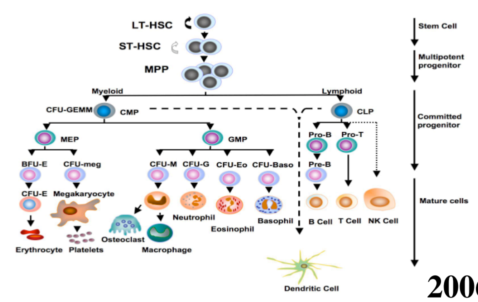

culture method

| Procedure for distinction | | Dicke | Toronto | Manchester | Bradley | Metcalf/Moore marrow | Metcalf/Moore embryo cells |
|---|---|---|---|---|---|---|---|
| Multiplication CFUs in vitro | | (yes) | no | no | no | no | |
| Separation obtained by | Velocity | no | yes | | | | |
| | Density-albumin step | no | | | | | |
| | Albumin continuous | | yes | | | yes | early - no<br>late - yes |
| | Ficoll continuous | | no | | | | |
| | 2 Dimensional dens.+ vel. | | | | | yes | |
| Vinblastine | c per $10^5$ cells | up | | up? | down | down | |
| | $\frac{\text{surv. s}}{\text{surv. c}}$ ratio | = | up | up | = | up | |
| $^3$H thym.suicide survival s>c | | small if any | yes | yes | | yes | |

Figure 2




1989

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