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THEMATIC ISSUE ARTICLE: NATURAL KINDS: NEW DAWN?

Cell Types as Natural Kinds

Matthew H. Slater

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Abstract Talk of different types of cells is commonplace in the biological sciences. We know a great deal, for example, about human muscle cells by studying the same type of cells in mice. Information about cell type is apparently largely projectible across species boundaries. But what defines cell type? Do cells come pre-packaged into different natural kinds? Philosophical attention to these questions has been extremely limited [see e.g., Wilson (*Species: New Interdisciplinary Essays*, pp 187–207, 1999; *Genes and the Agents of Life*, 2005; Wilson et al. Philos Top 35(1/2):189–215, 2007)]. On the face of it, the problems we face in individuating cellular kinds resemble those biologists and philosophers of biology encountered in thinking about species: there are apparently many different (and interconnected) bases on which we might legitimately classify cells. We could, for example, focus on their developmental history (a sort of analogue to a species' evolutionary history); or we might divide on the basis of certain structural features, functional role, location within larger systems, and so on. In this paper, I sketch an approach to cellular kinds inspired by Boyd's Homeostatic Property Cluster Theory, applying some lessons from this application back to general questions about the nature of natural kinds.

Keywords Cell types · Homeostatic property cluster kinds · Natural kinds · Stable property cluster kinds

M. H. Slater (✉)
Department of Philosophy, Bucknell University, Lewisburg, PA, USA
e-mail: matthew.slater@bucknell.edu

Cell Types in Scientific Practice

It's easy to be impressed with both the difference between and similarity among cells. A neuron and an erythrocyte resemble each other about as much as an orangutan resembles an oyster. But just as individual orangutans resemble each other in ways that are epistemically fruitful to biologists, so do individual erythrocytes resemble each other in ways that make them important pivots in our epistemic efforts.

The analogy between species and cell types also applies to the overall *structure* of their diversity. Though there are of course resemblances between species, we do not see a continuum of similarity among distinct organisms. Biological diversity is "clumpy" at many levels of organization. This sort of empirical fact is highly suggestive to enthusiasts about natural kinds. Brian Ellis, for example, writes at the outset of *Scientific Essentialism*:

> The distinctions between the chemical elements, for example, are real and absolute. There is no continuum of elementary chemical variety which we must arbitrarily divide somehow into chemical elements. The distinctions between the elements are there for us to discover, and are guaranteed by the limited variety of quantum mechanically possible atomic nuclei. (Ellis 2001, p. 3).

One of Ellis's chief goals in that book is to offer an essentialist account of natural kinds that places nomic facts on a secure footing. It is thus notable that the above "No Continuum Argument" lacks any reference to essences or essentialism.[1] Elsewhere, his essentialism is uncompromising: no wonder his warm-up example comes from

[1] See Mumford (2005) for a useful discussion of these issues.

chemistry, a domain of science often mined for examples by kind enthusiasts. Biological essences have appeared to be comparatively fewer.[2] In dark moments, some may even despair of identifying biological natural kinds at all. Given how thoroughly the biological sciences are committed to categories that operate in ways very similar to the categories identified as natural kinds (in, say, physics or chemistry) this would be an awkward conclusion indeed.

It seems to me, then, that the important philosophical question here is not *whether* such commitments can be vindicated, but precisely *how* we ought to vindicate them. In this article, I focus on the case of cellular kinds. Now, you will rarely hear biologists use the phrase "natural kind"—but "cell type" (and cognate phrases) is quite common. In his introduction to cellular mechanics, David Boal notes that while the number of individual cells in a typical human body is "literally astronomical, about three orders of magnitude more than the number of stars in the Milky Way," their *variety* can be captured by more pedestrian figures:

> for their immense number, the variety of cells is much smaller: only about 200 different cell types are represented in the collection of about 10^{14} cells that make up our bodies. These cells have diverse capabilities and, superficially, have remarkably different shapes.… (Boal 2002, p. 1).

Such estimates have been used to study other biological questions. For example, Arendt notes that "cell type number has been used as an index of complexity" (2008, p. 868; see also Bonner 1988).

The language of type is encouraged in the first place by the "clumpiness" of cellular diversity noted by many biologists; one classic text notes in Ellisian cadences that "there is no continuum of adult cell types intermediate in character" (quoted in Vickaryous and Hall 2006, p. 2; see http://www.ncbi.nlm.nih.gov/books/NBK28393/). In the second place, any neutrality of the language of type is belied by the epistemic uses to which biologists put cell types. Different cell types can readily be identified morphologically (e.g., via histological examination), and these identifications can in turn reliably indicate that a particular cell will have other properties and dispositions characteristic of a cell of that specialized type.[3] Our ability to derive useful information from knowledge of a cell's type plays a key role in certain medical contexts:

> In one tissue for example, the pivotal importance of a particular pathway in a specific cell type or lineage may dictate the possible ways in which growth control is likely to be regulated in this context. This type of consideration may explain, at least in part, the tissue specific combinations of genetic alterations found in tumours. (Knowles 2005, p. 130).

And just as biologists often drop reference to species when discussing homologous genes (orthologs), cell types also cross species boundaries (see, e.g., Gall et al. 1986). It is difficult to overstate the practical scientific importance of this fact. It is what allows us to learn about our own biology by studying that of model organisms.

While I cannot survey here the full variety of epistemic uses of cell types (both explanatory and inferential), hopefully it is plausible that we have compelling reason to make sense of such types having more than an artificial existence.

Though plausible that cell types enjoy some manner of objective existence, we still lack a philosophical account of them. This article starts work on this project. I begin (in Sect. 2) by briefly motivating a *general* approach for accommodating cell types in a natural kinds framework[4]—as non-essentialist property-cluster kinds—evaluating competing proposals along the way. However, I will argue in Sect. 3 that the details of this case legislate for altering some of the core theses involved in the most developed and well-known property-cluster account: Boyd's Homeostatic Property Cluster (HPC) account of natural kinds (Boyd 1988, 1991, 1999). While the HPC account departs in important ways from traditional essentialism, it carries on what I will call a "bottom-up" approach to natural kinds in its theoretical use of causal mechanisms. This stance, I argue, faces a number of theoretical and practical problems. I will sketch an account of natural kinds of cells which avoids these problems by adopting a more "top-down" (or multi-level) orientation (Sect. 4) and close (Sect. 5) with some reflections on the general project of developing such accounts in the context of recent criticism that this endeavor has taken on scholastic hue.

Candidate Theories of Cellular Kinds

Suppose that the above constitutes good prima facie reason for thinking that cells types, like species, are real.[5] What philosophical account of their reality might we offer? If previous inquiries into the subject can be a reliable guide,

[2] Just how few is controversial.

[3] Subject, of course, to variations due to cell cycle, context, stimuli, and so on.

[4] One important question that I will not address in much detail here: what is connoted by "natural" as a modifier of "kind"? I persist in using the phrase "natural kind" to signal my acceptance of the continuity between the account of kinds I offer and more traditional accounts. As will become clear in the final two sections, though, "naturalness" will take on a somewhat different cast on my account.

[5] We will take a more critical look at this supposition in the final two sections.

we have three basic options: (A) treat them as essentialist natural kinds, (B) treat them as non-essentialist, cluster kinds, or (C) treat them as individuals. I advocate (B). We can get there fairly readily by considering the merits of (A) and (C) and eliminating them.

Consider first the essentialist approach. As typically conceived, Essentialism has three tenets:

(1) That the essential properties be intrinsic,
(2) That they be possessed by all and only the members of a kind, and
(3) That they explain why members of the kind have a series of superficial properties more or less in common. (See Ereshefsky 2010, §2.1 for discussion.)

In the case of species, some sort of suite of genetic properties have been the obvious candidate for essences, particularly in fulfilling tenet (3) (Wilkerson 1995; Devitt 2008). While biologists have been more willing to question the primacy of this explanatory link in recent years, the real difficulty with genetic essentialism about species has always been with the first two conditions (Wilson 1999, p. 190; Okasha 2002, §4; Barker 2010). The main problem is the lack of genetic homogeneity among members of a species: the "all" direction of tenet (2) fails.[6]

Interestingly, essentialism faces something like the reverse problem when it comes to cellular kinds. Even while it was known that differences between cell types devolved from different combinations of gene products, it was not always clear how this was achieved. The apparent permanence of cellular differentiation suggested that genes were selectively lost during development (Alberts et al. 2008, p. 411). This turns out not to be the case.[7] Within an individual organism, the genetic code of each cell is largely conserved—making it a poor candidate for an essence. Genetic essences fail the "only" direction of tenet (2) for cell types.

Of course, such considerations tell only against a particular *candidate* essence rather than essentialism full stop. Perhaps there are other properties that might fulfill each of the three tenets. One can imagine different ways of filling out the basic genetic essentialist line, say, by construing cellular essences as certain kinds of regulatory adornments and packings of the genome. I am not overly sanguine about the prospects of this sort of suggestion, however. For one thing, a purely structural description of these modifications would seem likely to produce an overly fine-grained system of kinds. From the perspective of differential protein production and its consequences for cellular structure and function—the qualities by which biologists typically individuate cells—it does not matter *how* transcription is regulated. For two, such expression patterns are dynamic, both during development and as cells go through their various cycles (for a good discussion of the complications of cell cycle on our cell type specification, see MacLean and Hall 1987, §2.4).

But even setting aside this dynamism problem, infraspecific genetic heterogeneity will likely frustrate attempts to find a precise essence candidate. Arendt cites several comparative genomic studies that show how "important cell type-specific marker genes are often absent or strongly modified in fast-evolving species" (2008, p. 869). Finally, even if some proposal along these lines looked at all appealing, some cells like erythrocytes and sieve-tube cells in plants lack nuclei in their terminal stage of development.[8]

Non-genetic intrinsic essence candidates do not readily spring to mind. One might consider "ascending a level" to look for distinctive physiological or structural properties in virtue of which cells take on certain characteristic functions (e.g., delivering oxygen, digesting foreign materials, producing certain neurotransmitters, etc.). Could we divide cell types on the basis of such features? In practice, we often can and do; but these features are generally treated as *diagnostic* rather than as *defining* what it is to be a cell of that type. This strategy simply reinstates the problem the flight to genetic essence was supposed to solve: the intrinsic structural heterogeneity typical of biological categories.[9]

Focusing instead on the characteristic cellular functions themselves (rather than the collection of structural/physiological properties that give rise to them) is perhaps more tempting, but faces its own problems. On the philosophical side, it's not clear that we have a secure conception of biological function sufficiently precise (and objective) to play any useful essentialist role. On the empirical side, it does not appear that biologists are prepared to treat cellular function as essential to certain cell types. Highly specialized cells may be typical only to relatively complex organisms. Arendt argues that "multi-functionality has been a general feature of ancient cell types" and that "evolving cell types can also acquire new functions" (2008, pp. 868–870). It is also clear that, in pathological contexts, cells can *lose* characteristic functions.

[6] Certain aspects of biological practice—to wit, a broadly historical orientation in biological systematics—also tell against (1). I will circle back to this issue shortly.

[7] In fact, this explanandum (permanence) turns out to have been overemphasized. In eukaryotes, cells maintain their differentiated status only in particular contexts—say, in certain tissue types or in the company of other cells of that type. Outside those contexts, they tend to de-differentiate.

[8] As Maureen O'Malley reminds me, this does not mean that they no longer engage in transcriptional regulation. And indeed, while their transcriptional activities are quite low (below normal detection limits), recent studies suggest that mature erythrocytes contain "diverse and abundant microRNAs" that play important roles in signaling and other maintenance functions (Chen et al. 2008, p. 2).

[9] For further discussion of the difficulties with this approach, see Wilson (2005, pp. 104–107).

Rather than survey other implausible options—many of which I suspect would fail tenet (3)—let us follow the trail blazed by "neo-essentialists" about species (e.g., Griffiths 1999; Okasha 2002; LaPorte 2004): perhaps we can relax essentialism to allow for *extrinsic* properties to define cellular kinds, dropping tenet (1). One might attempt to divide cell types on the basis of their developmental histories within the organism—what we might call their "developmental phylogeny." On its face, this suggestion looks promising. In multicellular organisms, cells differentiate in regular patterns during development. In many (relatively) simple organisms the developmental pathways of cells and tissues have been mapped in detail. Plausibly, such histories satisfy tenet (3): since different developmental processes normally trigger the gene-regulatory events that give cells their distinctive qualities, there's a straightforward sense in which these histories *explain* why cells have the characteristic properties they have.

Unfortunately the analogy with historical essences for species is imperfect. Unlike species, cells do not fit into a *single* phylogenetic tree.[10] Rather, development in each organism defines its own local tree. These trees, of course, resemble one another in specific ways. Certain developmental events such as cleavage, gastrulation, and the establishment of different germ layers (Gilbert 2000, p. 26) can be grouped at different levels of organization. Can we then define cells on the basis of their "phylogenetic location" on certain developmental tree *types*; or more specifically, on the basis of their location with respect to various types of developmental events?

This general proposal faces a number of difficulties. The first is primarily conceptual. How might one identify these different developmental event types? One obvious and common strategy is to define them in terms of their products; e.g., particular types of tissue, organ systems, and cells. But this introduces a circularity: we cannot informatively use kinds of developmental events to define kinds of cells if the latter are also used to define the former. It is not at all clear how else one might proceed here, particularly when it comes to extending developmental event kinds across species boundaries.

Second, and closely related to this point, reflection on the level of developmental similarity across species suggests that an inter-specific developmental taxonomy of cells will be (at best) rather more granular than what biologists typically countenance. While we can, it seems, identify very basic inter-species stages in early development, it is doubtful that the more refined developmental event types needed to define the cell types biologists recognize across species boundaries exist. Homologous cell types are generally recognized on physiological or molecular bases.

Third, such a classification scheme is likely to be rather revisionary even at the level of individual organisms. Some cell types, such as cartilage cells, have their origins in different germ layers in the embryo.[11] And some cells of one developmental heritage can be induced to take on the intrinsic qualities and functions of cells of very different heritages (as demonstrated in, e.g., laser ablation studies). Accordingly, biologists are prepared to countenance such "developmental interlopers" as being of the same type. While "trans-differentiation" may be relatively rare (apart from experimental manipulation), these studies do show that cells indistinguishable in their structure, position, and function can have very different developmental trajectories (Tosh and Horb 2009, p. 111). Valentine (2003, p. 37) summarizes: "Cells that seem morphologically identical and are found in the same tissues, or in seemingly identical tissues in different regions, can have different developmental histories."

Does not homology, however it is to be conceptualized, point us in a better direction? I don't believe so. The issue deserves more discussion than I can give it in this context, but let me again briefly gesture toward some worries. First of all, it is not universally granted that the members of a certain cell type *are* homologous (Vickaryous and Hall 2006, p. 3). But even granting this doesn't clearly help with our present problem. Suppose we were to focus on a single organism about whose evolutionary history we knew nothing (an unrealistic supposition, to be sure). Say we find it to be composed of, among other things, 10^{14} distinct cells. Yet further physiological investigation might move to group those cells into mere tens (or hundreds) of distinct types. The question of how such types ought to be defined emerges before we attend to the problem of extending such categories to its conspecifics or evolutionary relatives—i.e., before we initiate the complex investigations required to assess homology. This suggests that the question of cell types is in an important sense conceptually prior to the question of cellular homologues. Identifying cell types in an organism (or a species) is roughly equivalent to identifying traits (like forelimbs) that are even candidates for being homologous with those of other species.[12]

[10] Of course, in some corners of biology this is a contentious thesis about species too; for entry into the debate see e.g., Doolittle (1999) and O'Malley et al. (2010).

[11] Some have their origin in the neural crest, some in the mesoderm. I thank Brian Hall for suggesting this example.

[12] I think that matters are somewhat more complex that this brief look allows. For example, our knowledge of cellular diversity in different species—what cells appear grouped across distant evolutionary spans—may well feed back on our classificatory practices in our own species. Trait identification need not be strictly prior to homologue identification.

What of option (C): that cell types are in fact individuals in analogy to the species-as-individuals thesis (Ghiselin 1974; Hull 1978)? To my knowledge, no one has actually argued for this view. Indeed, the only person I know to have even *considered* the idea brought it up in order to note its implausibility. Robert Wilson thinks that our disinclination to treat cells, among other biological categories, as individuals reflects badly on the (much more popular) application of the individuality thesis to species:

> It seems to me telling that while traditional realism is rendered implausible for [biological categories that are intrinsically heterogeneous and relationally taxonomized] for much the same reasons that we have seen it to be implausible for species, there is little inclination in these other cases to opt for either an individuality thesis about the corresponding "taxa"…. (2005, p. 104).

But what *explains* our disinclination to treat cell types as individuals? I suspect the disanalogy noted above between the way in which species and cells are supposed to form "trees" looms large here too. Whereas "members" of a particular species can be re-conceptualized as *parts* in virtue of their causal–spatiotemporal connection, instances of particular types of cells lack the same kind of causal cohesion. There is not a single tree of which cells of a particular type might be considered "chunks" (Hull 1998, p. 31).

Advocates of the species-as-individuals view often posit strong historical constraints on biological classification. Even a very "tiger-ish" organism outside the familiar phylogeny of *Panthera tigris*—say, an organism from Alpha Centauri that just happens to resemble Earthly tigers in various respects—should not count as a member of *Panthera tigris*. They contend that their metaphysics explains and justifies this norm of classification. However this may be in the case of species, the transplantation studies mentioned above reveal this norm's unpopularity when applied to cells. Biologists are apparently willing to treat cells from outside the normal developmental trees (products of cellular trans-differentiation, either naturally or artificially-induced) as cells of their "most recently adopted" type. This tells strongly against the individualist metaphysics for cells.

Perhaps there are ways of finessing the above difficulties. And perhaps one could offer an account along lines different from the (A–C) mentioned above. I cannot see clearly what any of those revisions or alternatives would look like, however. Thus, we turn to alternative (B): understanding cell types on the property cluster kind model.

The HPC Approach to Cellular Kinds

Richard Boyd's Homeostatic Property Cluster (HPC) approach to natural kinds has rightly garnered considerable attention from philosophers of biology who despair of accommodating the heterogeneity common in biological categories on an essentialist (or individualist) model. The HPC account is built for flexibility, allowing that such kinds may be associated with a *cluster* of properties, no single one (or subset) of which are necessary for being a thing of that kind.

This alone makes it a more plausible way of conceptualizing cell types than the theories we have already considered. It apparently accords nicely with biological practice. Wilson, a prominent HPC advocate, focuses on neural cell types:

> Standard taxonomic presentations of [two particular types of cells] proceeds by introducing a list of features that each cell type possesses, including typical original location in the neural crest, the types of dendritic connections they typically make to other cells, the neural pathways they take, and their final locations and functions. Adrenergic cells are heterogenous with respect to any single one of these properties or any set of them and it is for this reason that they do not have an essence as conceived by traditional realists. Yet in normal development, these properties tend to cluster together, and it is this feature of the form that the heterogeneity takes that allows us, I think, to articulate a view that stops short of individuality and pluralism. (Wilson 2005, pp. 105–106)

Of course, it takes more than having a list of properties more or less in common for some category to be a natural kind. The third tenet of essentialism mentioned above addresses our use of natural kinds in inference and explanation by providing a particular "ontological ground" for these practices: essences explain why natural kinds are projectible.

The HPC account replaces essences with the clusters of properties themselves. As generally conceived, such clusters—more precisely, *instantiations* of many of the clustered properties—comprise causal homeostatic mechanisms that maintain the coherence of the cluster. It is in virtue of this coherence that categories associated with such clusters are apt to play the roles they play in our epistemic practices. Essences are inessential to natural kinds.

Despite this picture's attractions, I think that it too faces a number of problems, specifically concerning the theoretical role of mechanisms. I have discussed these problems in a more general context elsewhere (Slater, manuscript); my present focus will be on the ways in which these problems become salient for the application of HPC to cell types. The HPC account retains from the traditional approach a sort of "bottom-up" stance about how kinds are to be defined. I will argue that a top-down (or at least multi-level) approach is more appropriate to the complex ways in which cells are understood.

The bottom-up orientation to kinds is quite apparent in the traditional essentialist account. As Putnam explicates the explanatory role of natural kinds, they are "classes of things that we regard as of explanatory importance: classes whose normal distinguishing characteristics are 'held together' or even explained by deep-lying mechanisms" (1975, p. 139). Such properties and mechanisms are "deep-lying," I suppose, in at least a mereological sense. Natural kinds in chemistry are often defined recursively in terms of structures formed by constituent sub-kinds (Slater 2005, pp. 25–26): water has the properties it has in virtue of the fact that its essence is having a particular structure of *other* natural kinds. Mereological "deepness" begets explanatory deepness; and explanatory deepness in turn grounds natural kinds' reality.[13] So the thinking goes—more or less—for HPC kinds too.[14] Early on, Boyd emphasized the importance of causal homeostatic mechanisms for grounding the reality of kinds. He writes that kinds "cut the world at its joints" in the sense that "successful induction and explanation always require that we accommodate our categories to the causal structure of the world" (Boyd 1991, p. 139). Other commentators have focused on the individuative role of such mechanisms. In his detailed discussions of the HPC approach, Paul Griffiths writes that, in general, "Phenomena with the same explanation should be placed together and phenomena with different explanations drawn apart" (1997, p. 171). Categories that are not held together with causal mechanisms, on the other hand, should be rejected (p. 191).

I have some general concerns about both of these roles for mechanisms that I will only briefly mention. First, there is an unanswered question of how to precisely analyze phrases like "the causal structure of the world." Second, the vagaries of individuating particular causal mechanisms seem poised to infect HPC kinds with an undue degree of subjectivity. Carl Craver (2009, p. 583) has pursued this line of thought forcefully: "One can be led to lump or split the same putative kind in different ways depending on which mechanism one consults in accommodating the taxonomy to the mechanistic structure of the world." Third, there are some distinctly theoretical problems with using mechanisms to individuate natural kinds. We must often rely on *types of* (rather than token) mechanisms. It would be natural to want to understand such types via the HPC approach itself (it seems doubtful that biological mechanisms will exhibit the sort of pristine homogeneity that makes them amenable to essentialist treatment). But this will initiate a regress.

A set of more specific concerns includes apparent violations of Griffiths' stance about kind individuation. We don't always divide phenomena with different explanations or treat categories not associated with a homeostatic mechanism as natural kinds. Consider a particular cell. It features, let us suppose, a certain cluster of properties by which we individuate cells of that type. This cluster is cohesive in the following sense: within certain tolerances and circumstances, properties from the cluster are reliably found together. The cluster is "stable"—not in the sense that any time it is instantiated[15] it *stays* instantiated, but in the sense that the *pattern* of these co-instantiations is stable across relevant counterfactual suppositions and (to some extent) across time. Simply put, it is a "robust" fact about the world that certain cells have features P, Q, R, S, T such that subsets of those features reliably betoken the existence of all of them.[16]

Now, what explains the robustness of this fact? The essentialist posits an essence; the HPCer posits a mechanism. Both accounts have these explanations serving a critical individuative/semantic role. In the context of the HPC account, if the stability of the same cluster of properties P, Q, R, S, T is maintained by two distinct mechanisms, we have two HPC kinds.[17] This in itself may not be objectionable. But consider: what is the mechanism that maintains the stability of the cluster associated with our (unspecified) cellular kind?

As it happens, we face an embarrassment of riches. The stability of the characteristic properties of our cellular cluster (call it "C") depends on the proper operation of the various mechanisms operating within and without the cell—not only for the continued operation of a particular cell itself, but in view of the various "quality-control" and environmental-maintenance mechanisms embedded in the larger organism. A host of other separately identifiable mechanisms and conditions—facts about developmental canalization, ecological factors relevant to development (Gilbert and Epel 2008), selective factors, and so on—are complicit in the stability of C.

But focus for now just on the first two: suppose that we have an intracellular mechanism (really an assemblage of

[13] Though this train of thought is rarely explicitly mentioned, it seems implicit in many late-20th century discussions of natural kinds; it is beyond the scope of this article to attend to its justification.

[14] This is a similarity also noted by Häggqvist (2005), §5), with whose views on HPC kinds I find myself in broad agreement.

[15] I use the idiom of "clusters being instantiated by an object" as a shorthand way of saying that (sufficiently many) properties in the relevant cluster are instantiated by that object (for the relevant purposes). I will address the issue of these qualifications shortly.

[16] I offer a more precise characterization of what I call "cliquish stability" in §5.2 of my ms.

[17] This possibility may depend on two further possibilities: (1) that the same properties can instantiate distinct mechanisms; or (2) that some mechanisms may be exogenous to the cluster (as, e.g., Boyd 1999 seems to allow).

various mechanisms) and an extracellular mechanism that underpins C's stability. What is *the* (emphasis definite article) explanation of C's stability? One response would be to "sum the mechanisms." Suppose we have an account of mechanisms up our sleeve (e.g., Machamer et al. 2000; Bechtel 2006). If it allows for the two lower-level mechanisms to be reckoned as parts of a larger mechanism, then we *also* have a single mechanism as required by our strict HPCer (just as a single block of wood can be composed of several smaller blocks of wood somehow fused together).

The problem is that such a multiplication of mechanisms opens the possibility that we will vastly over-multiply our kinds. Suppose that in two species, A and B, different quality-control mechanisms hold sway (though the same mechanism type acts intracellularly in the relevant cells of both species). Presumably, we then have two distinct *total* mechanisms and so two different cellular kinds. If this result complicates our epistemic lives—say, the differences in the extracellular mechanisms are incidental to their stability-maintaining operation (such differences might exhibit themselves elsewhere)—it is unacceptable. Since such situations seem perfectly possible (and are likely actual) and since we *should not* in those situations multiply our categories, I conclude that HPC theory is not well suited, as it stands, to accommodate our classificatory practices regarding cellular kinds. And since I believe that the theoretical problems with causal mechanisms mentioned above are serious, it again appears that we should be searching for an alternative.

Cell Types as SPC Kinds

Both the essentialist and HPC accounts of natural kinds take what I have called a bottom-up stance about kind individuation. The general problem with this stance, it seems, is that it tends to overestimate underlying homogeneity forcing us to over-split our categories. Fortunately, I believe that a (relatively) straightforward fix to the HPC account gets things right. In brief, the fix is this: drop the requirement that cluster kinds must be individuated by the mechanisms maintaining their stability. Indeed, drop the requirement that the cohesiveness of a natural kind must be maintained by mechanisms *at all*. Häggqvist makes a similar suggestion when he argues that "the demand for underlying mechanisms, even short of demanding internal micro-mechanisms, is still excessive. It is not at all clear why the lack of such mechanisms should impair the soundness of a kind" (2005, p. 80; cf. Lipton 1996, p. 493).

Though Häggqvist and I agree that causal homeostatic mechanisms are not necessary for grounding the reality of natural kinds, we differ about what should replace them. He claims that "projectibility is what matters for kindhood.… Dropping the appeal to explanation results in a position that might be dubbed *bare projectibilism*" (p. 82). While I am sympathetic to this view, I think Häggqvist is too quick to give up on finding a metaphysical explanation for the projectibility of natural kind categories. While we can think of the HPC and Essentialist views as offering us an explanation of the projectibility of a kind, it seems useful to me to conceptualize this explanation as running through an intermediate stage (see Fig. 1): a more proximate and general explanation of the projectibility of a kind is the fact that the properties characterizing that kind are—in a certain sense to be addressed shortly—*stable*. This stability may often be maintained by causal homeostatic mechanisms or essential properties, but it need not be.

The account of natural kinds that emerges—what I call the *Stable* Property Cluster (SPC) account of natural kinds—thus avoids the vagueness and theoretical difficulties involving causal mechanism. It affords a metaphysically neutral (yet theoretically specific) framework for understanding natural kind phenomena. In so doing, it effectively *unifies* previously theoretically disparate "kinds" of natural kinds: we can see essentialist and HPC kinds as different points on a spectrum of stability.

One might object to the SPC account's willingness to do without either causal mechanisms or essences. Can stability really be accidental or brute? In either case, the objection

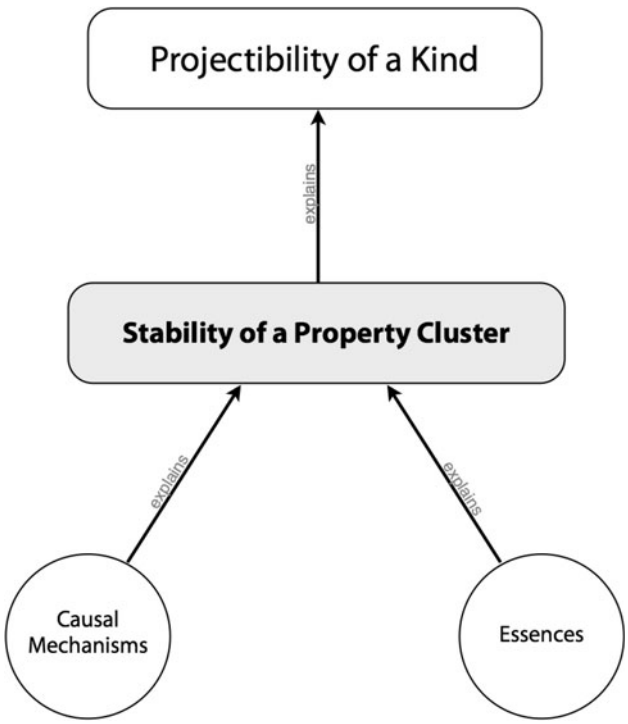

Fig. 1 Explanatory links between essence, mechanism, stability, and projectibility

continues, the category itself could not provide us with inductive knowledge. Häggqvist's response to the "accidentality" side of the objection (as exemplified by Millikan 2000, p. 17) serves my purpose too. It's not as though investigators find themselves "Gettierized" in such cases: "It is not a matter of believing something whose truth is accidental, relative to one's evidence" (Häggqvist 2005, p. 81).[18] On the brute side, it's far less clear what the specific worry would be—apart from a general suspicion of "bruteness." But again, as Häggqvist rightly points out (p. 81), we are often willing to tolerate an absence of a non-brute explanation for the projectibility of fundamental physical categories (such as electrons). I take no position on how common a phenomenon "brute stability" is. I am only committed to its possibility. The main point of the SPC account is just to refocus our philosophical approach to natural kind phenomena on stability rather than the various means by which stability is achieved.

I have not said much so far about stability. As the story turns out to be somewhat complex, I must again refer you elsewhere for the details,[19] but here's the big picture. Some properties are, as Chakravartty puts it, "systematically sociable" (2007, p. 170); they clump together. Their clumping, moreover, is a stable fact about the world. Now there are a few possible senses of stability that might apply here. One sense is that once instantiated by a particular, certain properties resist being non-instantiated. However, if we allow that the self-same object can change kinds (by absorbing a proton, say, or activating another suite of genes), this standard of stability is too demanding for an account of natural kinds.

Another sense—what I call "cliquish stability"—involves the tendency of some properties to show up together. Like cliques of teenagers, they may flit from place to place (in state space), but when you find a few of them, it's a good bet that the rest are close by. It is a good bet because their cliquishness (unlike that of teenagers, perhaps) is not easily disrupted—it is robust across the counterfactual suppositions consistent with the laws and facts about property clustering and interests of the relevant scientists.[20]

This description is necessarily schematic. But I hope that it is reasonably clear how it can apply to the case of cell types. We first identify properties of cells that are sometimes shared—be they physiological, genetic (e.g., patterns of gene expression), molecular—and look for patterns of clustering. How are such properties selected? Convenience doubtless plays a role. Much of our understanding of the physiology of cells stems from their examination in histological preparation—a complex process that highlights some features and obscures others.[21] In Vickaryous and Hall's (2006) approach, they selected 19 synapomorphies (shared derived characters), and employed standard cladistic techniques to analyze groupings. Though they did not explicitly seek out groupings that were stable in my proposed (cliquish) sense, this seems a clear implicit commitment we undertake given our willingness to project the resulting categories.

Cells are (imperfectly) associated with characteristic clusters of properties. Biologists recognize and use such types in a variety of contexts, across distinct organisms and species—evincing a commitment to the stability of their associated clusters. It is a very good—and as far as I can see unanswered—question how investigators uncover the sorts of subjunctive facts I contend ground stability. No doubt we often assess stability via investigations into the motley ways stability is typically achieved: by various physiological and developmental mechanisms, phyletic inertia, and so on. But it seems equally apparent that stability is often simply inferred by the mere fact that we see relevant clustering recur in a wide variety of contexts.

At the end of the day, norms of biological practice—concerning, among other things, the degree to which properties cluster, the sorts of properties particular disciplines and investigations attend to, and degree and circumstances of their stability—tell us whether a particular category is to be counted as a natural kind. Natural kinds, on the SPC view, are thus intimately connected with practice. An interesting consequence of this view is a sort of domain- and context-relativity of some natural kinds.

Let us consider a quick example of one of the many ways in which such nuances can get played out. Glial cells serve as a sort of neuronal "glue" (hence their name), helping to support, nourish, and buffer neurons. Presumably such dispositional properties would be included in any cluster associated with glia, along with morphological properties unrelated to these functions. However, when glia are removed from the organism, they lose some of their characteristic dispositions while retaining many of the

[18] We can go further in pointing out that even adding causal mechanisms doesn't clearly avoid accidentality: for such mechanisms might only operate on highly contingent bases. See §4.1 of my ms. for more discussion of this point.

[19] See my aforementioned ms., particularly §§5–6, for the full story.

[20] In the full account, I make use of the theoretical apparatus at work in Lange's (2000, 2009) account of natural laws and the interesting way in which he attenuates this construction in making room for laws in the so-called special sciences (Lange 1995).

[21] The most common histological preparation is rather involved and manipulative: one first dehydrates and fixes cells with formalin, then embeds them in paraffin, slices them with a microtome, mounts the slice on a slide, staining it first with hematoxylin and then eosin ("H&E staining"); see Ross and Pawlina (2011, p. 2) for a significantly more detailed description. Other techniques involve different stains (including antibody-linked fluorescent stains) and sectioning strategies.

structural properties by which we recognize them—i.e., the cluster comes apart in some investigative contexts.

Yet it may still be correct to say that this cell type is a natural kind in virtue of the fact that its property cluster is stable in the context where it normally functions and hence where it is epistemically most useful to us.[22] What should we say of the particular cell in the Petri dish, though? Of what kind is it? The particulars of the case matter, but there are a few obvious possibilities.

First possibility: the cell retains enough of the cluster of properties associated with the kind for the relevant domain (perhaps it retains its overt morphology but not its functional competence), but in its new solo context, those properties are unstable. Second possibility: the cell lacks sufficiently many properties to count as a member of the kind *glial cell* (and the glial cluster is unstable outside the proper organismal context). In either case, I think, we can retain the common practice of speaking of the cell as a glial cell. In the first case, we might consider the cultured (or frozen, or …) cell as a member of the *category* glial cell, but not treat that category as a natural kind in that extra-organismal context. In the second case, we could reckon it as a glial cell "by courtesy"—in virtue of its *history* of having been a glial cell and not its intrinsic features. We might extend this courtesy insofar as the cell can reliably teach us about its kin. The SPC view, I want to suggest, encourages us to think of "natural kindness" as a sort of *status* that categories can enjoy in certain circumstances. A theory of natural kinds was never (or *should* never have been) meant to provide *blanket* inductive license to project properties associated with a kind to an individual possessing some of those properties.[23] Rather, it helps us understand how certain categories *do* serve this role when they do. It is well known that inductive inference occurs only against the backdrop of background knowledge. This background can defeat the prima facie epistemic warrant provided by a category's kindhood. My interpretation of the background of the present case suggests that biologists treat cells in vitro as of the relevant kind in the first sense noted above in virtue of their largely unidirectional epistemic utility for shedding light on cells of the same kind in vivo. The case is isomorphic to that of medical students learning human anatomy and physiology by dissecting cadavers (or even to paleontologists learning about extinct species). Are such objects of the kind *human*? A "yes-and-no" answer seems compelling. They retain many of the properties of living human organisms in virtue of having a particular causal history (death need not disrupt the relevant structural properties when the cadaver is properly treated and stored), and so, studied in the proper context, allow us to reliably discover facts about living humans.

[22] That is not to say, of course, that such cells are not epistemically useful in vitro—doubtless, much of our understanding of the structure and function of different cells comes from careful histological work in contexts where the specific cells have *lost* many of their characteristic functions (being fixed, stained, frozen, metal-coated, or what have you). But the target of these studies is typically the physiological role these cells play in the their "native environments."

[23] This is one of the reasons I am reluctant to go in the direction of Häggqvist's "bare projectibilism."

Dawn or Twilight?

Ian Hacking has famously suggested that philosophical research into natural kinds has become "scholastic" in several senses. I want to comment on one in closing: Hacking contends that the project is scholastic in its centering on "an inbred set of degenerating problems that have increasingly little to do with issues that arise in a larger context" (2007, p. 229). Does this criticism hit home? That depends, for one, on how we construe this mix of metaphors, what issues we reckon arise in this "larger context," and whether those problems seem to us important.

One might plausibly respond to the latter question by urging pluralism about importance. The biological sciences will clearly not grind to a halt if, as Hacking suggests, we were to forswear use of the term "natural kind." But that doesn't mean that there aren't interesting and important questions to ask about whether there are biological natural kinds and how they are addressed by the biological sciences. It may simply be that little of practical importance hangs on the answer to this question.

This answer concedes too much, though. In investigating the patterns of diversity of cells within and among organisms of the same and different species—how such diversity arises, how it is maintained, and why it matters to us—we are, in my view, thereby caught up in inquiries concerning how and when cells form natural kinds. In employing talk of cell type in the epistemically potent sense, biologists are evincing a *commitment* to some cells being natural kinds. Perhaps not *all* cell types identified by biology are natural kinds in the sense I have in mind. Some may be taxa of convenience, contributing to our epistemic ends only by organizing discourse. But I strongly suspect that there is a common phenomenon behind our seeing erythrocytes and electrons alike as different kinds of items, each important to their respective sciences. That phenomenon, I think, is the stable clustering of properties captured by the SPC account.

Now, I have offered here only a brief sketch of this account and its application to the case of cells. But hopefully more will join the pursuit of greater understanding of the metaphysical and epistemological foundations of biological classification at more levels of organization. Even if Hacking's criticism overreaches, he offers us an important

reminder of the danger that our philosophical inquiries into science can have a tendency of losing contact with science over time. That is indeed a tendency we should fight.

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