Philosophical Problems of Immunology

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Abstract

At the dawn of the computational era, immunology is at a crossroads: Its efforts to frame microbial-host interactions in combative, war-related terms no longer fit the larger picture of immune protection, and its focus on antimicrobial responses barely captures the diverse functions of the immune system, from tissue maintenance to cancer surveillance to development. As the classical view of immune processes becomes increasingly complex, the problem of self, individuality, mind-body interactions, and disease causation have stimulated extensive philosophical comment. Relating these disparate research topics to changing avenues of theoretical studies, philosophy of immunology helps to reframe basic conceptions of the organism from an atomistic, insular entity to one characterized by fluidity, hybridity, and porosity. In addition, highlighting the role of the observer in experimental research, this interdisciplinary field has redefined classical

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demarcations between science and culture while advancing our understanding of biology as a fundamentally human endeavor.

Keywords

Biological identity · Biological individuality · Biological information · Burnet · Disease causation · Extended cognition · Holism in biology · Immune self · Immunolinguistics · Immunology · Immunopolitics · Immunosemiotics · Metaphor in biology · Microbiome · Mind-body interaction · Philosophy of immunology · Postmodern view of science · Psychoneuroimmunology · Reproductive immunology · Systems biology

Introduction: Modern View of the Immune System and Its Historical Basis

The traditional perspective of an organism as an integrated, unchanging, and autonomous entity faced scrutiny, notwithstanding early studies on secretin, acetylcholine, and other chemical mediators that seemed to suggest a seamless chemical coordination between body parts (Geroulanos and Meyers 2018). Rooted in Claude Bernard's idea of the radical separation of internal and external environment (Cohen 2009, pp. 191–205), this traditional vision helped to define immunological processes as involved in ensuring constancy of endogenous factors, and, accordingly, an organism portrayed as radically detached from its environment (Cannon 1963 [1932], p.38). Consolidated by the cybernetic movement and buttressed by an individualistic orientation of Western capitalism, this vision elevated autonomy to the rank of the essence of the living, as exemplified by André Lwoff's exclusion of viruses from the domain of life based on their apparent lack of independence (Lwoff 1957, p. 239).

As organisms were regarded as stable and autonomous, the immune system was assigned the role of a guardian of their constancy and autonomy, in which natural defenses assumedly "consists precisely in balancing and maintaining its stable state" (Richet 1900, p. 719). Authoring an early version of the concept of homeostasis, Charles Richet considered resistance against infection as a manifestation of a more general role of immunity in preventing disintegration of a living being in the face of changing environmental circumstances. Conceived as preserving stability and autonomy, the immune system is generally understood as assuring the animal's steady identity through its own "stable configuration in time and space, coordinating its components in a dynamic network" (Moulin 1989, p. 229). Thus, the immune system's role in host defense became associated with a view of an organism as fixed and autonomous. The organism's fixity was presumed to be evident in both the steadiness of its boundaries – what belongs to an organism is decided at birth – and the stability of its internal states, expected to remain constant despite environmental changes (homeostasis).

In a context in which the immune system was portrayed as the guardian of the organism's constancy and autonomy, the immune system was depicted as equally

stable and delineated, consisting of specialized lymphoid organs (both primary and secondary), as well as a network of lymphocytes, granulocytes, monocytes/macrophages that release a variety of molecular mediators to coordinate their activity (Murphy and Weaver 2016). By revisiting the idea of the immune self, individuality, mind-body interaction, and disease causation, philosophical studies of immunology are reevaluating this image, highlighting that immune functions are mediated not only by specialized cells and molecules but virtually all cells of the body, and that these functions consist not only in defense but also in an all-encompassing physiological coordination and adaptation influencing a variety of microbial, metabolic, neuroendocrine, and biochemical processes (Swiatczak and Tauber 2020; Pradeu 2020). In reflecting on this shift of immunology from a singular defensive function to a contextual orientation, philosophers of immunology have highlighted the conceptual implications of this more complex theoretical framework for understanding immunity and the placement of the organism in its environment.

Philosophy of Immunology

Self

At the heart of modern immunology is the concept of immune self, which, having been introduced by Macfarlane Burnet in the middle of the last century, is used to refer to the universe of tolerated antigens in the body (Burnet and Fenner 1949). The Australian researcher hypothesized that destructive autoimmunity is avoided by eliminating immune cells carrying receptors with affinity for endogenous molecules in an embryo (Burnet 1959). Speculating further, he proposed that lymphocytes, which survive this purging, persist in the organism into adulthood to respond to all kinds of foreign targets, including pathogenic microbes, transplanted foreign grafts, and other noxious substances (Burnet 1959). Once fixed at birth, Burnet assumed that the embryonic immune self persisted as an immutable antigenic core, which, like the personal self in human discourses, is uniquely sensed, enclosed, and protected (Tauber 1994, p. 173).

As an attribute of molecular identity and the basis for an organism's discernment from the foreign, immunological selfhood was conceived along the lines of classical philosophy, namely as the essence of the subject or the innermost ontological foundation of a living being (Tauber 1994; Howes 1998). Portrayed in the Cartesian philosophy as a disembodied core of identity (Descartes 2008 [1641]), *self* became a shorthand reference to depict the realm of antigens recognized as one's own during development (Baxter 2006). Resting on the Western idea of some personal essence, separated from the outside (Sampson 1993; Lakoff and Johnson 1980), such identification reinforced the vision of an organism as delineated, fixed, and protected and, in so far as immune responses were assumed to selectively target only foreign bodies, it portrayed one's own organism as sharply detached from the environment (Tauber 2017).

The notion of the immune self as unique, lasting, and circumscribed entity has been critically analyzed and reevaluated both in philosophy and science (Tauber 1994, 2000). Confounding the essentialist vision of the self were findings that disputed the fixity of immune parameters at birth, inasmuch as the domain of tolerated antigens changes during lifetime. As a result, there are no invariant immune parameters of self-identification. Clonal selection of lymphocytes proved to continue into adulthood (Silverstein and Rose 1997), and tolerance to an antigen was shown to be readily reversible by an addition of immunomodulatory molecules (i.e., adjuvants [Janeway 1989]). So, instead of immune identity formed at birth, ongoing peripheral processes mediated by regulatory T cells (abbreviated as "Tregs") and other mechanisms continue to modulate self/nonself discriminatory processes (Sakaguchi 2004). Hence, the idea of immune tolerance has been transformed from an inflexible definition determined at birth to a dynamic depiction in which immunity is malleable, fluctuating, and decentered.

Philosophically, the modified concept of the immune self turned out a better fit with a postmodern sense of the "I" than the classical version of the concept advocated by early philosophers (Tauber 1995). This is because postmodernism, akin to contemporary immunology, questions the stability of self, presenting it as fluid, unstable, situationally enacted, and a site of contestation, with various theorists offering differing perspectives within this framework. Indeed, starting from the critique of the modern idea of self by Nietzsche through post-Nietzschean accounts of personal identity by Heidegger, Foucault, and Derrida, the notion of selfhood has lost its original epistemic firmness and is now represented as an outcome of historical and societal contingencies (Seigel 2005). Deflationary accounts have been developed (Dennett 1992), and personal identity has become recognized as liquid, fragmented, and dispersed (Löwy 1991; Grignolio et al. 2014). The exchange of these ideas across disciplines has challenged essentialist frameworks and metanarrative structures in science, politics, and sociology. Thus, while the ontological status of self in philosophy lost its original Cartesian certainty, a parallel transformation also occurred in immunology in which changes in the cultural zeitgeist resonated with the shifting empirical and theoretical configurations in the science of biological identity (Fig. 1a, b).

Individuality

Littering of the soma by conspecific alien cells is a threat to singular individuality, and the adaptive value of the immune system has been considered to lie in its ability to ensure biological independence (Rinkevich 1999). Recognizing the capacity of the immune system to reject foreign grafts, Peter Medawar assumed that the immune system operates as a guardian of organismal individuality and an immune reaction assay became for him an ultimate test of biological distinctiveness (Medawar 1952, 1957). Later studies showed that graft rejection depends on T cell-mediated recognition of unique surface markers coded by products of major histocompatibility complex (MHC) genes (first described in Gorer et al. 1948), which were assumed to operate as "individuality differentials" or chemical indicators of biological uniqueness.

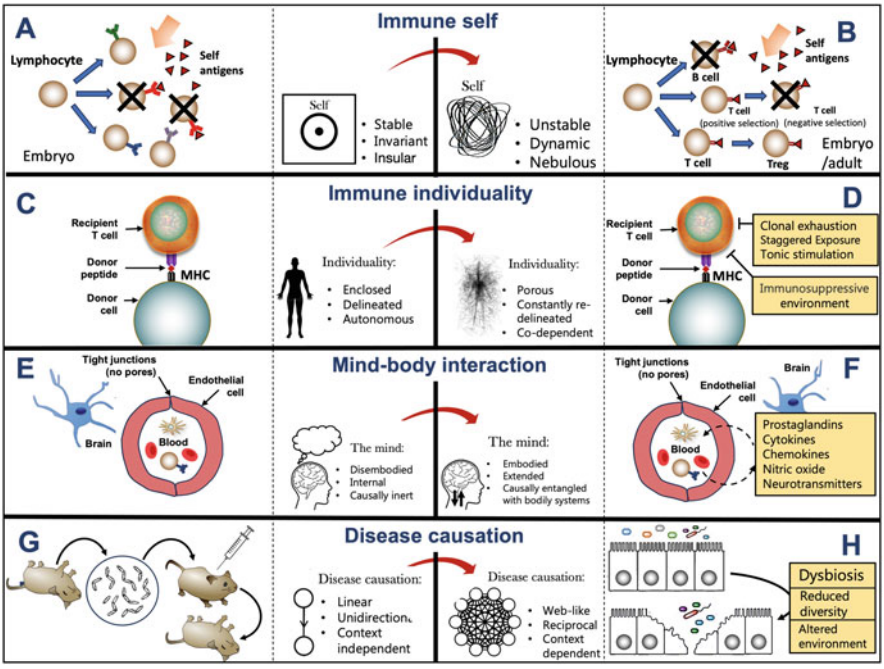

Fig. 1 *Changing views of self, individuality, mind-body interaction, and disease causation in immunology.* (**a**) The immune self was originally thought to be the result of the elimination of autoreactive lymphocytes in the embryo, a state of identity that was assumed to persist unchanged during adulthood. This corresponded to the philosophical view of the self as stable, invariant, and insular. (**b**) More recent discoveries have changed the simple view of immune identity, pointing to the role of tolerogenic processes in the adult and the importance of positive and negative selection of T lymphocytes. The discovery of Tregs further challenged the idea of a single centralized immune self. In this new framework, self appears unstable, dynamic, and nebulous. (**c**) Based on the original concept of the immune self, immune individuality was assumed to be fixed at birth, with each individual harboring a unique set of MHC molecules that underlay the basic mechanism of foreign tissue rejection. (**d**) The observation that clonal depletion, staggered exposure, tonic stimulation, and environmental fluctuations can promote compatibility of nonself grafts in some contexts changed the view of biological individuality as closed, delineated, and autonomous. Instead, the view of the animal's borders as porous, codependent, and constantly re-delineated has gained prominence. (**e**) The brain was thought to be sequestered from the immune system by an impermeable blood-brain barrier and thus segregated from immune-mediated processes. (**f**) Because of newly discovered bidirectional channels of communication between the immune and nervous systems, the mind has been recognized as embodied, extended, and causally potent. (**g**) Koch's postulates depicted disease causation as a linear, unidirectional, and context-independent process in which an invasion by an infectious agent triggers an inflammatory response. (**h**) In fact, the response to infectious agents is dependent on a broader context of ecological relationships, better represented as a multidimensional network rather than following linear causation. *MHC* major tissue compatibility complex, *Treg* regulatory T cell

Replacing the on/off model of self/nonself discrimination with a more dynamic conception of tolerance, concepts of individuality required redress (Hamburger 1978, pp. 42–43; Pradeu 2019). The simple model of organismal identity

demonstrated that cells expressing foreign MHC molecules may be tolerated in some contexts and that repeated exposure to a nonself antigen may attenuate responses to foreign molecules (Waldmann 2017; Pradeu et al. 2013). Indeed, dedicated mechanisms have been found to operate and prevent recognition of nonself or altered self-molecules as foreign and, as shown in cancer, specialized immune checkpoints (molecules that inhibit immune responses) prevent destructive reactions to transformed antigens (Baumeister et al. 2016). Furthermore, desensitization, clonal exhaustion, or reduced production of danger signals (molecules typically released during stress or damage) were shown to reverse destructive reactivity to foreign targets and induce tolerance to these molecules (Schwartz 2012; Schietinger and Greenberg 2014). Hence, immune individuality (the quality, which distinguishes one organism from another based on the immune system function) proved to be flexible and adaptable, defying the binary logic of rejection and acceptance determined by rigid self/nonself criteria.

The problem of biological individuality has been extensively considered in philosophy of biology, but no universal criteria for biological distinctiveness have been found (Clarke 2010). Philosophy of immunology has contributed to these debates by providing insight into the role of the immune system in establishing and maintaining multispecies consortia (Schneider 2021; Pradeu 2016), chimeric bodies (Martin 2010), and transgenerational identities (Veigl 2022a), as well as modifying our intuitions about what constitutes a single living being (Gilbert et al. 2012). Immune-mediated alteration of biological confines is particularly manifest in pregnancy in which certain forms of immune responses help to promote feto-maternal integration rather than inducing rejection of the fetus or causing autoimmunity (Howes 2008; Weasel 2001; Nuño de la Rosa et al. 2021). Hence, not only organismal identity but also individuality proves difficult to define, and by defying commonsensical intuitions about biological confines, philosophy of immunology contributes to similar debates in other areas of philosophy of biology (Fig. 1c, d).

Mind-Body Interaction

The idea of fixed biological confines and enduring essences has been challenged not only in the context of the debates over immune identity and individuality but also within the framework of research on the relationship between the immune and nervous systems, principally the changing view of the role of the blood-brain barrier (BBB) and neuro-immune-endocrine crosstalk in the body (Villabona-Rueda et al. 2019). Crucial for the discovery of BBB were studies by a nineteenth century pioneer of modern immunology, Paul Ehrlich, who observed that injection of a dye into the blood of an experimental animal stains its peripheral tissues but not the brain (Ehrlich 1885). This led to the identification of a layer of tightly sealed endothelial cells lining the vessels of the brain and the spinal cord that protect the nervous tissue from damaging effects of immune responses (Davson 1989). This early research supported the concept of the immune and nervous systems as

functionally and anatomically independent of each other, suggesting that not only organisms but also their bodily systems are relatively imporous.

Most notable integration of different physiological systems has occurred in psychoneuroimmunology, which has shown how the immune and nervous systems are inextricably linked through common phylogenetic and geological histories that explain their shared anatomic and biochemical relationships (Ader 2006). Beyond the significance of these findings for current immune theory, a version of the extended mind hypothesis in philosophy is supported by these findings (Ciaunica et al. 2023). According to this hypothesis, mental processes do not just happen in the head but also incorporate elements outside of the central nervous system as demonstrated by the release and response to neurotransmitters of immune cells that interact with nerve cells to establish an extended network of affective and cognitive processing (Greslehner et al. 2023). Multiple transport mechanisms have been identified in the brain blood vessel epithelium that mediate reciprocal exchanges of neuropeptides, prostaglandins, cytokines, chemokines, and other mediators redefining BBB as a dynamic interface rather than as a barrier or impenetrable wall (Banks 2015).

As an example of such coordinated neuroimmune communication, consider the stress response between the hypothalamus-pituitary-adrenal (HPA) axis and the microbiota-gut-brain (MGB) axis (Rusch et al. 2023). In the case of the HPA axis, psychological or physiological stress induces corticotropin-releasing hormone production by the hypothalamus resulting in the induction of cortisol in the adrenals accompanied by immune suppression. The more extensive MGB relies on components of the HPA as well as autonomic pathways to ensure a multimodal crosstalk between commensal microbes, the immune system, and the central nervous system (Herman et al. 2016). By enabling nonneuronal cells (leukocytes, commensals, etc.) to influence brain states, these bidirectional networks help offload the computational burden of the nervous system onto elements outside the central nervous system, effectively acting as an extended information processing system (Boem et al. 2021) (Fig. 1e, f).

Disease Causation

The intricacy of immune functions and the interconnectedness of bodily systems are further underscored by new views of the role of immunity in disease causation. Formulated in 1890 as a set of criteria to determine a link between a microbe and an infection, Robert Koch's postulates became a gold standard to determine the etiology and diagnosis of infectious diseases (Evans 1993). Based on these criteria, pathogens isolated from a sick organism, cultured, and transferred to another animal should make it equally sick or dead. However, the immune system confounds this simple model allowing for potentially pathogenic bacteria to reside in healthy organisms and nonpathogenic ones to acquire an invasive potential in a resistant host. Indeed, the role of microbes varies from one ecological context to another (Méthot and Alizon 2014; Swiatczak et al. 2011) – in some instances, inducing pathological consequences and in others, properly balanced, parasite-host interactions may

become mutually beneficial and long-lasting (Swiatczak 2014). Noting the role of the immune system in these shifting relationships, a newly developed ecologically oriented immunology ("eco-immunology") has focused attention on the contextual basis of immunity (Tauber 2008, 2017).

In the light of the immune system's role in shaping interactions with the microbiome, the causal link between a pathogenic microbe and a disease is not simple, and instead of being traceable to a defined causal agent, many pathologies appear to result from perturbed resident microbial ecosystems or compromised host factors (Lamont et al. 2018). The mere presence of a defined virulence factor in a microorganism is rarely sufficient to make it pathogenic or harmful. Indeed, the vast majority of respiratory tract infections result from a loss of stabilized balance between microbial communities that is a so-called dysbiosis rather than from a new intrusion of a microbe (Hakansson et al. 2018). Influenced by changes in the mucosal cell architecture, alterations in antimicrobial peptide production, or IgA repertoire transitions, these ecological perturbances may unleash opportunistic microbes to damage the host.

Further undermining the idea of disease mono-causation are studies of physiological inflammation. As a defense reaction of an organism to fight infection, inflammation has been traditionally considered to fall into the domain of pathology (Metchnikoff 1893). However, as already noted by Metchnikoff, innocuous forms of inflammation are part of normal tissue functioning, necessary for controlled microbial-host exchanges and debris clearance (Tauber 2003; Cohen 2007; Cohen and Efroni 2019). In so far as these studies indicate that pathological and physiological inflammation rely on similar mechanisms (dependent on active phagocytes and the so-called proinflammatory molecules such as IL-1, IL-6, and TNF-α), they challenge a simplistic divide between health and disease, inflammation and immune quiescence, suggesting that the immune system must navigate between various inflammatory modalities rather than relying on simple on-off activation states (Cohen 2000). At the same time, disease tolerance is increasingly recognized as an effective defense strategy in certain scenarios, allowing for the immune system to minimize damage without affecting pathogen burden (Soares et al. 2017). In sum, the simple view of an infectious agent has been cast aside and replaced with a dynamic systems-wide approach employing probabilistic causation mechanisms to analyze the complexity of microbial infections, some virulent while some others remain benign (Tauber 2017) (Fig. 1g, h).

A Novel View of the Immune System

As the changing views of self, individuality, mind-body interactions, and disease causation revolutionize our understanding of immunity, the associated picture of the immune system is also changing from a singular self-referring network to one that functions within a highly integrated psycho-neuro-immune-endocrine-metabolic supersystem (González-Díaz et al. 2017). Relying on a shared library of neurotransmitters, cytokines, and their receptors, immune and neurological functions are united, irreducible to the activity of singular components or structures

(Daëron 2022). Metabolic and immune functions are also linked, in which nutrient-derived signals influence leukocyte differentiation and activation and conversely, immune cells help regulate adipocyte and other metabolic functions (Saravia et al. 2020). The existence of combined immuno-endocrine activities is supported by a vast repertoire of leukocyte-derived hormones and hormone receptors, allowing these immune cells to become a part of a large regulatory and homeostatic network (Procaccini et al. 2014).

While the immune system partners with the nervous, endocrine, and metabolic systems in regulating their respective functions, other body systems have been implicated in expanding immunity beyond its classical formulation of immunocytes and their inflammatory mediators (Zhang et al. 2019). Examples include epithelial cells, which rely on pattern recognition receptors to activate the NF-κB signaling pathway and release an assortment of cytokines and chemokines in response to microbial and danger-associated signals while complementing leukocytes' functions in IgA transportation, cell migration, and signaling (Larsen et al. 2020). Similar to epithelial cells, nerve cells, stromal cells, and functional cells of various organs (e.g., hepatocytes, cardiomyocytes, and thyroid follicular cells) participate in immune processes based on a common mechanism of pattern recognition and cytokine production (Krausgruber et al. 2020). Most remarkably, the extended system of immunity incorporates symbiotic microbes, fungi, and bacteriophages, which like conventional immune cells release antimicrobial substances and immunomodulatory signals that assist to manage immune responses (Schneider 2021). The functional overlap between body systems challenges the idea of the immune system as fixed and encapsulated, to suggest that immunity stems from the coordinated activity of the entire organism rather than the exclusive prerogative of a dedicated immune network (Zach and Greslehner 2022).

When immunity is appraised across the vast variety of animal species, account must be made of its ubiquity in all life forms and the multiple mechanisms that have evolved to maintain host integrity. Indeed, evolutionary studies indicate that all organisms rely on some form of immune responses, and despite being initially considered unique to vertebrates, features such as immune memory, antigen specificity, and adaptive evolvability also exist in various forms in invertebrates (Rimer et al. 2014). Examples include small RNA responses and the CRISPR-Cas9 system, the latter of which relies on a repertoire of short variable DNA sequences acquired from viruses or mobile genetic elements that promote inheritable adaptation to viral challenges (Veigl 2019, 2022b). In-depth studies of the innate immune system suggest this evolutionarily primitive branch of the immune system also manifests adaptive features such as immune priming, memory, and specificity (Arts and Netea 2016). Hence, tracking phylogeny modes of host defense further contributes to the ontological ambiguity of the immune system by opening the definitional features of immunity and thus questioning what belongs or does not belong to the immune system.

Shifting and diffuse as well as lacking clear conceptual boundaries, the immune self has been decentered and thus resonates with postmodern depictions of the human subject (Haraway 1991). And similar to the linguistic analysis employed

by postmodern social and literary critics, immune information processing has been likened to a text that can be read, interpreted, and analyzed (Leem et al. 2022; Ostrovsky-Berman et al. 2021). Suggested by Niels Jerne in his 1984 Nobel lecture (Jerne 1985) and further developed by semiotic models (Sercarz et al. 1988), a textual view of immune sequences in the context of computational linguistics and aided by machine learning tools now suggests that the principles of receptor assembly and ligand binding follow syntactic rules of language (Vu et al. 2023). These findings are expected to help generate novel sequences that when translated into proteins will offer novel therapeutics (Huang and Li 2023). This linguistic orientation changes the focus of immunology from mechanical models to strategies directed at defining the role of information, means of communication, and the basis of immune meaning (Chevrier 2019). In short, conceptual developments in computational immunology align with contemporary advances in data technology and the centrality of discerning informational patterning and processing (Haraway 1991; Hayles 1999).

Immunology's Social Dimensions

Current views of immune selfhood, individuality, mind-body interaction, and disease causation reveal parallels between philosophical and immunological discourses in which researchers reach into cultural sources for metaphors and tropes that serve to help model their scientific findings (Tauber 1995, 2016). This transfer is reciprocal, and once incorporated in immunology, the cultural meanings reverberate throughout society, shaping perception of issues pertaining to identifying *self* and *other* (Napier 2003). In fact, the idiom of invasion, discrimination, resistance, immunity, and tolerance so prominent in the immunological lexicon are also found at the heart of social and political thinking. Indeed, the co-option of this vocabulary by the scientific discourse reciprocally helps to validate the social categories and responses because of the power of naturalizing social relationships (Brown 2019). Drawing on these cultural tropes, immunology effectively reconfigures itself as a political science to become a key participant in current disputes concerning how to legitimate the interactions of individuals and communities in various socio-physiological contexts (Neocleous 2023).

The import of cultural meanings to immunological arbitration is evident in the very concept of "exception" that immunity borrowed from a political discourse about social duties and obligations (Cohen 2009). In fact, the word immunity derives from the Latin word *immunitas*, which means exemption from social duties, a relief from paying taxes or performing military services granted to selected classes of citizens in ancient Rome. Thus, a resistance to a disease was for Romans an analogue of immunity in the social, legal sense. Mirroring sociopolitical concern with participation of an individual in a society, the scaffold of immunity provokes questions about sovereignty of the self in relation to the other (Esposito 2011). The concept of immunity, in this context, is invoked to capture the ways in which individuals define themselves by establishing boundaries and protecting against perceived threats in a

society. This concept lies at the heart of sociopolitical studies by Esposito, E. Cohen, Neocleous, and other authors to frame the tension between the individual and the community, and the immune system becomes an analogy for understanding such societal dynamics (Esposito 2011; Cohen 2009; Neocleous 2023).

Politically conservative, Burnet and Peter Medawar readily considered the immune system in terms of self/nonself discrimination, capturing the imagination of a research community in the mid-century individualist era (Lafferty 1995). While the aforementioned intellectual changes may seem to indicate a departure from the dominance of liberal Western thinking, the stress on boundary-crossing, plasticity, flexibility, and adaptability equally describes the new modes of production under late capitalism (Bartlett and Byers 2003) and, as shown by Martin, the portrayal of the immune system in these post-Fordist terms aggravates the stigma of immunodeficiency-suffering patients, who come across as weak and inept (E. Martin 1994). The unique blend of facts, values, and social images is apparent also in the notion of strong immunity as remaining in the grips of patriarchal ideology. From a feminist standpoint, a science based on stark self-versus-other distinctions is culturally biased, associated with masculinity, autonomy, and dominance. The critique suggests that this construct may perpetuate a need for control over the "other" to maintain a defined sense of self (Weasel 2001). The emphasis on *strong* immunity further reinforces the patriarchal ethos through the use of militaristic metaphors, binary oppositions, narratives of dominance, and the preservation of individualistic ideals. Analyzing these aspects from a feminist perspective helps uncover the potential connections between scientific discourse on immunity and broader cultural narratives. In the grips of thinking about immunity in terms of power and strength, Western society has taken the efforts to boost immunity as a political imperative, despite evidence showing that balanced and tailored responses are more desirable in most clinical contexts (Zach and Greslehner 2023).

Operating as conduits of cultural transfer, metaphors do not just establish a platform of shared conceptual coherence with society but help to transform the reality they represent (Reynolds 2022). As a metaphorical offshoot of the imperialistic rhetoric of late nineteenth century Germany (Gradmann 2000), the images of war and struggle keep informing medical conduct and in the scenario in which destruction is recognized as the only viable treatment option against infection, they help to transform microbial communities to match their perception as scourges of humanity. Indeed, as attested by the expanding population of antibiotic-resistant species, the growing use of germicides distorts ecological relationships between microbes that thereby augments their negative impact *on* human hosts by changing mutualistic interactions into war-like ones (Bottery et al. 2021). Acting as self-fulfilling prophecies, these and other images do not only frame the interpretation schemes in the field but also shape medical and social conduct.

The transmission of metaphors between immunology and the larger culture is bidirectional and while culture remains a rich receptacle for these figures of speech, immunology itself is becoming a source for our understanding of self-other relationships (Napier 2003). This is exemplified by the analysis of the risk of excessive self-protection and defensive security in society in terms of aggressive autoimmunity and

death (Derrida 2003). Assuming that self-preservation frenzy may incite excessive defense responses, Derrida posited autoimmunity as equally destructive as constructive, creating opportunities for reconsideration of the relationship with nonself. At this juncture of science and culture, immunological images help to depict the current condition of human society, and with the recent crisis of identity politics in the globalist era, the notion of immunity helps to portray human society as porous or micro-compartmentalized in a bubble-like pattern (Sloterdijk 2011). The immunological perspective has also been adopted to understand the roots of the societal contract and mutual obligation by illustrating the complex interplay between community and immunity on both social and biological planes (Esposito 2011).

All in all, philosophy and immunology rest on a shared cultural matrix, and in so far as they rely on similar imagery and social experience, they resonate with shared themes and value systems (Tauber 2016). While rarely acknowledged by experimental scientists, this intellectual cohabitation continues to make the science highly influential in how the public considers personal identity and other themes. As highlighted above, cultural narratives in both fields shape perspectives on self and others. When integrated with philosophical ideas, this shared cultural framework may impact public discourse on personal identity, influencing beliefs about the self, its boundaries, and interactions with the external world. Immunology has thus burst open the doors of the laboratory to reveal its broad cultural influence beyond the obvious ways nature is understood or manipulated by derivative technologies.

Conclusions and Future Perspectives

Immunology, like all sciences, builds on its empirical observations framed by underlying methodological commitments and metaphysical assumptions. Philosophy of immunology has focused on the conceptual suppositions of immunity as protecting a core identity and the implications of changing notions of individuality. Growing appreciation of immune tolerance required for beneficial commensal relationships and assimilative nutrition has radically modified the original immunological construct of host defense based on a core self. With loosened criteria of identity required to account for dynamically shifting ecological relationships, notions of individuality have shifted from rigid self/nonself demarcations to more fluid conceptions of identity. Philosophically, the implications of this new conception of immunity have had a profound effect on the very definition of organismic identity, which has been destabilized as boundaries between self and nonself become ill-defined. In this conceptual shift, the immune system becomes redefined as an icon of fluidity, flexibility, and hybridity, a conception that richly resonates with postmodern views of the subject, whose contingent boundary-transgressive cultural images now seem corroborated by the science of biological identity. Thus, the governing ideas about organismic autonomy have been radically transformed, and considering the paradigmatic status of individuality in Western core values, these alterations of the biology of identity undoubtedly will have wide cultural ramifications.

A second theorical modulation is based on the recognition that immunocytes play pleiotropic roles that contribute to metabolic, neurocognitive, and endocrine physiologies. Accordingly, internal communication has been added as a central feature of the immune system. That integrative function places immunity at the nexus of homeostasis and thus expands its characterization as an effector system employed for host defense to a much broader function as a regulator of the organism's internal milieu. So, from the clinical perspective, the disciplinary standing of immunology is also changing as more comprehensive ways of understanding pathophysiology and developing strategies for health maintenance increasingly appears to demand a joint effort of experts from neurobiology, endocrinology, computational linguistics, artificial intelligence, and systems science.

In tandem with these expanded understandings of the immune system's diverse communicative roles, the cognitive metaphor in immunity gains traction. Whether mediating "foreign" relations both with internal symbionts and the external environment or coordinating internal physiological systems, the immune system is becoming aptly portrayed as an information processing faculty analogous to well-known systems in our daily life. As immunology is better integrated with other disciplines through cross-disciplinary bridges, basic conceptions of organic economies will be deepened. The philosophical implications for biology seem apparent.

Definition of the Key Terms

Antigen (antigenic) – a substance that can bind to a specific antibody or T cell receptor.

Chemokine (chemoattractant cytokine) – a molecule that directs migration of immune cells (leukocytes).

Cytokine – a molecule that influences the activity of leukocytes.

Dysbiosis – a loss of balance between microbial populations colonizing a multicellular host. It is often associated with inflammatory diseases and other disorders.

Immune identity of an organism – a feature that allows the immune system to recognize an organism as the same entity over time.

Immune individuality of an organism – a feature that allows the immune system to recognize an organism as a separate entity, distinct from anything else.

Immune receptor – a molecule that can cause a change in the activity of the immune system upon binding of another molecule (a ligand). This includes pattern recognition receptors, antibodies, T cell receptors, etc.

Immune recognition – a process that upon activation of an immune receptor initiates a cellular reaction.

Immune self – a universe of mostly endogenous molecules that are tolerated by the immune system.

Immune tolerance – the state of unresponsiveness to a particular antigen.

Lymphocyte – a class of immune cells including B cells and T cells, which are able to bind antigens with high specificity.

Major histocompatibility complex (MHC) – a set of highly diverse (polymorphic) genes, which are unique to each individual.

Summary Points

1. Focusing on epistemic and ontological foundations of our understanding of immunity, philosophy of immunology offers an opportunity to reconsider some of the fundamental questions related to the role of theory, metaphor, and social factors in science.
2. Establishing a bridge between medical knowledge and the humanities, philosophy of immunology helps reconsider deeply held intuitions about organismal identity, individuality, cognition, and disease causation.
3. Philosophical studies of immunology suggest that our understanding of disease protection relies on a shared cultural reservoir of metaphors and images to reexpress some of the complex tensions between community and immunity that arise in social and political settings.

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