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Selfhood, Immunity, and the Biological Imagination: The Thought of Frank Macfarlane Burnet

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Abstract. The language of self and nonself has had a prominent place in immunology. This paper examines Frank Macfarlane Burnet's introduction of the language of selfhood into the science. The distinction between self and nonself was an integral part of Burnet's biological outlook – of his interest in the living organism in its totality, its activities, and interactions. We show the empirical and conceptual work of the language of selfhood in the science. The relation between self and nonself tied into Burnet's ecological vision of host-parasite interaction. The idiom of selfhood also enabled Burnet to organize and unify a diversity of immune phenomena. Rather than approach the language of self and nonself as a bluntly imposed metaphor, we focus on its endogenous origins and immanent uses in immunology.

Key words: biological thought-style, immunology, self and nonself

The self and the biological angle on immunity

The *self* assumed a central role in contemporary immunology soon after its introduction by Frank Macfarlane Burnet (1899–1985) in 1949.[1] The swift prevalence of the idea of self was in part a consequence of its familiarity and rhetorical appeal. Yet the establishment of what we refer to as "the idiom of selfhood" – the distinction between self and nonself to encapsulate phenomena of immunity and infection – bespeaks more than the power of metaphor to anchor itself in scientific language: selfhood reflects an abiding concern for what may be referred to as the "biological" tradition in immunology. Throughout its history, immunology has been marked by the interface

between two traditions of thought, recently characterized as chemical and biological, or in analytic terms as reductionist and holist (Silverstein 1989; Tauber 1994; Mazumdar 1995). With his attention to cells and their interactions, and his conception of infection and immunity in terms of life-and-death struggle between organisms, immunologist Elie Metchnikoff (1845–1916) had already laid the foundations of the biological orientation to immunity (1892–1905). While his work inaugurated the biological orientation, this approach saw a temporary eclipse during the first half of the twentieth century (Siverstein 1989; Tauber and Chernyak 1991).

Burnet restored the biological thought-style within immunology. His entire oeuvre, through a long career, is integrated by a consistent vision of living phenomena that nay be referred to as a "biological thought-style" (see Fleck [1935] 1979 and Lowy 1991). This reading of Burnet is consistent with his own understanding, which he called "biological" in implicit or open juxtaposition to "chemical". He labeled himself a "physician naturalist" (1967), remarking that when struggling to find a title for his work "the first that came to mind was nearly always 'A biological approach', or 'The natural history of (infectious disease, cancer, war, woman or what not)' " (1959: p. 1).[2] Burnet's approach to immunological phenomena was thus self-consciously biological. His use of the language of *self-nonself* was intrinsically a part of this orientation.

Burnet contributed to immunology the idiom of selfhood, which soon became ubiquitous within the science, conceptually organizing an array of phenomena – for example, infectious disease, autoimmunity, transplantation, and tolerance. Before Burnet, Metchnikoff had introduced a language of warfare and intentionality in immunology. These idioms are indeed closely aligned: "self- nonself" expressed, but importantly also expanded, the Metchnikovian image of competitive struggle between organisms and infectious agents (such as bacteria and viruses); and intentional acts of identification – particularly of "recognition" of the foreign – underlie the division and relation between self and nonself. The assimilation of Metchnikoff's and Burnet's idioms in immunology reveals the power of the biological perspective to integrate and clarify a range of phenomena, thereby conceptually guiding the imagination toward a unifying foundation. While reductionist approaches within immunology (such as early twentieth century serological studies or contemporary molecular biological techniques) are often heralded for their powerful practical consequences and regarded as objective science-proper, the influence of the biological thought-style is equally, if more tacitly, as powerful on the level of conceptual organization of immune phenomena. The idioms introduced by Burnet (and Metchnikoff before him) have become nearly invisible as the pervasive linguistic currency of immunology.

In this paper, we examine Frank Macfarlane Burnet's thought – the scientist who was the major force behind the reinstatement of the biological approach in immunology – focusing especially on his idiom of selfhood. Burnet's conception of self epitomized his biological vision. Knowledge built upon, or formulated through, the immunological conception of "self" is epistemically affiliated with a biological way of thinking. We elucidate this knowledge in examining how an interactional dimension of self-nonself underskirts Burnet's ecological perspective on health and disease; and in seeing how his overall use of a language of *self* comprehensively unifies and orders phenomena of infection and immunity. Before turning to these topics, we briefly discuss the biological perspective on life.

Wholes and parts

A common characterization of the biological perspective on living phenomena is that it embraces holism rather than reductionism. The idea of holism implicates a regard for the nature of life as *sui generis* – a phenomenon with its own integrity. The biological perspective takes as its units of analysis, or fundamental model, *the living organism in its totality*, regarded both epistemically and methodologically as whole. This view stems from treating life as fundamentally integrated, with its different constituents only having meaning as parts of a whole. While component parts may be separately studied – elemental analysis being regarded as not only possible, but necessary – for biological thinkers such dissection is not an end in itself. The true object of inquiry is to understand the nature of organisms as functioning whole; thus interest in such matters as hierarchical control and integration is an overarching concern. For the biological thought-style *organization* is the starting and ending point of inquiry into living processes (Tauber 1991: p. 24); the counterpart of "organization" is *assemblage*, which tends to characterize the chemical approach to the understanding of life.[3] On the biological view, knowledge about life does not involve decomposing the whole, and coming to understand the work of its constituents. Rather, it is a matter of deciphering the form and properties of the parts within the perennial foreground of the whole, as organizational rather than unattached units.

The priority of the whole organism is perhaps all the more evident in the understanding of the composite parts of the organism. For example, the biological orientation is vivid in a passage where Burnet describes the surface of the bacterium. His description reflects the essential characteristic of the biological thought-style, namely, the conceptual mediation through features of the living organism in its totality, regardless of whether the substantive focus is on the whole, on parts, or on parts of parts.

> The surface of the bacterium is not like an animal's skin, just a relatively inactive protective layer, it is the most important part of the organism, and every part of it is, and must be, intensely *alive* ...

After describing the bacterial surface as a "mosaic of enzymes", and defining enzymes as "large molecules which have the power to induce chemical changes in other molecules", Burnet returns to complete his conception of the bacterial surface:

> All we want to stress is the vitally active *interfering* nature of the bacterial surface. It is easy to see that the introduction of such a surface into the living substance of an animal cell will be very liable to disorganize the delicate co-ordination of functions therein. It will be irritant or dangerous, and actively resented by the invaded cell (1940: p. 42, emphasis in original).

Burnet describes the bacterial surface in light of the attributes and imagery of the living organism. While he telescopes onto the "bacterial surface" as a component of the organism – "the most important part" – his account of it is, on multiple levels, holistic. In writing that the bacterium's surface is "not like" the animal's skin, Burnet invites a comparison between them: bacterial surface and animal skin form the physical boundaries of bacterium and animal, respectively. The image of whole organisms – bacterium and animal – is tacitly invoked. And beyond circumscribing the entire organism, the "intensely alive" bacterial surface *itself* behaves as a whole. The organismal trait of *activity* is attributed to a component part, as Burnet generously describes the bacterial surface as a "vitally active interfering nature." The deleterious effect of the bacterial surface within the animal cell is, moreover, rendered in terms of the disruption of the cell's wholeness: the bacterial surface "disorganizes [its] delicate co-ordination of functions." Finally, the intentional ideas of "interference," "invasion," and "resentment" amplify the interactional nature of the bacterium-animal cell encounter.

In the biological perspective, the emphasis on wholes emerges on a phenomenological level in a form of reasoning that intensely accentuates *activity*. The "whole" comes through, not as an emergent of composite parts, but at the level of perceiving the action of living entities and their processes *en tout*.[4] Meaningful action is paradigmatically manifested at the level of the organism, but it is not limited to that level; it may be an aspect of a component of the organism. Burnet's analysis of the bacterium's surface reveals that disagreement between chemical and biological perspectives does not arise with respect to the level of analysis of life processes. The surface action of the bacterium is ascribed to its component *enzymes* – an understanding confluent with a chemical view of the destructive effects of pathogenic bacteria. However, Burnet never loses sight of the bacterium as integrated

and alive. For Burnet its entire surface is alive, and its vitality is conveyed in a language of action and intention: it has "interfering" capacities that are "actively resented." The organization of component parts, chiefly enzymes, into a whole living surface is conveyed in terms of a capacity to act, to interfere.

The integrated view of life is not an approach necessarily founded in a deliberate philosophical or metaphysical stance, nor does it reflect a proclivity to mystify the nature of life. While analysts of scientific thought often characterize holism as an emergent effect of the relation of parts, for the scientist with a biological orientation holism is not expressed in metascientific terms, but as a way of approaching phenomena while maintaining a view upon *life*. Life is manifest even in constituent parts of the organism: in Burnet's words, every part of the bacterial surface is "intensely alive," and the substance of a cell is "living."

Burnet's ecological view

The biological perspective is enthralled with the living organism. By keeping the living organism in the perennial foreground, it seeks to understand the nature of life. Biological thinkers query the phenomenon of life, by focusing on the existential and interactional boundaries of the organism. As something existent-in-itself, the boundaries of the organism are drawn by its birth and death. As something complete-in-itself, the boundaries of the organism are clear, for it stands apart from its environment, exhibiting an autonomy registered by its actions upon the world. And as something dependent-on-the-world, the boundaries of the organism are also flexible and permeable, for the organism is always intimately connected to its inanimate and animate environment, being both sustained and endangered by its world. All these elements – of history, of autonomous action, and dependency – make the life of the organism turbulent and its boundaries potentially unstable. The organism is mortal, active, and dependent, hence its vulnerable boundaries are simultaneously well-defined and fluid. While its boundaries are constantly crossed or negotiated, yielded or violated, for the organism to continue existing its integrity must not be challenged beyond certain limits which, themselves, are elusive and variable.

Elie Metchnikoff, who originated the biological orientation to immunity, propounded a view of disease and health in terms of a Darwinian life-and-death struggle between organisms. He grasped parasitic infection and host defense in terms of aggression and competition, writing that "phenomena [of infection and defense] ... are more or less directly connected with the struggle for survival that is always going on between the representatives of

the different orders of living beings" (1892: p. 28). Burnet also endorsed the evolutionary view of *strife*, describing infectious disease as a "manifestation of the interaction of living beings" and "part of that eternal struggle in which every living organism strives to convert all the available foodstuff in its universe into living organisms of its own species" (1940: pp. 4, 37). However, Burnet expanded this perspective on infection and immunity as life-and-death struggle. With the framework of *self-nonself*, he sustained a focus on how living organisms interface, while moving away from the understanding of interaction as a strictly competitive affair. The distinction between self and nonself invokes the idea that there are fairly clear boundaries between organisms; yet these concepts do not implicate a commitment about the nature or outcome of their relations. The concept of self thus enabled Burnet to articulate a more encompassing vision of immunity and infection.

Burnet's ecological perspective on the relationship between organism and parasite was intimately allied to his more encompassing vision, for ecological thinking is inclusive not only of the competitive struggle between organisms, but of the ways in which they are interdependent.[5] Exploring the interrelations of organisms is an expression of the biological interest in boundaries. Indeed, the biological orientation in immunology has always been preoccupied with the interactive boundaries between organisms: this preoccupation has been at the core of the science from the moment the microorganismal cause of infectious disease was identified. Immunity and infection are quintessentially, although never straightforwardly, connected with the interpenetration of organisms. So, for example, discussing disease caused by protozoa, Burnet observes that "there is probably no species of vertebrate which is free of infestation by protozoa in its intestinal tract" (1940: p. 51). Infection stems from this sort of infestation – from the transgression of the organism's bodily space – yet it is never a simple consequence of microbial presence in the body, for organisms are always already "invaded."

Burnet's ecological perspective introduced an angle of Darwinian thinking that had remained unexplored in the more narrow fixation on struggle and competition between organisms. For Burnet interaction signified not only competition but also balance, an "uneasy equilibrium" that develops between species since "all food chains are naturally interwoven" (1940: p. 13). Burnet's ecological perspective was evolutionary, not only in the emphasis on the "struggle for survival," but also in drawing on Darwin's image of life as an "entangled bank": as Darwin put it in *On the Origin of Species*, organisms "so different from each other ... [are] dependent on each other in so complex a manner" (1859[1964]: p. 489). Variability is always present in the "delicate unstable balance" of interacting and interdependent organisms, a balance that is fluctuating and precarious, rather than static and predictable. In his 1940

work *Biological Aspects of Infectious Disease*, Burnet's "unstable balance" is expressed both in his understanding of the immunological dimension of disease, viz., in the variable responses of individuals to microorganismal pathogens, and in his epidemiological picture of disease, viz., in the fluctuating patterns of the spread of infections. Burnet's dynamic picture of disease stems from his appreciation of the multifactorial, interactive determination of phenomena of infection and immunity. Epidemiological patterns emerge through the intersection of various factors: the relationship between host and parasite (including the physical condition of the host and the degree of virulence of the infectious agent), environmental conditions, as well as population, since infectious diseases have different trajectories of contagion in different population densities.

Like Metchnikoff, Burnet thought of parasites as predators and defined infectious disease as a form of predation of the parasite on the host. "The micro-organisms of disease," he writes, "are using the tissues of their host simply as the source of food they require for growth and multiplication" (1940: p. 8). This view of parasites living at the expense of the host understands survival as a matter of life-and-death struggle. Yet Burnet added to this nature-red-in-tooth-and-claw picture a broadened Darwinian insight, by incorporating a new adaptational angle upon the host-parasite interaction: rather than a contest to the death, he reasoned that the host-parasite relationship should tend toward a delicate equilibrium. With the exception of certain microorganisms – that spread from the host carcass or survive indefinitely outside the host environment (anthrax, for example, can survive for long periods in the form of spores) – most pathogens require a *living* host as a viable vessel for survival, for food and shelter as well as for reproduction and proliferation by transfer to other viable hosts.

Given the requirement for a living host, Burnet arrived at the intriguing conclusion that death from infectious disease must essentially be an *accidental side-effect* of parasite and host interaction – a consequence of the parasite's extraordinary virulence and/or the host's constitutional weakness. These circumstances aside, death from infectious disease is not *intrinsic* to parasitic form of life. Referring specifically to human infectious disease, Burnet writes that "the general point of view that we must adopt in regard to infectious disease [is that] it is a conflict between man and parasites which, in a constant environment, would tend to result in a virtual equilibrium ... in which both species would survive indefinitely" (1940: p. 23). Elsewhere, Burnet elaborates on this idea of host-parasite equilibrium, arguing that it is an oversimplification to regard their relation as pure conflict:

> It was once easy to think of the interaction between man and some pathogenic microorganism as a simple antagonism, success for the pathogen

> being measured by it own overwhelming multiplication with death of the host, success for the patient by recovery with annihilation of the invaders. But once the pathogen began to be thought of as a living organism dependent for its existence on a means of continuous survival, such a point of view became obviously untenable. Success for a parasite as for any other living organism is measurable only by the size and persistence of the population ... It is irrelevant to that success whether infection is fatal to every host individual or to none. But it is relevant that ... once an animal has died of microorganismal infection there is no further possibility of the pathogen being transferred to new hosts except in very special circumstances. An acutely fatal infection is, therefore, disadvantageous for the survival of the parasite. Conversely, a low-grade infection with no more than trivial symptoms but with free liberation of the pathogen over a considerable period of time will usually provide the maximum opportunity for dissemination of the parasite. With many sorts of qualification and limitation the normal end result of long-period interaction under approximately constant conditions between host and parasite is a state in which the host suffers no significant disability and the parasite persists long enough to ensure transfer by one or other method to a new susceptible host (1946: pp. 25–26).

As this passage discloses, the ecological perspective emphasizes the fluidity of boundaries. Multifactorial determination tends to underlie life processes in general, and disease and health in particular. Moreover, adaptation toward interdependence or uneasy co-existence is, if not the overriding trend, at least on a par with adaptation and survival at the price of the extermination of the other, whether host or parasite.

What in epidemiological analysis is considered the attainment of an "equilibrium" between organisms, became cast in Burnet's immunological thought as a matter of "immune tolerance." Indeed, Burnet's very first use of the concept of tolerance (1940: p. 24) is synonymous with the idea of "a virtual equilibrium" in which both host and parasite "survive indefinitely" (1940: p. 23). Ecological thinking focuses on patterns and consequences of interaction between organisms; it is, therefore, equally applicable to the outer and inner environments of organisms. Epidemiological trends pertain to the interface between organisms in the *outer* environment, while phenomena of parasitism, infection, and tolerance pertain to organismal interactions transpiring *inside* host bodies. Burnet's ecological thinking provided a unifying framework for the interaction between organisms in both outer and inner environments.

Reasoning on the basis of evolutionary pressures favoring adaptation and continued survival, Burnet arrived at the counter-intuitive picture of infectious disease with trivial or even non-existent symptoms for the host; he later referred to this condition "subclinical infection" (1962: p. 20). He expanded the vision of the host-parasite relationship, moving beyond a rigid identification of parasitism with predation, in the recognition that a deadly predatory-parasitic assault on the host is equally counter-adaptive for the parasite: by destroying the environment of its livelihood, the parasite brings about its own annihilation. The microorganismal infiltration of the host is thus profiled by Burnet as more complex than a straightforward disease-causing phenomenon. The boundaries between interpenetrating organisms are pliable, and thus the lines between parasitism, tolerance, and symbiosis – the latter consisting in a mutually advantageous association between organisms – are variable and fluid both intra- and inter-individually. As a consequence, Burnet notes the difficulty of finding "an objective standard of virulence by which different strains of micro-organism can be experimentally compared" (1940: p. 143). Corollary to this reasoning, in Burnet's thought states of health and disease are on a continuum, rather than being understood as two sharply distinct – not to say absolute – conditions of being.

Burnet's ecological view of the entangled bank of organisms was intimately linked with his immunological conception of selfhood. The ecological understanding of host-parasite interaction extended the entire gamut from deadly and antagonistic, to uneasy equilibrium, to indifferent co-existence. The relation between self and nonself transposed the ecological perspective to a higher, more inclusive level of abstraction. Just as the ecological view of the host-parasite interface encompassed states of health and disease as a continuum, so the idiom of selfhood united a variety of immunological phenomena within a single conceptual scheme. We now turn to trace how the language of selfhood arose in Burnet's thought and what role it played in his biological orientation.

Immunology as the science of self and nonself

In western thought the idea of *self*, in the sense of individual, person, or subject, has a long philosophical, and a more recent psychological, history. The intellectual history of the concept has been explored elsewhere (see Tauber 1994, 1995). Our interest here is in the connection between self-nonself and the biological thought-style, and hence we investigate the idiom of selfhood as a conceptual model *within* the science. Instead of approaching the idea of selfhood as *imported* from a cultural and historical milieu into a scientific context, we analyze it as an idiom that *grew roots* within the science, thereby becoming a virtually immanent component of immunology. Remaining close to the uses of self and nonself in Burnet's thought, we show

their intrinsic force in the science. This intrinsic force is especially evident in how immunological thinking was conceptually reorganized through "the idiom of selfhood." In calling selfhood an *idiom* we underscore its pervasive range in application and implication; we aim to convey its multi-tiered operation: the self-nonself ecounter incorporates an array of divergent phenomena, conjoining them in a single semantic universe. The idiom of selfhood has had a profound epistemic effect on the science, and on this count we argue that the uses of "self" and "nonself" defy classification as metaphorical or literal.

After Burnet's introduction, the language of self-nonself swiftly became prominent in immunology. The question that arises concerning its alacrity of reception in immunology is Why has it been so successful? Ilana Lowy has addressed this question, arguing that the strength of the immunological concept of self stems from its "loosely defined" quality (1992: p. 375 and *passim*). She accounts for the swift dissemination of the concept within immunology precisely in terms of its indeterminacy of meaning. According to Lowy, the success of the concept "self" in immunology has hinged on its being a "boundary object" between different biological subdisciplines and communities. It has had network value, providing a common language that has facilitated interdisciplinary communication about immune phenomena. Questions of autoimmunity and tolerance, for example, are not only theoretically fascinating to the biologist, but crucial practical matters for the medical community; or to take another example, the nature of infection intersects the fields of biochemistry, cellular and humoral immunology, and medical science. As Lowy argues, the language of self-nonself, loosely describing phenomena coming under these topics, has worked as a valuable communicative vehicle across different fields in the life sciences.[6]

We want to complement Lowy's insightful analysis by exploring her idea of a "loose definition" from a somewhat different angle. We interpret the open- endedness of the concept of self in immunology not so much as a consequence of its indeterminacy of meaning, as a quality of its *polysemy*. From an epistemological standpoint, the resilience of selfhood does not reside in its institutional-communicational function alone – its ability to function as a boundary object across biological communities – but in its power to organize and represent different biological topics under a single conception. This aspect of its appeal is intellectual: the epistemic force of self-nonself resides in its truth effects via making manifest the intimate interconnections between key immune phenomena. The diffusibility and productivity of selfhood is thus *not a matter of its nebulous character, but rather of its multiplicity of meaning*. Indeed, the immune concept of self ceases to appear semantically indeterminate, when concrete instances of its application are considered.

SELF	referential	illocutionary	perlocutionary
reflexive			
individual subject			

Figure 1. The polysemy of selfhood.

The force of the selfhood idiom flows from its polysemy which may be analytically delivered on a matrix of vertical and horizontal dimensions (Figure 1). The vertical axis focuses on the definition of the *word* "self," while the horizontal axis considers the different facets of the *concept* "self." The word self has two central uses: one, an emphatic use, appearing as an auxiliary suffix, prefix, or qualifier of another word; and two, a use synonymous to "individual subject." On the horizontal axis, the import of the concept self can be analyzed in terms of referential application (level of content), organizational accomplishment (illocutionary level), and evocative connotation (perlocutionary level).

Focusing for the moment on the vertical axis, we note that the word self has an abstract usage and a more concrete meaning. "Self" permeates our language almost unnoticeably as an integrated suffix or prefix of other words (as, for example, "itself," "myself," "self-sacrificing," and the like). It thereby qualifies particular entities or ideas in a *emphatic* or *reflexive* mode. The first definition of self given in the Oxford English Dictionary is "in concord with a substantive or pronoun, to indicate emphatically that the reference is to the person or thing mentioned, and not, or not merely, to some other." In this sense "self" refers reflexively to an entity, *qua* that entity, underscoring that it is circumscribed, separate, (quasi-) autonomous, or of singular quality, unique existence, or uniform essence. On the other hand, the more concrete meaning of self – according to the dictionary, "the realization or embodiment of an abstraction" – applies to the synonymous use of the term with the "human individual." This meaning is unambiguously delivered in the second, pleonastic definition of self found in the Oxford Dictionary: "the entire person of an individual."

The immunological usage of self imbricates the divalent meaning of self as emphatic reference and circumscribed individuality. In disentangling the two senses we want to show that the emergence of self within immunological thinking does not have a singular point of origin. Self makes its very first appearance in Burnet's 1940 *Biological Aspects of Infectious Disease*, where he describes an amoeba digesting its prey. Looking at this act, Burnet raises a question about an aspect so obvious, as to be often taken-for-granted. Why do the enzymes or ferments that digest the bacterium within the amoeba's body

"not digest the amoeba's *own* substance, chemically so similar to that of its prey?" (1940: p. 29, emphasis added). The question Burnet posed is thematically redolent. That digestion is not directed against the organism's "own" substance, foreshadows the seminal role that phenomena of autoimmunity were to play in Burnet's thought, namely, that the immune processes of the body do not normally turn against the body's own components. Moreover, the observation that the bacterium is "chemically so similar" to the amoeba identifies the elusive problem of defining the boundary between self and nonself. And at the same time, the idea of "the amoeba's *own* substance" anticipates the reflexive application of self, by lexically turning our focus on the amoeba *itself*. After posing the above question, Burnet introduces the self-nonself distinction:

> If we are to describe and discuss such phenomena scientifically, we must for the present at least be satisfied with a ... biological approach. Is there any simpler way of looking at this relationship between the eater and the eaten? It may be that something useful can be gained by concentrating on the most obvious aspect of all – that the engulfed micro-organism is not the amoeba *itself*. The fact that the *one* is digested, the *other* not, demands that in some way or other the living substance of the amoeba can distinguish between the chemical structure characteristic of "*self*" and any sufficiently different chemical structure which is recognized as "*not self*." Here we seem to have an important general character of animal protoplasm which may provide *a connecting thread to help link up some of the very diverse manifestations of the defense processes* which we shall have to consider. For with one very important exception, every disease-producing invasion of the body is by some type of organism whose intimate structure is *foreign* to the body. All such invasions can, in at least a proportion of instances, be overcome by natural processes. Perhaps it is significant that when invasion by the unco-ordinated growth of the body's own cells (cancer) occurs, natural processes never succeed in overcoming it (1940: p. 29, emphases added).

The variety of themes touched adumbrates the broad scope of self-nonself. The idiom of selfhood may be likened to a tool – a spindel. To extend Burnet's analogy of "connecting thread," selfhood has the essentially dialectical task of threading together the relationships between the amoeba and itself, the amoeba and the bacterium, immune defense processes and invasions in general, and immunity and abnormal self (cancer). The vast immunological topics implicated are readily appreciated: autoimmunity, nutrition and immune defense, tolerance and self-surveillance. With the very first appearance of "self" and "not self," in Burnet's work, the different levels of their application are already implicit. From the outset, the idiom of self-

hood emerges as a conceptual tool that spins together key immunological phenomena.

The birth of the selfhood idiom lacks a singular genealogical trajectory. This observation contravenes the idea that the origin of selfhood is purely exogenous to immunology – viz., a bluntly imposed metaphor. A subtle, far less dramatic, and *endogenous* aspect of the nascence of self-nonself can be discerned: these terms emerge in tandem, firstly, with the emphatic use of the word self in the phrase "the engulfed micro-organism is not the amoeba *itself*" and, secondly, with the use of the oppositional pair "the one" and "the other" that follows. The semantic progression, culminating in the novel application of "self versus nonself" in immunology, is a three-fold immanent movement:

(1) the engulfed micro-organism is not the amoeba *itself*
(2) the *one* is digested, the *other* not
(3) the chemical structure characteristic of "*self*" and any sufficiently different chemical structure which is recognized as "*not self*."

It could scarcely go unnoticed that Burnet cautiously enclosed the terms "self" and "not self" in quotation marks. (Though later in his work Burnet largely abandoned this convention of scare-quoting.) These self-conscious insignia betray his apprehension, or recognition, of a metaphoric status of self; while using the term, there is some aspect of its meaning that he demurs to extend to the amoeba. So while there is a textually internal progression from (1) the "amoeba itself" to (3) "self and not self" – mediated by the lexical bridge (2) "the one and the other" – there is also a lacuna between them, for *self* includes the semantic dimension of "the entire person of an individual," and its corollary implications of subjectivity, agency, and will. Because the human subject is the prototype of "the entire person of an individual," the application of self and nonself to the amoeba-bacterium encounter may imply analogies with a human interactional context: Burnet's quotation marks apparently aim to void such a tacit analogy.

By contrast "the amoeba itself," which anticipates "self," requires no qualification in its usage. This simple phrase vividly contours the amoeba, as such, against a momentarily undefined inanimate and animate environmental background. The work of *itself* is almost deictic: it is the linguistic equivalent to showing or pointing out directly the amoeba as an organism that has a separate existence, a living entity that is visually witnessable as complete-in-itself. Hence one of the pathways to "self" and "nonself" is the perceptual experience of the organism as separate, whole, and above all as *living*. Indeed, the very first usage of Burnet's distinction of *self* and *not self* is not only textually adumbrated within the same passage (lines 1 and 2 above), but foreshadowed three pages earlier in his brief discussion of the origin of life. In that context the distinction preoccupying Burnet is not that between two

organisms, but between "living" and "not living;" self- nonself also emerges more deeply at the border between living and not living. After recognizing the possible futility of speculating about chemical intermediates between not living and living matter, he goes on to characterize the first living forms as follows:

> All we can say is that they commenced the process of incorporating dissolved compounds of carbon and other elements into growing *self*-persisting units. The essence of life is this quality of incessant incorporation of any chemically suitable material into living substance which, in its turn, continues the process (1940: p. 26).

We find again the emphatic or reflexive self in the idea of organisms as "self-persisting units." The mutual reflection between *self* and *unit* delivers the perception of the living organism as a complete and separate entity. At the same time, the first identifying act of a living unit – "the essence of life" – is the nutritive act, which immediately implicates the encounter between the self and nonself. *Self*-persistence stems from the incessant incorporation of *other* substance into self. Self-persisting unit, then, encloses the duality of an autonomous existent that depends upon a relational context for its continued existence. Burnet's idiom of selfhood dives into the primordial waters of *seeing* an entity as living and interacting with its environment. Again we underscore the ever-present theme of the biological thought-style – the living organism in its totality, the prototype of life.

The complexity of the genealogy of the idiom of selfhood, with the interplay between the two uses of self, reveals that "self versus nonself" was not simply metaphorically imported into immunology. Such a view is partial to the familiar, commonsense meaning of self as "human subject." Yet the richness and evocative quality of the idiom of selfhood rests precisely on its defying the metaphor-literal divide. The idea that the encounter between, say, amoeba and bacterium is an empty screen onto which an anthropomorphic theatre of interacting "selves" is metaphorically projected elides the deep-rooted perceptual dimension of witnessing this encounter as one between two separate, living entities. The emphatic self expresses perceptual knowledge: writing about the "amoeba itself" is equivalent of pointing to the direct and simple way that the amoeba is perceived as living. To put it somewhat differently, if the sense of self as "the entire person of the individual" is only metaphorically extendable to amoebas, the emphatic (that is, deictic) sense of self is a literal application.

The immunological idiom of selfhood thus straddles the divalent meaning of self: it is presented immanently as an extension abstracted from its emphatic usage (viz., itself becomes self) and, at the same time, invokes the concrete synonym of "individual person," self-consciously flagged by quotation marks. The application of self-nonself to phenomena of infection and immunity becomes a meeting point of endogenous and exogenous genealogical trajectories. The passage in which the terms are introduced has been analyzed as expressing the heterogeneous origin of the idiom of selfhood. The complexity of self-nonself can already be discerned in one dimension of analysis (designated in Figure 1 as the "vertical"). The alloyed quality of selfhood can also be seen in the conceptual facets embodied in the "horizontal" dimension. The versatile, yet robust and productive idiom of selfhood thus takes shape through its polysemy.

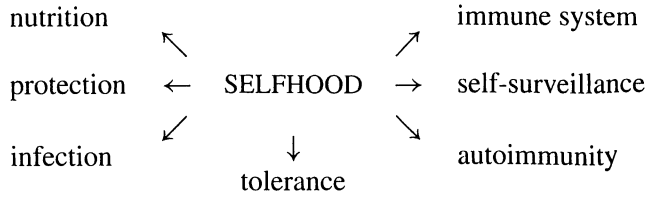

Figure 2. Immunological topics integrated through selfhood.

The vertical axis highlights the divalent meaning of "self" – which is constitutional of the word, rather than a tension in need of resolution. On a horizontal axis, the complexity of the concept of self may be analytically discerned on three levels: the propositional, viz., what it *refers* to in terms of the immune phenomena it directly characterizes; the illocutionary, viz., what it *accomplishes* in terms of organizing and unifying defferent phenomena in a single idiom; and the perlocutionary, viz., what it *implicates* in terms of its evocative effects as a concept with broader cultural and historical extensions – intellectual, political, moral, or psychological. Borrowing from J.L. Austin's analysis of language (1962), we disentangle these levels of propositional, illocutionary, and perlocutionary as an analytic strategy for expositing the semantic richness of immunological selfhood.

Figure 2 loosely catalogues an array of immunological topics conceptually and empirically tied together with the idiom of selfhood. The figure inventories what for Burnet forms the *scientific content* of the self-nonself division. These topics constitute the reference loci of the idiom. The idiom of selfhood is the conceptual pathway that reveals the essential similarity or interconnectedness of diverse immunological phenomena. The role "selfhood" plays as a semantic nexus constitutes its illocutionary force: it *organizes and unifies* different realms of immunological knowledge. We briefly overview certain of these immunological topics, showing how they are clarified and tied together through the self-nonself scheme.

The first act of the living entity is the incorporation of materials into self- substance. The first act of the self is nutritive – the transformation of nonself into self. Indeed, the *primeval immunologial act* is that of the predatory amoeba engulfing and digesting its prey, the bacterium. This is the microorganismal prototype of phagocytosis that Burnet acknowledged as fundamental in immunity:

> The phagocytic cells of the blood and of the fixed tissues *are* the final defenders of the body. The whole complex process of immunity involving the co- operation of blood vessels, tissue cells and both the fluid and cellular elements of the blood is directed toward bringing the various phagocytic cells to bear on the invaders at the most effective time and place (Burnet 1940: pp. 36–37, emphasis in original).

The nutritive act of engulfing and digesting is understood as a cellular preadaptation for the protective immune function of phagocytes. Phagocytosis is understood as the transfiguration of the nutritive into the prophylactic function. The nutritive act enables the continued existence of the living entity; yet its also places the organism at jeopardy, for to engulf a foreign entity is potentially a dangerous, even lethal, action. The typical outcome of the amoeba-bacterium encounter is the disintegration of the bacterium by digestion. But there is another possible twist to this story:

> Let us look at the process from the point of view of the victim, the eaten rather than the eater. Suppose that by some modification perhaps of its surface, the bacterium on which the amoeba ... feeds becomes resistant to the digesting effect. If it is taken in by the protozoon it will be retained for an hour or two, and then discarded as useless, passing out like Jonah, none the worse for its sojourn in a primitive digestive organ. From this stage it is only one step further for the smaller organism to develop the power on its side of utilizing for food the substance of the organism which engulfs it. If the microorganism can multiply within and cause the death of the protozoon, we can quite reasonably say that the protozoon dies of infectious disease (1940: pp. 30–31).

The nutritive act is thus not only the basis of self-persistence and the evolutionary portal to protection, but the possible pathway to infection. Both protection from and infection by nonself, both growth by digestion and death by parasitism, are phylogetically linked through the nutritive act of the self. The "self" takes an unavoidable risk in bringing "nonself" into itself. The evolutionary and functional transformations – from nutrition to protection, from nutrition to infection – are all mediated in the encounters between self and foreign and their diverse effects. Protection and infection are thereby apprehended as two sides of the same coin, being inverse outcomes of the

self- nonself encounter. These phenomena of life-and-death consequence become conceptually interconnected through the idiom of selfhood.

According to Burnet, immune protection is mediated both by humoral elements, fundamentally primary and secondary antibody response, and by cellular response. As a biological thinker it is not surprising that he maintained that immune phenomena are ultimately cellular, for humoral antibodies are themselves the products of cells – specifically of clone of cells: he considered the development of cell populations as "the most basic aspect of immunity" (1962: p. 45). Burnet demonstrates the functional priority of cells by describing a simple experiment. If, using genetically uniform mice, the serum of an immunized animal is transferred to a normal one, the latter ceases to respond to the corresponding antigen[7] within a few days. However, if the spleen cells of the immunized animal are transferred to the nonimmune animal, the latter will show a secondary response to the antigen even months later. Burnet concludes that "this experiment has the important implication that all the 'information' needed to allow antibody production can be transferred from the spleen of an immune animal" (1962: p. 50).

While affirming the importance of phagocytes, Burnet did not identify all cellular immunity with their actions. He recognized the significance of those ubiquitous immunocytes – known as "lymphocytes" – and of plasma cells. Given their respective morphologies, Burnet reasoned that the lymphocyte, with its large nucleus and scant cytoplasm, must be the carrier of information for the derivation of new cells, while the plasma cell with its extensive cytoplasm must produce antibodies (1962: pp. 54–55).[8] About lymphocytes he observes that "enormous numbers are present in the lining membranes of throat and bowel and appreciable numbers will be found wandering through almost every tissue in the body" (1962: p. 54). Thus, as in the amoeba so in the vertebrate animal, the potential tight link between nutrition and infection persists – whence the adaptation of protective cells along the interfacing surfaces between self and nonself.

Working in unison, the protective responses of lymphocytes, antibody-producing plasma cells, and phagocytes ensure the integrity of the self when they successfully destroy, or control, foreign elements; "microorganismal invaders can be recognized as something alien and inappropriate to the body" (1962: p. 39). Inversely, infectious disease is the consequence of invading parasites - - bacteria, viruses, or protozoa – not being successfully opposed by the host. According to Burnet, such failure is due either to the excessive virulence of the foreign element or to some deficiency in the responsive immune functions of self. Yet as the relational neutrality of the terms self and nonself conveys, far from being absolute states, infection/disease and immunity/health are pictured by Burnet on a continuum. "Nonself" is not

necessarily synonymous with a hostile, parasitic entity, and parasitic entities can vary enormously in degree of virulence. Therefore, between protection and infection looms a gray, undetermined but vast territory in the encounter between self and nonself: in immunology the phenomena within this gray territory come under the heading of *tolerance* (discussed below).

Indeed, the hostile encounter between self and nonself – with its attendant imagery of combat, invasion, aggression, or counter-attack – is the archetypical description not because it represents the norm, but because its attendant events are the most arresting and consequential. For example, the logarithmic secondary response in acquired immunity is a dramatic physiological phenomenon, and its evident evolutionary utility in overcoming microbial threats is almost axiomatic. Further, the desire to oppose the catastrophic succumbing of the body to infectious disease has been the motivational epicenter of immunology and the most public theatre of its activities. And yet as Burnet recognized, especially in formulating his ecological outlook, encounter between self and nonself are usually inconsequential, if not innocuous: if there is a norm in such encounters it is truce rather than war, tolerance instead of destruction. Tentatively claiming that "surely it is axiomatic that a virus getting into the body and damaging cells will automatically be recognized as something foreign and inimical," Burnet swiftly adds: "But its is not axiomatic" (1962: p. 39).

Immunological tolerance is open-ended, ranging from an indifferent to a tense proximity between self and nonself. Burnet introduced the idea of tolerance synchronously with the language of selfhood. Their semantically intimated affiliation is one of the most central expressions of the terminological productivity of the idiom of selfhood (see Tauber 1994: p. 100ff). As the first uses of the term in Burnet demonstrate (see above, 1940: p. 24), "tolerance" enters the science in the guise of its *vernacular* meaning – as that condition where something is tolerated, endured, or indulged. Through this initial vernacular use, tolerance swiftly transformed into a *technical* term in immunology, being defined, in general terms, as the failure of the immune system to respond to antigen (or more specifically, as the induction of non-reactivity to a specific antigen capable in other circumstances of inducing a cellular or humoral response) (Janeway and Travers 1994). Burnet was pivotal in making the idea of tolerance central to immunological concerns, by foregrounding certain revealing yet neglected phenomena. Of prominent importance were emerging embryological studies of patterns of immune response and problems surrounding successful organ transplantation or blood transfusion. Burnet's drive as a biological thinker was to formulate a unitary, cogent account encompassing these varied phenomena. His synthetic genius was to integrate topics like skin grafting, embryological

experiments, and transfusion problems under the auspices of the self-nonself encounter.

By way of introducing his discussion of skin grafting in *The Integrity of the Body* (1962), Burnet offers the self-nonself distinction as the guiding scheme of the observations described: "It has already been noted that no ordinary component of the body will provoke an immunological response. Antibody production or any other type of immunological reaction is against foreign material – against something that is not self" (1962: p. 68). He goes on to note that while skin can be grafted from one part of the body to another in the same individual, skin from another individual, within a few days, becomes inflamed, then separated, and finally rejected from the body. "The body," concludes Burnet, "is clearly rejecting tissue that in some way it can recognize as foreign to itself" (ibid.). He then reminds his readers of the hemolytic disease of newborns described in an earlier chapter of the same work. This condition ensues if the cells of an Rh+ embryo leak into the circulation of the Rh– mother who then produces antibodies against Rh+ which, passing across the placenta, produce massive damage of the newborn's red cells in the period after birth (1962: p. 32ff). Comparing graft rejection and hemolytic disease, Burnet writes that "*they are clearly of similar character*" (1962: p. 69, emphasis added).

His insight of similarity between these diverse phenomena is mediated through the self-nonself relationship. Far from being "clearly similar," at face value graft rejection and hemolytic disease appear quite different. Yet for Burnet both cases involve recognition of the foreign: the grafted, foreign tissue is antigenic to host immunity, as the baby's Rh+ blood cells are antigenic to the Rh– mother's antibody. The abstract conceptual quality of *self versus nonself* is evident here in describing biological interactions, regardless of either the specific body components involved or their relative size to one another. The conceptual pair self-nonself thus arranges diverse phenomena in a manner revealing a core identity. The epistemological contribution of the idiom of selfhood lies in unifying disparate phenomena – in this case, graft rejection and hemolytic disease.

Blood transfusion problems, embryological immune studies, and experiments and observations involving twins are similarly made confluent through the idiom of selfhood. Burnet claims that the "difficulties and catastrophes" of blood transfusion "probably more than anything else . . . has been responsible for defining th[e] central problem of the differentiation of self and not-self" (1962: p. 36). Red cells introduced into the body of an individual who does not possess the type trigger the production of antibody. Yet some individuals were found to possess two different sorts of cells in their blood. Burnet discusses the case of a woman who had 61% of group O cells and 39% of

group A; while the former were her own, the latter were her twin brother's who had died at birth. In this context, Burnet notes that "there are also two pairs of living twins who are known to have shared their blood cells in this same fashion and the phenomenon is regularly seen in cattle twins;" he goes on to note that "the occurrence of two genetically distinct types of cell in one individual constitutes him as a chimera" (1962: p. 38).

"Nature's experiments," as Burnet terms them, point toward a critical intersection between embryological development and immune response. A term referring to mythological creatures with body parts of different animals, *chimera* in immunology is respecified as an alloy of self and foreign. The foreign – derived from another individual – is treated by the body as self, as long as it is introduced into the body during embryonic life. This sort of "implantation" may arise naturally in the case of dissimilar twins, but its implications can be pursued in experimentation: "the same phenomenon can be studied experimentally by prenatal injection of suitable animals" (1962: p. 76). Burnet then describes an experiment where embryos of mice of stock A (white) are injected with spleen or kidney cells of mice of stock B (black). Once the A mice become 6 to 8 weeks, they are grafted with skin from the B mice. While in normal A mice the skin is rejected, in the experimental mice the graft grows normally.

This sort of experimental work ramified into diverse embryological studies collected under *the problem of tolerance*, which Burnet ultimately summarizes in the following unifying manner:

> We have seen that if, at the very beginning of independent life, foreign material, whether cells from related though genetically distinct individuals of the same species, purified foreign proteins, or a rather unusual virus, is implanted and can remain present it is likely to be accepted as "self" and no immune response will be involved against it (1962: p. 83).

The language of self and foreign becomes a device for the imagination to penetrate the surface of diversity to discern a single underlying pattern that recurs. The idiom of selfhood, then, is not so much a descriptive or explanatory scheme, as a tool allowing diverse findings to emerge as permutations, as empirically different expressions of the same phenomenon.

The relation between self-nonself is so fluidly conceived in Burnet's thinking that self can actually *be* nonself in contexts where the immune system treats "self" components as though they were "foreign." This is the case with autoimmunity – meaning "self-immunity" (the Greek prefix *auto* means self) – where the very distinction between self and nonself implodes. The possibility of autoimmune phenomena was recognized early on by immunologists, and Paul Ehrlich (1854–1915) coined the expressive phrase of *horror autoxicus*, viz., horror of the body treating its self as toxic.

Viewed as a state so unthinkable as to have the ring of something almost nightmarish, horror autoxicus was not investigated for the light it might shed on immune process; it was regarded as something aberrant and pathological. Horror autoxicus remained an evocative ideality with uncertain worldly moorings, until Burnet turned his biological lens on autoimmunity, both as a phenomenon that is absent and one that is sometimes present in various disease states.

Indeed, the double character of autoimmunity as absence and presence does not emerge as a paradox. For the biological thinker, it is a natural and expected consequence of evolution. According to Burnet, evolutionary reasoning would predict that autoimmune phenomena ought to be absent or exceedingly rare. "It is axiomatic," writes Burnet, "that no immunological reaction takes place against the normal constituents of the boy" (1959: p. 33). At the same time, on a sophisticated understanding of evolution, autoimmunity recurs precisely because "the whole of the control mechanisms have had to be developed not by an infinitely intelligent designer but under the pressure of evolutionary selection" (1962: p. 83). As an evolutionary thinker, Burnet regarded autoimmunity as a rare yet at the same time intrinsic dimension of immune function. He was not at all partial to Ehrlich's notion of "horror autoxicus," indirectly labeling it as superstitious by comparing it with the idea that "nature abhors a vacuum."

To summarize, from an epistemological perspective, the most striking feature of the idiom of selfhood is its conceptual unification of key immunological phenomena. Nutrition, protection (by phagocytosis and primary/secondary response), infection, autoimmune disease, phenomena of tolerance, natural or experimentally created chimeras, and autoimmunity all become conceived as a network of interlinked or interrelated functions, of evolutionary transformation and adaptive imperfection. Through the idiom of selfhood all these topics mirror and play off one another; they represent states or processes that arise in the playing field between body and environment, at different evolutionary stages and development moments, given different circumstances or starting states. Burnet, the biological thinker, introduced self-nonself as a framework able to unify, in both empirical and conceptual ways, various immunological phenomena.

Conclusion

Emphasis on the antagonistic relationship between self and foreign can be the mainspring for a language of conflict or warfare in immunology. Indeed, Burnet himself occasionally exploited the rhetorical possibilities of the self-nonself encounter. For example, he describes antibodies as:

> Plain-clothes detectives with perfect memories for criminal faces; when they come into contact with their "opposite number," this is recognized as a dangerous individual which has on some former occasion penetrated the defenses of the body or of society. It or he must be apprehended (1940: p. 125).

Certain analysts have found this sort of language-use and imagery in immunology to be covertly political. Besides the violence of surveillance or warfare imagery, cultural critics uncover a stratified, iniquitous society projected onto processes and functions of the body; a system of difference between people becomes mapped onto the immune system. Emily Martin writes that "in the new science of immunology, social differences – between men and women, managers and workers, or citizens and foreigners – are written metaphorically into the character of various immune system cells" (1990: p. 410). She cites Donna Haraway's claim that "the immune system is an elaborate icon for principal systems of symbolic and material 'difference' in late capitalism" (Haraway 1991: p. 204). The implication of such assessments is that scientific thought can function as ideology.

While immunological knowledge is not insulated from its cultural milieu, nor from the nature of the society in which it is produced (see Tauber 1995), a view of immunology as cloaked politics is misguiding. Such analysis misunderstands the work of language in science, by reducing the genealogy and effects of linguistic idioms to a single level of analysis. The basis of such a critical angle on the language is that it is *metaphorically* imposed on phenomena of immunity. We have argued, however, that the idiom of selfhood cannot be neatly classified as either metaphorical or literal language-use. In its emphatic uses, *self* reflects the witnessability of the organism as a separate and living entity. In its extensions as "individual subject," *self* can be exploited to personify immune objects and processes in colorful ways. And in its thematic uses, the illocutionary power of the selfhood idiom lies in scientifically unifying a diversity of immunological phenomena.

Our interest has been to underscore the intrinsic force of the selfhood idiom, how it is rooted within scientific thinking. The idiom of self-nonself did not originate solely form the sense of "individual personhood," but also from the more humble origins of the emphatic, barely noticeable use of *self* as suffix, seen in the immanent textual transformation from "the amoeba itself" into "self." This is not to deny the significance of the semantic leap, nor to downplay its rhetorical effects: it is to emphasize that the complexity of selfhood is not so much a matter of its anthropomorphic resonances, as of its heterogeneous genealogy and diverse applicability. The effectiveness of self- nonself flows from its polysemy, rather than its insinuation of social antagonisms. The concept of self extends into vernacular uses and

connotations, yet its applications in immunology take root in the phenomena, allowing the penetration and constitution of immune phenomena in a unified language. At the same time, this language is intimately familiar allowing resonances of individuality, intentionality, will, aggression, and autonomous action to be brought into rhetorical play; after Austin, we have called this aspect the perlocutionary dimension of the idiom. The perlocutionary dimension, however, should not be treated as the most overriding, for such a view oversimplifies the role of the idiom of selfhood in immunology.

To conclude, we have examined Burnet's self-nonself framework, focusing in particular on its epistemic uses and effects. Rather than approaching it as a bluntly imposed metaphor, we have focused on its immanent work in the science. The idiom of selfhood was an integral part of Burnet's biological outlook – expressing the interest in the living organism in its totality, its activities, and the definition, integrity, and negotiation of its boundaries. Within the ecological perspective, self-nonself allowed for a comprehensive gamut of outcomes, a Darwinian vision inclusive of competition, equilibrium, and even cooperation in the interaction of organisms. In its broader applications, the idiom of selfhood has enabled tying together a diversity of immune phenomena. As mentioned in the introduction, the ubiquity of the self-nonself (and self- foreign) framework reveals the power of the biological perspective to organize and unify biological phenomena. Even in this era of triumph for the reductionist approach of molecular biology within the science, the idiom of selfhood – introduced by a biological thinker – has been the pervasive conceptual currency of immunology. While the scientific basis of selfhood is increasingly questioned (Podolsky and Tauber 1997), the self's heuristic standing continues to be accepted. Indications are that even if it were to be eclipsed, other biological metaphors are waiting in the wings to assume its functions.

Notes

[1] Burnet was a prolific scientist talented as experimenter, theoretical thinker, and synthesizer of empirical findings; he was broadly educated as a biologist, besides immunology, being conversant in virology, ecology, embryology, biochemistry, genetics, and epidemiology (see Tauber and Podolsky 1994; Podolsky and Tauber 1997).

[2] Elsewhere, not without irony, he noted that physicists and chemists "are not deeply interested in evolution, adaptation, survival and such nebulous and unmeasurable concepts" (1940: p. 74).

[3] Richard Lewontin expresses the sensibility of the biological outlook when he maintains that " 'assembly' is the wrong metaphor for living beings" (1991: p. xvii). In the context of the problematic of "wholes" and "parts," a biological orientation denies neither that the whole organism often be fruitfully studied in isolation. Instead, what is implicitly affirmed in

biological reasoning is that the parts can ultimately only be understood and analyzed in light of the whole (Levins and Lewontin 1985).

[4] This feature of meaningful action is also encountered in Metchnikoff's portrayal of phagocytic action. Phagocytes, or "eating cells," were first understood by Metchnikoff as amoeba-type, motile cells that engulf and digest invading microorganisms or foreign elements, thereby protecting the body from their harmful effects.

[5] Burnet defined ecology as the "economics of living being," including activities, modes of feeding and reproduction, environmental conditions of well-being, and enemies (1940; pp. 4–5ff). For a detailed analysis of Burnet's ecological view, see Tauber and Podolsky (1994), Tauber (1994).

[6] There are indications in the past decade, in both theoretical and experimental reports, that the versatility and utility of the "self" in immunology may be eclipsed by alternative formulations (Podolsky and Tauber 1997: chapter 9). At the same time, this potential erosion of the "self" is not widely accepted; notwithstanding its possible problematic status, it has served as an essential model of immune function for almost three decades.

[7] Antigens are foreign substances that produce an immune response in the body. Their name arises form their ability to generate antibodies (Janeway and Travers 1994: G: 2).

[8] In his *Integrity of the Body*, Burnet describes three sorts of immunocompetent cells, namely, the lymphocyte, the plasma cell, and the monocyte. He speculated that because it is sometimes difficult to classify these cells when looking microscopically at a tissue section, perhaps "they can change into one another" (1962: pp. 55–56). From a contemporary vantage he was partially correct. Lymphocytes are today classified into B-cells and T-cells, with B-cells developing into antibody-secreting plasma cells; monocytes belong to the separate family of cells called polymorphonuclear leucocytes. (See Burnet 1962: chapter 5; cf. Janeway and Travers 1994 1:8).

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