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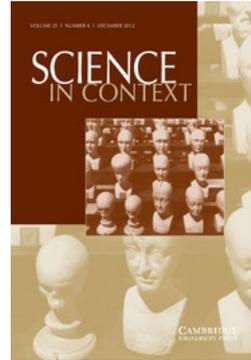
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## Postmodernism and Immune Selfhood

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# Postmodernism and Immune Selfhood

## The Argument

Two research traditions in immunology, supposedly centered on the same issue of immune identification, have followed different theoretical goals and originated from competing philosophical foundations. These may be labelled modernist and postmodernist, respectively, thereby applying cultural and philosophical categories to immunology in order to articulate potential scientific resonances with the broader culture. To accept that exercise an important caveat is imposed, namely, this translation is most appropriately discussed at the level of metaphor. In other words, I will structure my treatment of these issues as expressed in the metaphorical language of the discipline, and thus the bulk of this discussion will focus on how the language and modeling of the science draws from the culture-at-large. Scientists seek images from their everyday lives to describe phenomena that may be poorly articulated in their technical discourse; such is the utility and importance of metaphors generally, and thus it is not surprising that we might discern echoes of a postmodernist sentiment in the metaphors borrowed from post-World War II culture. I will also discuss, to a more limited extent, how postmodernists have sought support for their own ideological arguments in immunology. This last topic serves only to illustrate the bidirectionality of scientific discourse with the society in which it is embedded.

## Introduction

Selfhood, that is the definition of the self and its ability to discriminate the other, has been the governing issue in immune theory since shortly after World War II. As the declared “science of self/nonsel self discrimination,” immunology’s central concern is the definition of the self and its defense. To examine the immune self is particularly relevant for this discussion, because the self has arguably been the target of the heaviest postmodernist barrage. Thus it is most likely that if we are to discern postmodern effects in this science, we would find them revolving around the question concerning immune identity. I have addressed how immunology might be construed as a “postmodern science” by tacking my sail to the following course: The common element of a postmodernist view of selfhood is that the self, like the rest of the world, has no reference point and must be regarded as having melted away. As C. S. Lewis quipped, “the Subject is as empty as the Object”

(Lewis 1952, 10). When the subject is “de-centered,” no longer an origin or a source, it becomes only the contingent result or product of multiple social and psychological forces. In this view, the unity of the self was at best a deceptive construction. Its very authenticity has been fundamentally challenged. In short, from this perspective, the self should more appropriately be viewed as a contingency or an interpretive scheme. If the self is a contingency, there is no unity by which it may be organized to confront its world. The postmodern view of the self disallows Kant’s modern subject to determine for itself, completely and unconditionally, what to accept as evidence about the nature of its world or its organization. Self-determination has been replaced by arbitrary choice, a construction based on the unsteady assumptions of cultural practice and historical chance. This view, derived from literary and social critiques, will serve as the template upon which I will attempt to place our current understanding of immune selfhood.

How have I come to assume this orientation? After all, virtually every discussion of postmodernism begins with some attempt to define what postmodern *is*.<sup>1</sup> The problem fundamentally resides in defining “modernity,” which may be collapsed or extended to almost any dimension. It may refer to a historical period beginning with Darwin, or perhaps Rousseau, or even Descartes. Depending on the context, modernity is a capitalist project, the Enlightenment program, or a set of ideals originating in the Renaissance. Modernity’s veritable soup of ideas include technology, dualism, positivism, instrumental rationalism, and bureaucracy on the one hand, and romanticism, individualism, transcendentalism, liberalism, democracy, the unconscious, and indeterminacy, on the other. The only reasonable conclusion is that the intellectual and cultural events of the past 500 years may be grouped in various sets and called “modern,” leaving a rather ill-defined foundation upon which to build a definition of “postmodernism.” Given this rather damning caveat, it is still possible within proscribed disciplines to agree upon a generally understood meaning of the respective terms, although they do not necessarily coincide. For instance, in literature, the modern period refers to roughly 1880 to 1945 (e.g., Posnock 1991), whereas in philosophy, modernity is bracketed by

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<sup>1</sup> The term “postmodern” was probably used for the first time in 1934 by the Spanish author Federico De Onis to describe a reaction within modernism, and soon thereafter by Arnold Toynbee, who apparently rediscovered the term and used it to signify the end of an era marked by Western domination (Rose 1991, 171). In this latter sense, postmodernism referred to the last phase of Western history, an era of irrationalism, anxiety, and lost hope. But the term has assumed many other connotations as it was applied to art, literature, film, architecture, political theory, philosophy, psychology, sociology, science, and religion (e.g., Jencks 1992). It is notoriously difficult to offer a coherent definition of “postmodernism” because of the myriad ways it has been used in the past sixty years. After a rather exhaustive survey of these various meanings, Margaret Rose concluded: “It is up to ourselves to understand and evaluate both the new ideals or goals set up by its [postmodernist] authors and their evaluations of the past” (1991, 177). Stanley Fish, for instance, takes an even more circumspect view: “The whole modernism/postmodernism context of discussion simply mystifies me because I don’t have any handle on any of your terms” (1987, 96). In any case, the orientation adopted here, in particular regarding a definition of the “modern” from which any understanding of postmodernism must derive, is based on an unpublished lecture given by Leslie Menand to the MacArthur Fellows in Chicago, February 1994.

Descartes and Kant. It is from this philosophical tradition that I will contrast modern and postmodern views of the self.

"In the wake of Descartes's meditations, modern philosophy becomes a *philosophy of the subject*" (M. C. Taylor 1987, xxii). The modernist view of the self that serves as the implicit contrast to postmodern notions throughout this discussion is the one offered by Kant, namely, the transcendental apperception of the ego. This was, to a large extent an operational definition of selfhood — namely, the inner, fundamental, and unchanging sense of a unity of our consciousness.<sup>2</sup> From the mid-seventeenth century through the Kantian project, the self, although difficult to define, still remains to offer a perspective on the world and thus order it, becoming the locus of certainty and truth (Nagel 1986; C. Taylor 1989; Pippin 1991). From this orientation, the nineteenth century witnessed a significant philosophical turn, which we may refer to as postmodern. Beginning with Hegel, and most clearly articulated with Nietzsche, the sovereign subject relates only to that which it constructs or confronts. The realization of the self is determined in a complex duality of its own self-consciousness, which is intimately dependent on its relation to the other — whether God, nature, culture, history, or other selves. In other words, otherness becomes constitutive, quite a different vision of the self from that of Kant for instance. Perhaps Kierkegaard offered the best precis of this relational definition of the self:

The self is a relation which relates itself to its own self, or it is that in the relation which relates itself to its own self, or it is that in the relation [which accounts for it] that the relation relates itself to its own self. . . . Man is a synthesis of the infinite and the finite. . . . A synthesis is a relation between two factors. So regarded, man is not yet a self. . . . Such a relation which relates itself to its own self (that is to say, a self) must either have constituted itself or have been constituted by another. If this relation which relates itself to its own self is constituted by another, the relation doubtless is the third term, but this relation (the third term) is in turn a relation relating itself to that which constituted the whole relation. Such a derived, constituted, relation is the human self, a relation which relates itself to its own self, and in relating itself to its own self relates itself to another. (Kierkegaard [1849] 1955, 146)

Kierkegaard's espousal became a major philosophical pillar of twentieth-century responses to the problem of personal identity. Alterity serves as a major focus of how postmodern phenomenologists, beginning with Husserl, define selfhood. Briefly, the self, to the extent that it can be actualized, is, in varying views, defined by the other (e.g., Theunissen 1984; Taylor 1987). Obviously different critics see

<sup>2</sup> For Kant, transcendental apperception is the structured unity — pure ego or self — of consciousness, which precedes (transcends) the content of our perceptions and makes possible their experienced order and meaning. Transcendental apperception was thus thought to be the necessary condition for having an experience and for synthesizing experience into a unity. In this sense, the self is posited.

such a project with different degrees of optimism, but at least the problem is shared, and when the issue of alterity is discussed, we know roughly what is being debated. The question revolves around whether, and how, in response to an encounter, the self articulates itself or is altered as a consequence of that engagement. Also considered is how the engaged self might alter its object and their shared world. In short, the phenomenological approach explores how the self lives in its world, essentially in a universe of others. The self alone is either alienated — that is, alienated in its selfness — or it actively engages the world and thereby becomes actualized. The debate revolves about the contingency of this process and its problematic opportunities for success. But by and large the parties agree that the potential for self-aggrandizement must be realized *in* the world, and the self must ultimately actualize itself in the encounter with the other (Tauber 1995).

The centrality of the self's relation to the other assumes its more radical postmodern orientation as an expression of post-structuralism. Structuralism understands meaning to be a function of the relations among the components of any cultural formation, or our very consciousness. For instance, the pictures of our mind's world assume their meaning, value, and significance from their relations — that is, their “place” in a structure. But the deconstructionists broadly argued that any structure crumbles when we recognize that no part can assume participation outside its relation to other parts. In other words, there is no center, no organizing principle privileged over structure and thus able to dominate its structural domain. From this perspective, there is nothing “natural” about cultural structures (e.g., language, kinship systems, social and economic hierarchies, sexual norms, religious beliefs), no transcendental significance to limit “meanings,” and only power explains the hegemony of one view over another. Similarly, “the self” may be regarded as constructed by arbitrary criteria, and thus occupied no natural habitat. In this scenario, the phenomenological insistence on the self's dependence on the other has been radically challenged: Not only has the self's autonomy been rendered meaningless, *any* construction of the self is regarded as arbitrary.<sup>3</sup>

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<sup>3</sup> Another crucial tributary from which the self has been assaulted is from the Wittgensteinian perspective: “Of this ‘I’ itself one can say nothing. It can only be manifested, and that in silence. Any discourse about this *subject* (about the subject of the subject) is merely speaking to say nothing: words that do not mean to say anything, that are there *in order* to say nothing, an isolated abracadabra without context. Just like someone outside a closed door who, to the question ‘Who’s there?’, responds, ‘It’s me’; but we do not recognize his voice, and before we can open up he vanishes without a trace” (Atlan 1993, 401). The self “exists” only as part of a “language game,” a convention from which it possesses some explanatory meaning; but to define that meaning is a seemingly hopeless task and, more important, a vacuous aspiration. I will not further explore this profoundly disturbing philosophical critique, other than to note that within this postanalytical context, the self is no longer decentered, it is dissolved. The very question of selfhood is rendered meaningless altogether. This is the extreme radicalism of a postphilosophical analysis, and for this discussion I mention it only to point to where the selfhood problem may ultimately be resolved: Beyond the self as a relational construction (phenomenologists) or a decentered subject defined by arbitrary cultural constructions (deconstructionists), the self as an *entity* simply does not exist. But this position, irrespective of its philosophical merits need not be further explored here, for I believe immunology still employs the self in various metaphorical guises (Tauber 1994d).

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From the deconstructive Derridean perspective, we are able to appreciate the importance of indeterminacy and why it holds such powerful dominion in current debates of the postmodernist agenda. The terminology originated in literary criticism,<sup>4</sup> but it has in fact a strong resonance, albeit in a somewhat different context, with nineteenth-century philosophy (e.g., Nietzsche [Tauber 1994a]) and biology ([Tauber 1991; 1994b]). After Darwin, evolution, as an ongoing and everpresent characteristic of life, drove us into a deep insecurity regarding any notions of nature as constant and stable. Species were now defined not as static entities, but as subject to change dependent on the vicissitudes of time and happenstance. The scientific agenda directed itself to explain how each life form responded to endless competition and collectively adapted. But biologists pursued these issues with a very different understanding of the organism from that assumed in the pre-Darwinian era. By postulating an ever-changing biosphere, a consequence of evolutionary necessity, a new element of indeterminacy was introduced. Beyond the evolution of species, the organism would now also be viewed as subject to evolutionary forces. Beyond the role assigned to the organism as a unit of selection (a major problem in its own right — viz., the relation of the individual to the collective), how was the individual organism in this evolutionary context to be defined in its own individual life history? The developmental process was reexamined as a *process* of emergence. No longer viewed as a static entity, the process character of the organism was recognized as its dominant defining element. The organism's boundaries and mechanisms of self-actualization represented analogous definitional problems to that posed for the species at large. *What* was the organism that must always adapt and change? This became the key question, for the indeterminacy reached into all levels of investigation: To what degree did genetics program the life history of the individual? What was the adaptive capacity of the organism? In what sense could biological "potentiality" be understood? How did the organism protect itself in its environs? Thus the core issue of organismal identity for the first time became a problem, and it is here that immunology was born.

The differentiation of self from nonself was articulated as a scientific problem when the self was recognized not as given but rather as defined in *process*. A mechanism of identification was required. And, in turn, the dynamic interaction of the self with its other demanded a means to recognize the foreign. The historic origins of this issue have been detailed elsewhere (Tauber and Chernyak 1991; Tauber 1994c, 1994d), and here it is sufficient simply to state that immunology grew from the aspiration of identifying the mechanisms that protected the self and, more fundamentally, the processes by which the self developed. Note that deep

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<sup>4</sup> Indeterminacy arising from a poststructural reading of a text, signals that there is no single correct interpretation, not simply because different readers may differ as to their respective understandings, but more profoundly because language has no restraints on its reference. Since there is no fixed point within or outside the text, meanings proliferate and change with time, and the meaning of the text as a whole becomes indeterminate (Leslie Menand, unpublished lecture, 1994).

within the foundations of immunology, fundamental concerns with such an entity as the self resided as a *problem*. What later would be articulated as a concern of defining the self in postmodernist critiques was earlier posed in this post-Darwinian science. In this sense, then, we might easily argue that immunology *contributed* to the postmodern ethos at least as much as being defined by it. In either case, the postmodern self remained implicit in the nascent discipline, only to emerge clearly during the mid-twentieth century in the struggle of two competing research traditions. I will now trace how the immune self was first presented, and how in recent years, this nebulous metaphor has assumed a clearer articulation that closely approximates a postmodern construction. The history of the concept of the self in immunology has been summarized elsewhere (Tauber 1994d); here I wish to emphasize those elements that most clearly echo themes characteristic of postmodernism.

### **The Introduction of the Immune Self**

The concept of self was formally introduced into the immunological lexicon in 1949 in a book written by Frank Macfarlane Burnet and Frank Fenner, *The Production of Antibodies* (1949). This was the second edition of a short monograph which was largely devoted to elucidating regulatory mechanisms of antibody production. Recall that antibodies are proteins that recognize foreign substances as foreign and initiate reactions to neutralize or destroy them. The antibodies represent a vocabulary that recognizes a universe of substances or microorganisms that might be deleterious to the host organism. This is, of course, the teleological framework that immunology was generally regarded as following. Immunology emerged as a new discipline at the turn of the century in the wake of the discovery of infectious diseases and new understanding of the host response to such insults (Tauber and Chernyak 1991). Thus antibodies were first described in the context of repelling pathogenic invaders or neutralizing their toxins. Antibodies assumed the function of chemically identifying nonhost elements. This narrow concern with the foreign as external was soon expanded to include any internal host element that no longer served its designated function. Thus, damaged, effete, senile, or malignant cells were regarded as appropriate targets for immune destruction. To be historically accurate, this latter function was most readily observed to be mediated defensively by immune cells rather than antibodies per se, but it was known by 1900 that antibodies were also reactive against host constituents (Silverstein 1989). The pathological significance of such activity was not apparent, and it is of considerable interest to investigate why immunology chose to follow the path of immunochemistry rather than pursuing such intriguing pathophysiological findings. In any case, the immune system through the 1940s was generally regarded as a system of defense, and lying in wait for the postwar expansion of immunology's domain was the concern with immune surveillance of the host itself. The antecedent

observations had been made, but had not yet been incorporated into the mainstream of immune theorizing and experimental programs.

It is important to note that in the most general sense immune selfhood was equated with normality — in fact with ideality (Tauber 1994a; 1994b). This already heralds a postmodern orientation in that a static “norm” is replaced with an endless quest for idealization. The organism not only ceaselessly strives for its self-aggrandizement vis-à-vis others, but engages in a constant surveillance to achieve inner perfection. This concern of self-directed immune activity did not become a focus of interest until after World War II, but its nascent principles may be discerned from the earliest days of immune theorizing (Tauber and Chernyak 1991). In 1949 Burnet was to make this agenda explicit by articulating this “self-oriented” function (Tauber and Podolsky 1994; Tauber 1995d). He proposed that the immune system not only identified the foreign, but defined the self. The so-called self-marker hypothesis stated that during embryonic development, the organism went through a learning process, wherein the immune system encountered a set of what were called “self-markers” (Burnet and Fenner 1949). The recognition of these markers by the embryonic immune system initiated the elimination, or control, of those immune cells that might react against such constituents of the self. This purging of self-reactive immunocytes ensured that later, in the mature organism, the immune system would direct its activities solely against the outside world. In this view, then, immunity was designed to combat pathogens that might penetrate the host’s boundaries. In a sense, the self was thus defined negatively: it was that which the immune system ignored, a lacuna in the immune vocabulary. In other words, as a result of an embryonic learning process, the immune system would not react against the self.

So in 1949 the self made its formal appearance in immunology. It did so as a passive entity, even an a priori one. In this sense, it assumed a modernist construction. Perhaps it is ironic that it existed only as a shadow — i.e., as an entity that would not be subject to immune reactions, in privileged immune dormancy. In this view, the immune system was in a sense turned off (so as not to attack) with respect to its fellow cells (allowing host elements to live in harmony with their aggressive protectors) and, at the same time, poised to destroy all that had not been identified as self during early development. Boundaries between self and other were conceived as in principle well-circumscribed. It was clear that when the self was invaded by pathogens, the immune system was called forth to do battle to preserve the self’s very life. And when the immune system bizarrely turned on its own host in pathological autoimmune reactions, this was evidence of immunity run amok. Immunity was a mechanism directed normally against the outside world to preserve the self against insult. Implicit here is the assumption that the self, under normal conditions, is inviolate, and the agency of its integrity is the immune system.

The definition was crudely operational — the self was that to which the immune system did not react. This is an impoverished characterization of the immune self, as Burnet did not deal with two major deficiencies of such a formulation —

namely, that (1) there are myriad cases of the immune system ignoring microbes or the ingestion of foreign substances,<sup>5</sup> and (2) there are important cases where the host's antibodies in fact recognize self-constituents as a normal part of the body's economy. The immune system plays an important role in destroying malignant cells, remodeling tissue which is damaged (to then allow normal repair and growth processes to ensue), and removing effete or senile elements, which must be digested to make room for their replacements. Thus beyond host defense proper, immunity includes the surveillance of host cells, monitoring their state of health and refurbishing as necessary. These functions may be viewed as examples of altered self and thus susceptible to immune identification and subsequent destruction. Although a reasonable conjecture, and undoubtedly correct, this hypothesis is based on the assumption that the immune system is designed to identify the other, not the self. However, in the past three decades, the inward-directedness of the immune system, its so-called surveillance function, has received increased scrutiny as theorists argue that perhaps the immune system in fact identifies the self in a positive fashion. In other words, in contrast to Burnet's formulation of the negative self, immunity is now conceived by some as derivative, being in actuality a product of a positive process of self-identification. With this revised notion of immune identity, a new dimension of complexity has been introduced. I will return to this matter. For now, I turn to a basic outline of Burnet's notion of the immune self, in order to consider where it might be placed on the modernist/postmodernist axis.

At first glance, Burnet's theory appears to fulfill the key modernist criteria of selfhood — namely through a tacit appeal to the existence of such an entity as the self. Why is this a modernist notion? One might argue that Burnet employed the 'self' as a Kantian category. Analogous to the apperception of the transcendental ego (see footnote 2 above), Burnet's self is based upon a notion of unity — a coherent whole — that functioned as the inner, fundamentally integrated organism. An additional feature which was not fully appreciated at the time but later became a central focus of immune theory — was that in defending the self, the immune system also defined it. The final element — again not explicitly declared — was the bewildered search for the source of immune function. In other words, what constituted organismic identity? Recall that the molecular basis for a genetics that might account for immune identity was yet to come; but it is this conceptual problem of identity that must be recognized as the truest modernist aspiration, though the formulation of the problem remained hidden and implicit in its earliest presentation. Thus Burnet's formulation consisted of three elements: (1) the basic

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<sup>5</sup> In some abnormal cases, food allergies illustrate that it is not simply given that we can ingest with impunity. The body may or may not accept the challenge of specific foodstuff as nutritive. Immune rejection is one way control is exercised, and it clearly illustrates that milk, eggs, fish, or whatever, are in fact "foreign" though generally tolerated. The same is true of what we breathe. Some unfortunate souls suffer seasonal allergies, miserable immune reactions to pollens of various kinds. Again, the rest of us tolerate these same foreign insults without notice.

notion that there was such an entity as the self; (2) that it was functionally identified by the immune system; and (3) that in some unspecified fashion it represented the source of immune activity. These represent different levels of organization, each of which, in the modernist orientation, corresponds to an implicit certitude that there are definable borders and that a self exists. The self, never articulated by Burnet in anything resembling a cogent scientific definition, remained a functional construct. Simply put, the self was that which under normal circumstances was not reacted upon by its own immune system, and in this sense, possessed coherence. It is noteworthy that Burnet barely elucidated what he meant by 'self', in any sense. He was no more specific than the self connoted a vague sense of identity. More concretized meanings would later be assumed, and as discussed below, these were conducive to a postmodernist interpretation. Burnet himself eventually attempted to describe immune function in terms of information theory and cognitive models, opening the door to powerful postmodernist influences (not necessarily advocated by him but developed quite explicitly by others). However in 1949 the self remained a nebulous, undefined construct which served as an elusive metaphor. (I have described it as an "ontological" attempt to allude to the elusive source of immune activity [Tauber 1994d].)

In concluding this description of the "modernist" phase of immunology, we must appreciate how Burnet evoked a powerful sense of personal identity. His self hypothesis was developed along Kantian lines: in using the term 'self', he explicitly used language evocatively to conjure intuitively available images of ourselves, thus construing the immune system as protecting a coherent entity, one with definable immune borders. There is a clear scientific tradition that built on this version of selfhood — namely, the effort to define the self genetically. A molecular definition of selfhood emerged from transplant biology, where the very limits of successfully transplanting tissue from one individual to another demanded exploration of the factors that identified a transplanted organ as self or foreign. Spectacular success has been achieved in defining the molecular signature of the self in genetic terms. Defined by such means, the self would gain a certain finitude. In its simplest form, the issue is whether the genetic constitution of the host programs the self-markers that Burnet originally hypothesized, and whether they are operationally active in immune function. If these markers were in fact coded for in the genome, this would then be given, a priori. Defined through a given set of genes, the immune self would then take on a specific character, one given by the particular sequence of an individual's genetic endowment. That query has been remarkably successful. In exquisite detail, we have the structural and genetic definition of the protein complex that serves as the major identification system of the immune self. This so-called major histocompatibility complex binds foreign substances, and thus becomes altered from its embryonic state so that immune cells recognize the foreign element. Note that the foreign is perceived in the context of altered self. The important upshot is that immunologists who seek a ready definition of the self can now point to the genome and cite a genetic signature which regulates immune

recognition mechanisms. I suggest that this line of research and pursuit represents the modernist background assumption that there is a self. *Because* the immune self is now definable in molecular terms, at both the genetic and protein levels, a degree of exactitude has satisfied the epistemological and materialistic yearnings of the field, confirming that our commonsensical notions of identity can at some “basic” level be successfully applied to the problem of immune identity. With that success firmly established, let us now turn to what may be referred to as postmodern developments. To do this, we must broaden our definition of the immune self from the implicit passive, even negative, sense originally used by Burnet, to a more active, cognitive entity.

### **Echoes of Postmodernism in Immunology?**

The defining characteristic that corresponds with the spirit of postmodernism is the understanding of the nature of the organism as decentered and indeterminate. Thus in contrast to the modernist vision of the self, the postmodern view stresses the dynamic, if not dialogical, character of the organism. And here we discern a close affinity with the phenomenological theme of authenticity. Specifically, I am referring to alterity (the other) discussed in the introductory section. I have already mentioned that the immune system identifies the foreign as a result of antigen binding to the major histocompatibility complex. The self is thus altered, allowing the foreign to be “seen” as it modifies the natural state of the self’s signature. The immune response ensues. This is not only a fascinating finding in itself, but also on account of its resonance with a postmodernist perspective. There are those immunologists who resist defining immune activity as based upon the mutually affecting presence of the other. They are wedded to a modernist notion of the self as a given entity, neatly defined and entailed by its own “selfness.” This self is guarded by the immune system, which is then conceptualized as a sub-system fully (i.e., firmly) determined by a genetic prescription. I believe this is fundamentally a simple mechanical conception, where well-integrated parts function together like Descartes’ clock: If only we understood its workings better, we would perceive the mechanical order and operative causal relationships of this complex system. This is a rigid modernist aspiration, one which in my view is limited in its explanatory power. The phenomenologist rejects this formulation and replaces it with one centered on defining the self as emerging in the process of its encounter with the world. This issue of emergence deserves extended treatment, but suffice it simply to note that I am not referring to some vague metaphysical transformation, but rather to organic function and complexity which clearly differ in character from simple machines. Such “entities” can not be characterized by metaphorical approximations, but require organizational principles to describe new kinds of mechanistic models, perhaps best described by nonlinear logic, complexity theory,

and self-organizational precepts of various ilk.<sup>6</sup> In immune theory this general view is represented by the cognitive paradigm which I discuss in detail in the next section.

I will not assert that the cognitive metaphor was self-consciously developed as a postmodernist construct, but simply note that embedded in Burnet's original formulation was an obvious understanding of personal (i.e., psychological) identity from which he borrowed to express his own theoretical propositions. These were in fact presented in a vague fashion that I believe he intended to be metaphorical. He invoked our deep, intuitive understanding of selfhood to articulate an organismic approach to immune identity. I suspect that postmodern analogies were hidden in the metaphor, only to become more clearly articulated as the theory was espoused in its different guises by later theorists, who also recognized the resonances of such an articulation, and in the process built their conception of immune identity on the same borrowed cultural language. I have found no explicit admission of immune selfhood mirroring the prominent philosophical discussions concerning personal identity or postmodernism per se, but there is such a close correspondence in the manner in which the science has been explicated that I find it difficult to see them as two totally separate phenomena. How, or why, they are coordinated is another, far more complex question. I surmise that the most obvious connection is the rich metaphorical context of the language, whose broadly shared significance and flexible meanings led to its wide adoption. The immune self taps into an imprecise lexicon that carries a complex cultural construction, some of whose elements possess postmodern literary and social critical overtones. One might argue the extent of correspondence, but the analogies are, at the very least, highly suggestive. This is not to contend that immune theory supports particular postmodern tenets, only that I believe there are deep resonances between certain hypotheses regarding immune models and the language — with its cultural meanings attached — used to describe those theories. In sum, I regard this matter as a case study of how a science reflects the contextuality of its practice.

These tentative observations are reinforced by examining another element — although I regard it as logically derivative from the issues of alterity and dialectical encounter — namely, how a postmodern biology formulates and utilizes a holistic scientific strategy. This challenge to a modernist reductionist science has been argued by some critics as the key distinguishing element of postmodern biology, one firmly committed to organicism (Griffin 1988). This characterization from a historical perspective is problematic. The organismic views of the Romantic teleomechanists and *Naturphilosophen* clearly precede the German reductionists whose research commitment to determine the biophysical and biochemical basis of life processes were formulated in the 1840s and gained firm hegemony fifty years

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<sup>6</sup> The literature concerning biological complexity and self-organization is immense and growing. The reader is referred to this sampling of symposia, anthologies, and monographs: Atlan (1992), Kauffman (1993), Krohn, Kuppers, and Nowotny (1990), Peacocke (1983), Pines (1988), and Yates (1987).

later (Lenoir 1982). But the argument rests on recognizing that Cartesian reductionism is a major pillar of the modernist strategy and, irrespective of its historical appearance in biology, the reductionist physiologists pursued deterministic and mechanical ideals alien to postmodernism's emphasis on holism, chance, emergence, and, most important, process. Barely submerged beneath these concepts are vague notions of organismic contingency and self-actualization (Tauber 1991). These are easily found in the postmodern vocabulary but not generally regarded as suitable "scientific" terms; they lurk, hardly hidden, in our general understanding of the organism defined by its immune system.

Before I develop the so-called cognitive "postmodern" influences in immunology, I wish to offer a general orientation that rests on the appreciation that a postmodernist biology is one that regards process functions and holistic constructions as central to its interests. I have already mentioned that in light of recent developments the organism has come to be regarded as a complicated compound entity. I am referring to the symbiotic relationships organisms have with other species. (For instance, humans cannot exist without certain bacterial flora, as for instance bacteria in the colon produce vitamin K, a critical cofactor in the production of clotting proteins.) Without embarking on a discussion of microecology, I do wish to emphasize that the boundaries of self and nonself are not always clear. The point is that the immune system may ignore a putative challenge to the integrity of the organism, so that immune unresponsiveness per se is not a sufficient criterion for defining the self. The lesson to be gleaned is not that our body has learned in the course of evolutionary history what is beneficial to it and what is not, but rather that the boundaries of self and nonself become individually tailored and may be blurred. What is becoming increasingly evident is that the immune system ignores much of what it sees. It allows the organism to engage its environment. And this is the key element in the "postmodern" construction of the immune self: the self/nonself border is ever-changing.

As the immune system evolves in the life history of the organism, it constantly modifies the focus of its activities. As a result, certain immune clones are expanded while others are reduced, and thus the profile of the immune repertoire undergoes modification in time. There are two major parameters by which we assess immune reactivity. First, there is a dynamic economy of immuno-reactive cells, which are in shifting anatomic pools and coordinated by a complex system of inhibitors and activators (both cells and molecules). Additionally, there is a shifting genetic composition of the antibody library. One of the major wonders of modern biology is how readily adaptive the antibody pool is in its response. Through shuffling of several genetic elements that are assembled to make the antibody molecule, and adding genetic regions that are highly susceptible to mutation, the immune activation represents a fine tuning of the antibody library that is engineered to produce the best fitting antibodies to match their targets for destruction. The immune system is thus a highly adaptive organ, changing in response to the requirements of the organism at large.

In short, the immune self is not a static entity, but is best understood through its functional behavior. Throughout the life experience of the organism, there are changing environments, new insults, encounters with novel challenges, and it is the immune adaptability and versatility that determines its overall success. This is the primary lesson of evolutionary biology, and it is a radically different conception of the organism from that of the pre-Darwinian era. As already mentioned, prior to *On the Origin of Species* the organism was a "given." It was viewed as essentially unchanging and stable. We now appreciate a much more dynamic image. The organism is in a dialectical relationship with its world. In an ever-changing set of relationships, at many different levels of engagement, the organism lives in response to its environment. As it changes in response, its very character may be altered. The immune system is an integral part of that view (Tauber 1994d).

### Information, Cognition, and the Immune System

Thus far I have suggested a broad orientation by which we might regard immunology as having resonance with postmodernist perspectives. These overarching considerations will come into sharper resolution by examining specific issues pertinent to current immune theory. To this end, I will summarize the development of certain recent views of immunity as a cognitive process, namely the attempts to model immune function by a systems approach that explicitly utilizes linguistic and mental metaphors.

From the very inception of immunology, the presence of the idea of "recognition" was evident. The identification of the foreign implicitly requires that something is doing the recognizing. Recognizing is a perceptive event and must rely on a cognitive apparatus. This view reflects the richness hidden in the term *recognition*, perhaps because we now appreciate the surrounding meaning that must support such a metaphor. A retrospective overview of the historical development of the cognitive perspective reveals that the ready analogy of the immune system to the nervous system awaited a complex metaphorical extension of the self. Only when the *self* was in place, could a cognitive apparatus be added to develop the model's full inherent potential. Not surprisingly, such a formulation was articulated by Burnet shortly after he presented his *self* theory. I believe the faint outline of what was to become a novel conception of immune function may be discerned in Burnet's earliest use of the word *information*. And for our purposes, it becomes a key point of entry for postmodernist interpretations.

Information, throughout postmodernist critiques, has served as a powerful axiom for a hermeneutic interpretation of culture. As Donna Haraway observes:

Genesis is a serious joke, when the body is theorized as a coded text whose secrets yield only to the proper reading conventions, and when the laboratory seems best characterized as a vast assemblage of technological and organic

inscription devices. The central dogma was about a master control system for information flow in the codes that determine meaning in the great technological communication systems that organisms progressively have become since World War II. The body is an artificial intelligence system, and the relation to copy and original is reversed and then exploded. (1993, 367)

In this view, the postmodern scientist reads

as a text coded systems of recognition . . . embodied in objects like computers and immune systems. The extraordinarily close tie of language and technology could hardly be overstressed in postmodernism. The “construct” is at the center of attention: making, reading, writing, and meaning seem to be very close to the same thing. (Ibid., 372)

If the body fulfills the basic criteria of a semiotic system, it is a small leap to conclude that “bodies, then, are not born; they are made. Bodies have been as thoroughly denaturalized as sign, context, and time” (ibid.). Information then serves as an evocative and crucial fulcrum for this postmodernist view of our culture.

Information — its manipulation and control — has had a complex and important history in biology. The novelty of information theory in the mid-1940s was not concerned with its measurement or transmission, which date to the nineteenth century, but with new notions concerning the logistics of information storage (Kay 1994). With the development of the modern computer, information technologies and their powerful epistemic repercussions began to permeate other academic disciplines and the broader cultural sphere. The impact of automated control systems on modeling biological processes was anticipated and promoted by Norbert Wiener and his colleagues during the early 1940s, and with John von Neumann grandiose schemes for applying complex field control and communication engineering to several areas of biomedicine were planned (ibid. 1994; Heims 1980). Their interests ranged from modeling neural function to viral replication. Just as Burnet and Fenner published *The Production of Antibodies* (1949), Wiener’s *Cybernetics* captured attention in diverse fields, as information theory was offered as a new paradigm. There was much speculation concerning the application of cybernetic theory to biological systems in general.<sup>7</sup> The most aggressive proponent of cybernetic theory application to biology was Henry Quastler, who organized a symposium to integrate information theory and biology (1953). Of particular note,

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<sup>7</sup> For example, despite lack of experimental support, J. B. S. Haldane, in a 1948 unpublished paper, attempted a calculation of the “total amount of control (information = instruction) in a fertilized egg, and various other similar points” (Kay 1994). H. Kalmus made similar attempts and concluded that genes could be described as messages or sources of messages, and thus could be regarded as the basic elements of biological control (1950). Note that it was von Neumann’s notion of reproducing machines that copied via coded instructions, which introduced such “copiers” (or cybergs) as models for genes (Kay 1994). These matters are discussed in greater detail in Kay’s article found in this issue of *SiC*, p. 609.

the general proposal that each protein might be regarded as the “message” and amino acid residues as an “alphabet” was applied to the specificity of antibodies by Haurowitz at this meeting (1953). This history is important in as much as we should recognize that cybernetics was considered the new means for understanding genetic transmission prior to the Watson-Crick paper of 1953, and immunologists were keenly aware of its possible application to the production of antibodies. In fact, the generation of diverse proteins with directed immune specificity was viewed as an important problem of protein synthesis, and thus it is not surprising that Burnet would also comment on the possible ramifications of information theory.

The so-called template theory is now only of historical interest, in that it predated the current understanding of how protein is translated from genomic DNA. However in 1955, shortly after the self-marker theory was proposed, Burnet, like most of his contemporaries, believed that protein formed in some as yet unspecified fashion on the template of some preexisting molecular structure. In his work *Enzyme, Antigen and Virus* (1956), as in his earlier monographs, Burnet struggled to account for protein synthesis and more specifically antibody production, but now further modified to account for the information contained in DNA. It is not necessary to summarize the particular issues in order to appreciate the appearance of the concept of *information* in the immunological literature.<sup>8</sup> Consider, for instance, how *information* is introduced (albeit enveloped in quotation marks) in the overview printed on the book’s cover jacket:

The problem [protein, virus and antibody production] is discussed from the point of view of the way in which “pattern” can be manifested in protein or other macromolecules and an attempt is made to sketch the outline of something like an “information theory” of the cell in which macromolecular pattern serves as a means of conveying “information” within the organism.

In a section entitled “Information theory in biology,” Burnet acknowledged the profound impact cybernetics made on his own theorizing:

Since 1945 there has been widespread recognition amongst scientists and the public generally of the importance of the principles which have emerged from experience in the development of electronic communications and

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<sup>8</sup> Burnet’s vision of the template mechanism, built on a vague notion of biological patterning, was an intermediate stage in acknowledging the basic information flow from DNA to protein that was in the air so to speak, but had no experimental basis. In his words, “it is the thesis of this monograph that, where biological matters above a certain level of complexity are concerned, most interpretations must be in terms of macromolecular pattern which, by interacting with complementary or near complementary pattern in some other functional situation, can induce action or, if it is more convenient so to express it, convey information or instructions” (Burnet 1956, 58). The details of how Burnet accounted for antibody synthesis are not of concern here, but only the acknowledgement of the early appearance of “information” as a governing principle. In this regard, he was well aware of the theories expounded by Haldane and Haurowitz (*ibid.*, 17).

control systems. . . . In our field, the relation is a good deal more distant, but one cannot escape the attraction of the general approach.

This monograph was originally conceived as an attempt to develop something analogous to a communications theory that would be applicable to the concepts of general biology. However, it has not been found possible to make any serious use of the already extensively developed concepts of information theory in the strict sense. In part this is due to . . . only the most generalized sketch of an outline [that] has yet to be given of how information theory at the strict level can be applied to biology. The only extended account of such an approach that I have been able to find is the symposium edited by Quastler (1953). (1956, 164–65)

Although Burnet felt confident that macromolecular pattern replication was the basis of information flow in the cell — just like “the printed word is the basis of the flow of information” — this hypothesis, and so the overall thesis of the book, was attenuated by lack of experimental support. Thus while Burnet sensed the general power of information theory, its application as a research program remained highly problematic in his day.

Within five years, immunology was marked by a major conceptual turn. The generation of diverse antibody sufficient to recognize the myriad universe of foreign substances became, in some sense, a simpler regulative problem. The so-called clonal selection theory proposed that through differences in binding avidity the antigen selects antibody-producing cells (lymphocytes), which are stimulated to produce antibody as a result of the antigen binding to the antibody coating the cell surface. Although the genetic mechanism by which diverse antibodies were synthesized in the first place remained a critical problem (solved in the mid-1970s), biologically oriented immunologists could train their sights on the matters relevant to immune regulation. In Burnet's monograph, *The Clonal Selection Theory of Acquired Immunity* (1959), the notion of information is again used, but now in a completely different context. No longer directly concerned with transfer of genetic instructions, information appears as a library of ready-to-serve lymphocytes. Information would have “to be stored, either individually or collectively, in the cells of the antibody-producing system” and “long-lasting retention of information” was required to account for immunological memory (p. 47). The clonal selection theory established *information* firmly within immune theory, where it has served as the nexus of diverse concerns: geneticists pondered how the genome could accommodate the extraordinary diversity required of the mammalian immune repertoire (1 to 10 billion different specificities); cellular biologists sought to explain how such a complex system could be regulated. In fact, “system” became a widely operative term as a result of modeling such an information-generating entity (Moulin 1989).

When Burnet formally introduced the *self* metaphor in 1949 (it actually appeared a decade earlier, but without any theoretical significance [Tauber and Podolsky

1994; Tauber 1994d]), he prepared the critical context for the admission of other terms that were consistent with the idea of personal identity or, with what will soon become explicit, of a *knowing* entity. For instance, immunological “training,” “recognition,” “learning,” and “memory,” are terms that rely on a creature that has cognitive abilities. Thus in erecting a new theoretical edifice on the foundation of the self, the appearance of *information* finds a conducive environment for evoking a rich metaphorical potential. Information is certainly a tool that a mind uses, and thus its appearance might be construed as a natural member of the newly emerging immunological lexicon. And the move from “information” to “cognition” is effected on the basis of a close conceptual link. Although Burnet first uses “cognate” in passing in 1959 (p. 70), by 1963, in *The Integrity of the Body*, a short book written for a nontechnical audience, he invokes an analogy with language to account for antibody selection.<sup>9</sup> The cognitive metaphor, however, was to be more fully developed by others.

Niels Jerne (who along with Burnet are widely acknowledged as the leading immunologists of their era) must be regarded as the true author of the cognitive immune model. In 1960 he wrote of the antibody-producing system as “comparable to a typewriter” (p. 348) or “analogous to an electronic translation machine” (p. 341), thus invoking models of mind derived from cybernetics. In his words, “we would probably conclude that an important feature of the machine would have to be an ability to recognize single foreign words, and that the mechanism by which it functions must, in some form or other, include the consultation of a Foreign-English dictionary” (ibid.). By the mid-1960s, Jerne was dealing explicitly with the metaphorical meaning of immunological “memory” and “learning.” In an anthology devoted to diverse systems of learning behavior, he noted how immunologists used metaphors such as “recognition” that were obviously derived from brain function. His own seminal contribution to immunology was the insight that antibody proliferation resulted from the “natural selection” of preexisting antibody, an insight which he later developed into a network theory. Before the network hypothesis was formally proposed in the mid-1970s, Jerne tentatively regarded the

<sup>9</sup> In the section where Burnet is explaining the clonal selection theory, he illustrates how “the body acquires or generates the information which allows it to differentiate immunologically between what is self and what is not self” (Burnet 1963, 94). He draws an analogy with another information transfer example, that of words:

If it is true that around four amino acids units are responsible for each specific immune patterns . . . we are in a position to make use of the analogy between 20 common biological amino acids and the letters of the alphabet. Each pattern could be represented by a four-letter combination. . . . [W]e can imagine an electronic computer set to produce at random four-letter groups from a 26 letter alphabet. If 10<sup>7</sup> words are asked for, we should have a 99-percent probability of getting at least one example of every possible four-letter word. . . . Our computer has another characteristic. Once the selection has been completed [to create the reactive library], all the remaining “words” are stored in the memory and when any combination is asked for it can be produced in unlimited numbers, but only if it is in the memory. (Ibid., 94–95).

Here Burnet utilizes analogies from language, information processing and the emerging powerful model of cybernetics to explain immune function.

immune system as analogous to the preexisting structure of the nervous system, which changes as learning occurs. Remarkably, he reaches far back into philosophical tradition to buttress his argument: "As pointed out by Socrates (375 BC) and Kierkegaard (1844), understanding must be preceded by recognition, and all learning, therefore, must consist of a "recollection" of knowledge already present in the soul" (Jerne 1966, 157). In another article, Jerne went on to draw more explicit comparisons and contrasts with the nervous system (1967). He saw that each system has a history of encounters with the world that remain present both in the form of irreversible changes and in the form of memories that always affect the next response. Thus both systems change with, and learn from, experience. Jerne further speculated that the nervous system might well share similar molecular mechanisms to those found to generate antibody diversity.

By 1974 Jerne's inferences have become bolder: there were functional parallels ("... the immune system, when viewed as a functional network dominated by a mainly suppressive Eigen-behavior, but open to stimuli from the outside, bears a striking resemblance to the nervous system" [Jerne 1974, 384]), which in turn suggested the possibility of phenotypic similarities. In his view, the brain was likely to reflect the same basic structure proposed for the immune system, due to, in his words, "similarities in the sets of genes that govern their expression and regulation" (ibid.). Over the next decade, Jerne continued to draw explicit parallels between the immune and nervous systems. Without detailing the theoretical basis of his argument, I wish to draw attention to the dramatic and evocative sense of selfhood Jerne used to couch his argument: "... the immune system (like the brain) reflects first ourselves, then produces a reflection of this reflection, and then subsequently it reflects the outside world: a hall of mirrors. . . . The mirror images of the outside world, however, do have permanency in the genome. Every individual must start with self" (Jerne 1984, 19–20). There is a striking "bridge" of the self as *entity* and the self as *process* in these few short lines. Jerne invokes the relational basis of Kierkegaard's formulation of the self in the image of the mirrors endlessly reflecting the self's image and at the same time he notes the genetic basis of the self as the "starting point" of this dialectical identity. In a curious way, Jerne would have it both ways, seeming to acknowledge the inner tension of resolving what is fundamentally a philosophical conundrum.

In a paper published the next year, Jerne drew a more explicit parallel with language by turning to Noam Chomsky's theory of generative grammar, specifically the hypothesis that certain deep universal features of language acquisition is dependent upon a DNA-encoded function. The flexibility and fine specificity of the immune system dwells in the ability of genetic components to sort, select, and assemble into diverse antibodies, a process fully delineated by the mid-1970s. Why Jerne chose to parallel such a process to language acquisition and competence reveals a metaphor of great complexity. Drawing on Chomsky's generative grammar, Jerne repeatedly attempted to crystallize the analogy between linguistics and immunology (Jerne 1984; 1985). He used the linguistic theory as a model for

explaining how the immune system reacts to the universe of antigens with such adaptive, versatile precision. But in forming this analogy, Jerne had to invoke the role of the brain and thereby found himself entangled in the entire issue of mind-body modeling. Reflecting his earlier ambivalence already discussed, he alludes to characteristics of body as entity and of mind as process. The immune system parallels this structure: the antibody library is the entity, and network function its process. In so situating his theory, Jerne placed himself in a classical predicament: Is language the *voice* of the mind or the mind itself?

Not surprisingly, in the wake of Jerne's contributions much discussion ensued as to whether the immune system might be regarded as semiotic (e.g., Sercarz et al. 1988); and more generally, an entire school of thought has emerged that views the immune system as a cognitive system.<sup>10</sup> Elsewhere I have reviewed this development in detail (Tauber 1994d), and suffice it here to make a brief summary. Irun Cohen, Antonio Coutinho, Francisco Varela and their respective colleagues, regard immunology's focus as having shifted from the task of discriminating self from nonself, to understanding the more basic function of how the immune system serves as a cognitive faculty. In their general view, the self has quietly slipped away as a definable (viz., modernist) entity and has been replaced with a "knowing system," one conceptually centered on a process orientation. They argue for a "cognitive paradigm" building on the fundamental notion of information:

Simply put, a cognitive system is a system that extracts information and fashions experience out of raw input by deploying information already built into the system; in a sense, a cognitive system is one that knows what it should be looking for. This internal information, which precedes and imposes order on experience, can be seen conceptually as a blueprint for dealing with the world. In the abstract, cognitive systems can be said to behave with a sense of direction; their internal organization endows them with a kind of intentionality. Cognitive systems, then, are not passive processors or recorders of information; they are designed to seek very particular information from the domain in which they operate. (Cohen 1992a)

The implications of this statement represent an important theoretical development. The argument maintains that the immune system is directed inward, constantly sensing and affirming itself. Reaction to the foreign becomes secondary, or perhaps a by-product of this central self-defining function. This is the maturation of an orientation introduced after World War II, namely that immunology is fundamentally concerned with defining the self. Before the immune system can protect the organism from the foreign, it must *know* itself. The logic demands that establishing *identity* must precede protecting the host's *integrity* (Tauber 1994d). I regard this as the crucial conceptual turn in current immunology, a turn buttressed by the cognitive paradigm.

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<sup>10</sup> These views are not necessarily widely held by the immunological community, but serious attention is paid to its proponents.

When the immune system is viewed as a cognitive entity, immunologists most clearly reveal their intellectual debts to various extra-curricular sources in their quest to model immune identity. In this view, the immune system represents a complement to the nervous system; indeed, contemporary theorists represent immune function using models similar to those proposed for understanding neural cognition. To engage its targets, the immune system must first perceive them and then, in a sense, decide whether to react. This is a cognitive model, where the immune and the nervous systems are regarded analogously. Each has perceptive properties; each has capabilities to discern both internal and external universes. Information processing is central to both the nervous and the immune systems, and thus their respective perceptive properties are linked to effector systems. In the case of the nervous system, it is the musculoskeletal system that enables movement in response to stimuli, and the autonomic neuroendocrine system that effects changes in the body's energy economy and visceral control, as, for instance, making glucose available for the acceleration of heart rate and breathing upon sight of a predator. Similarly, the immune system has its own effector system of antibodies and immune cells to carry out the immune reaction. This may be the rejection of invading bacteria, the inflammatory response to a burn, or the allergic rhinitis of hay fever. Beyond the functional analogy, there is growing evidence that the nervous and immune systems are highly integrated with each other (Ader et al. 1991). They share many of the same messenger molecules, have close developmental histories — both in phylogeny and in ontogeny — and finally intersect biochemically to achieve a common purpose. But beyond these interdependencies, there is a growing appreciation of a strong parallel in how these complex systems might be organized; increasingly, system analyses applicable to one discipline are carefully examined for their applicability to the other.

As a cognitive apparatus, the immune system's structure may well mimic the architecture of the nervous system. Following Jerne's original musings, models based on neural networks, complete with analogous computer program simulations (e.g., Stewart et al. 1989), suggest new research directions. Most models set up systems of differential equations that serve to represent the behavior of the system, but a recent alternative approach employing cellular automata attempts a more "biological" model simulating dynamic conditions; the system's evolution is then described as the outcome of local and unique interactions (Cohen and Atlan 1989; Celada and Seiden 1992). This latter approach clearly falls under the rubric of a process-oriented biology, which is the mature development of a cognitive metaphor introduced by Burnet and Jerne. Beginning with the self that must recognize and order information, parallels with language were soon developed. These in turn were expanded into more explicit analogies with the brain and mind. More recently this self metaphor has been deliberately extended to that most intimate of the self's function, cognition. After all, Descartes proclaimed, *cogito ergo sum*. It is from this modernist manifesto that postmodernist responses were to be built.

Insofar as we model the immune system as a cognitive entity, the same issues arise concerning the knowing entity as those that challenge the disciplines attempting to characterize the mind. I would not venture to propose that immunologists are overly concerned with postmodernist objections to situating such an entity as *The Mind*, but I do believe there is a general awareness that any explanation of the immune system must ultimately deal with its emergent properties, its self-organization, its hierarchical structure, and its integrating mechanisms. These concerns are very much at the heart of a postmodern science that is no longer content either with simply defining an entity (be it the nervous or the immune system) or with believing that through biochemical or structural analyses of molecular components, the properties and dynamic controls will simply follow. The cognitive sciences are very sensitive to the drastic limitations of a simple mechanistic ideal, and I believe they are distinguished from those biological disciplines that may still aspire to reduce the organism to a collection of clockwork-like mechanisms. This pervasive concern with discerning how properties arise from structure — for instance, how the mind emerges from the brain — quite dramatically separates the anatomists, whether gross or molecular, from their colleagues concerned with emergent process phenomena. It is in this sense that I believe it fair to say that when immunologists refer to the immune self they are keenly aware of the dynamic character of immune identity. I am specifically referring to how the immune molecular and cellular profile is altered in response to new challenges. In this sense, the immune system is always changing in composition and character, suggesting a certain “indeterminateness”; a focused center, a postulated organizing principle, remains elusive and undefined.

Perhaps the most explicit conception of a decentered self in current immunological theorizing is that of Irun Cohen’s immune homunculus (Cohen and Young 1991; Cohen 1992a, 1992b). He has proposed that the differentiation of self and nonself is ambiguous, because in contrast to the dominant paradigm of the clonal selection theory, the immune system is in fact organized to recognize particular host constituents. In this view, immune cells are keyed to a library of targeted self antigens that represent an “outline” of the normal body analogously to the mapping of the homunculus of the cerebral cortex or late seventeenth-century embryological depictions of the preformed miniature adult in the head of the sperm (Gasking 1967, 53–54; Farley 1982, 20–22). Foreign antigens then are recognized as “other” not by their intrinsic foreignness (that is, their novelty), but because they are presented in a *context* that changes their shared “selfness” to a representation that declares their pathology. In other words, the foreign is destroyed not so much because of differences in the molecular structure that might distinguish a foreign substance from host constituents, but because shared antigens do not appear “normal” in the context of infection, for instance.<sup>11</sup> Cohen uses the

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<sup>11</sup> The reasons for this sharing of antigenic constituents between host and parasite pertain to close evolutionary relationships that govern the interactions of pathogens with their targeted hosts. There seems to be highly conserved homology between certain shared proteins that the immune system has

analogy of Escher's ambiguous ground/representation etchings, where diverse figures emerge depending on what the viewer perceives as the background context (Cohen 1994). The trope is the alternate way one views what is figure and what is its context, so that what first appeared as ground may assume new form as a figure. When visual cognition perceives their interplay, representation — i.e., the figure — is shown to be constructed from an ambiguous universe, where background and image are exchanged at liberty. Meaning is thus actively sought and not given. This is an important postmodern aesthetic principle, which Cohen has tapped to depict the immune system as defining self and nonself in a contextual dynamic. He argues that self antigens in their "normal" setting are made tolerant by the animal's control mechanisms, which are loosened or abandoned when the context of these "self" antigens is altered in the setting of microbial invasion.

In this scheme, the self is operationally defined as that which elicits immune recognition in a positive fashion, albeit at a level below that evoked by the appearance of recognizable (i.e., still "self"), antigen in the context of infection. In other words, autoimmunity is a normal characteristic of the immune system, which constantly seeks to identify and monitor key host constituents. If these self antigens are altered in a contextual sense, their "meaning" changes and an active immune response is initiated. Thus the self is no longer an entity but dynamically emerges in a process of self-identification, which presumably changes and adapts continuously throughout the life of the individual.<sup>12</sup> This so-called cognitive theory of immune recognition has been claimed to be a "paradigm shift" because of the radical reversal of how the self is regarded (Cohen 1992a). Not only are the dynamic elements emphasized but how the immune system is structured as self-defining challenges earlier conceptions of the immune selfhood as a given entity. This newer view of immune function is fundamentally formulated on self-seeking, self-organizing activity, whose structure is decentered from any bounded self. Immune identity can be defined only in particular contexts, and from such histories, selfhood emerges.

This centerless notion of immune selfhood resonates with a post-structuralist orientation, which in other discourses is referred to as indeterminacy.<sup>13</sup> Closely keyed upon to recognize the foreign. To what extent self-recognition is then a by-product of this primary defensive function, or the converse, is not yet discerned (Cohen and Young 1991; Cohen 1992a; 1992b).

<sup>12</sup> A conceptually similar self-directed theory has been developed by Antonio Coutinho and his colleagues, who also emphasize the cognitive nature of immune function (Coutinho et al. 1984; Varela et al. 1988). Parallel to Cohen, they have been instrumental in demonstrating the inner-directedness of normal immune function. Differences arise from their division of the immune system into central and peripheral components, where the central division is responsible for surveillance of the self. Although they are now adopting the notion of the "immunculus" (Cohen's discovery that only certain self antigens are key to immune self recognition), in their articulation a self entity remains implicit (Nobrega et al. 1993). In an important sense Burnet's formulation remains hidden in a reversed model of a self, now defined positively (Chernyak and Tauber 1991), and the decenteredness of the immune system as an Escher picture is not articulated. My own view is closer to Cohen's (*ibid.*).

<sup>13</sup> Cohen has no conscious ambitions to link his theory to postmodern critiques from other fields. When interviewed in April 1994, he appeared unaware of postmodern criticism (e.g., the views of Derrida and Foucault), and generally unconscious of any resonance his decentered depiction of immune selfhood might have with similar arguments from literary or social criticism.

linked is the subordinate matter of how to account for the immune system's holistic properties, which again reflects a powerful postmodern biological ethos that seeks such understanding. But note, I regard this holistic concern as arising from the destabilizing character of structureless phenomena that we metaphorically refer to as *The Self*. And in this same vein, the cognitive nature of the metaphor only reflects the underlying problem of the subject as process. The difficulty of conceptually grasping the self may reside within the very foundations of our subject-verb structured language. Only a subject can act. How can there be immune activity without a definable entity — a self that acts? At this point it seems that all the postmodern concerns converge to leave us with the task of erecting a new grammar. The self is neither subject nor object, but is actualized in action; the self becomes, in this view, a subjectless verb. These questions uncannily reflect issues pertinent to our personal identities and project the same kinds of responses that we label as postmodern.

### **Culture and the Immune Self**

I believe that we might readily accept that there are two visions of immunology beckoning for attention. Each has exerted important influence on the growth of the discipline, and I suspect that these views will continue to compete for dominance. The first, which I have referred to as modernist, is that older research tradition based in immunochemistry. It has followed a reductionist program culminating in our sophisticated understanding of genetic control of immune identity. The second major research tradition, which I have tentatively labeled as analogous to postmodernist tenets, refers to those efforts of (1) defining immune function in terms of a holistic systems approach, and (2) stressing the indeterminateness of immune identity. Such an analysis emphasizes the process characteristics of the immune reaction. In this scheme, the self is functionally defined (as opposed to genetically prescribed), and such a program utilizes immune cognition (to constitute the self's "otherness") as part of its theoretical edifice.<sup>14</sup>

In closing, I will simply offer an example of how cultural critics have used immunology as a weapon in their ideological wars. This represents a converse illustration to the one I have developed, so that now immune theory is invoked to

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<sup>14</sup> It is still unclear to me whether there are postmodernist criteria of scientific methodology and epistemology that are clearly distinguishable from modernist science. New work in Bayesian inference, for instance, may have wide repercussions that will redefine the rules governing "scientific objectivity." Do these matters qualify as postmodern, and if so, on what basis? This is a matter well beyond the boundaries of this discussion, but I refer to them only to alert ourselves that these issues may be obscuring our ability to situate the dramatic changes in immunology. Perhaps it is fair to refer to certain programs in immunology as postmodern not on the basis of the criteria that I have listed, but because the epistemological foundations of the science may be adopting new modes, fundamentally reorientating our basic scientific style. If we are in fact in the midst of such a sea change, "postmodernism" becomes a convenient code for indicating that older modes of inquiry are inadequate. (See note 6.)

support a postmodern argument. The case is useful in simply emphasizing the free correspondence and contextualization of the science in its culture. The suggestion that there might be postmodern effects in science immediately implies that the science, as a product of culture, is also a participant in larger social phenomena. This is undoubtedly true at some level, but I resist the cavalier use of immune theory for political agendas. Although I readily accept that the older notion of self has been replaced by an expanded, if not “looser” functional definition, I have doubts as to the applicability of anthropomorphic concepts to what must remain at some fundamental level an abstraction. The self is a metaphor; it fulfills an operational role for immunology. This should not be confused with what the self “is.” After all, immune function deals with cells and genes and proteins, not selves! The extraordinary power of the self metaphor is reflected in this conflation. On the one hand, we must recognize that we are not defined as *egos* by our immune system, but on the other hand, immunology has thrust itself into a position where it serves as an important component of our personal identity. In short, the potency of immunology has resulted in the imposition of its own definitions on how we now regard ourselves. In this sense, immunology has been both imperialistic and triumphant. When the science becomes too intimate with its culture, there are dangers of surreptitious use of the presumed objective findings for ideological arguments. But there are those who more readily, if not enthusiastically, would utilize immunology to explain ourselves, sociologically.

When regarding immunology as both a possible product of, and a contributor to postmodernism — that is, as a cultural construct — it is but a small leap to shift immune theory from representing an epistemological challenge to being merely a thinly veiled political ideology. Donna Haraway, a leading proponent of the latter view, claims that the “immune system is an elaborate icon for principal systems of symbolic and material ‘difference’ in late capitalism” (1993, 366). Immunology, according to Haraway, is particularly effective in portraying our cultural structure and values because it so closely resonates with our own inner and social being. She attempts to marshal evidence that our own image of selfhood is projected onto immune theory and that beyond reflecting the metaphoric construction of models, the theory might in turn be used to legitimate particular power relations. She argues that immunology, marshaling the power of scientific legitimacy, can be used as a map to guide the “recognition and misrecognition of the self and other in the dialectics of Western biopolitics” (ibid.). The science, in her view, thus bestows a certain authority to differentiating, and by implication to affirming, difference in society. Her point is not to dispute such difference, but to expose how immunology regards relationships between diverse kinds as combative, when other modes of encounter might be envisioned (specifically those that emphasize cooperation and symbiosis). The power of the immune system as an icon is in assuming it to verify and legitimate an inequitable social structure. In Haraway’s analysis, the science has achieved an imperialistic prominence, perhaps matched in intensity “only in the biopolitics of sex and reproduction” (ibid.), in effectively offering us a scientific

rationale for declaring not only the scientific basis of difference, but the “natural” state of different kinds. There is us, and then there is the foreign, and the relationship is one of conflict. Haraway perceives this self-empowering as an assertion of dominance, reflecting the basis of a social metaphysic where the other may be excluded.

Beyond the post-structuralist modes of Haraway’s argument, there is obviously an ideological agenda here that I will not criticize. I have summarized her views only to illustrate how immune theory is being invoked both to characterize ourselves and to serve as a focus of cultural criticism in a postmodernist vein. I do not share Haraway’s analysis that immune theory so closely reflects our cultural values; but I do respect the general observation that immunology is firmly embedded in its culture, and that we are witnessing a rich dialogue between the science and its broader context. Rather than taking its cues exclusively from literary critics, artists, and philosophers, I suspect that culture at large is seeking in immunology an expression of certain precepts that are perhaps better articulated by the immune scenario than by others. Or at least so such critics as Haraway (*ibid.*) and Emily Martin (1990, 1992) would have us believe. The important distinction to maintain is that their critiques are sociological, not scientific; and their use of the science outside of its context immediately translates, if not distorts, the original conceptual formulations.

Immunology’s seductiveness is so powerful because the science is in such free communication with its supporting culture. Immunology borrows extensively from common experience to articulate itself. This is evident in simply listing the common metaphors found in the immunological literature. I have already used several, not only so as to employ language that the general reader might understand, but also because these words are the ones used in technical publications. I am referring to *immune response, recognition, immune surveillance, immunologic learning, tolerance, foreign, repertoire, presentation*, and of course the *self*. Other common metaphors used by immunologists include *internal image, collaboration, memory cells, virgin B cells, killer cells, suppressor cells, framework regions, avidity, and rejection*. There is ample evidence, from many cases, of how scientific theory and practice depend on the prototheoretic constructions of metaphor, and I need not here further illustrate this point. Suffice it to conclude that immunology not only borrows freely from the broader culture in which its practitioners live, but is beginning to articulate an epistemology that has deep reverberations beyond its own circumscribed audience. Whether immunology manifests postmodern influences or only exhibits certain analogies to a cultural lexicon seems to me largely to depend on an assessment of how one wishes to situate its key metaphors in their cultural matrix. In other words, the critical exercise is to decipher the underlying metaphorical structure of the discourse. It is an open dialogue, and we should be wary of the free correspondence between two very different kinds of language. Finally, this overarching concern with the metaphorical construction of the science might be regarded as a postmodern conclusion. The vision of immunology as

intercontextualized, integrated, and to varying degrees constructed from other sources than its narrow purview, represents the view of science, at least in part, externalized from its parochial internalist interests, forced to engage its culture and admit its deepest intellectual roots as originating in that cultural experience.

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