

# Perplexity as a provocation: revisiting the role of metaphor as a 'place holder' for the potential of COVID-19 antibodies

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Accepted 10 May 2022

## ABSTRACT

This article revisits long-standing critiques of the role of metaphor in immunological discourse. Drawing on Alfred North Whitehead's speculative philosophy of organism, I focus on the use of metaphor to explain the process by which COVID-19 vaccine research is able to generate protective antibodies, the challenge of autoimmune disease and dengue fever antibodies. I suggest that metaphors are provoked by the perplexity that arises from presupposing that distinct morphological substances are the first order of reality. I conclude that rather than seeing metaphors as typically skewing conceptions of the body, as has been previously argued, those of memory, recognition and misrecognition may be instructive of a body in transition. Indeed, a process of transition that shows degrees of creativity. When gesturing towards the processual nature of infection and immunity, metaphors invite new modes of shared thinking across the disciplinary divide.

In 1995, *Scientific American* published an article titled 'From Complexity to Perplexity'. It cited many prominent figures in complexity studies attending a conference at the Santa Fe Institute to decide if a unified theory of existence was possible. According to the author of the article, John Horgan, if there were a definitive outcome from the talkfest, even if the most advanced computers were to capture Nature's complexities, the knowledge generated would still elude human understanding. Horgan concluded his article with a comment by one of the participants, Francisco Antonio Doria that summed this up: 'We go from complexity to perplexity', to which Horgan says, 'everyone nodded' (Horgan 1995, 109). However, the nod is somewhat perplexing because the content of the article suggests that some participants did believe a unified theory is possible. Thus, it would seem that perplexity is the final answer, whereas, for others, it merely marks a stumbling block in the search for an explanation. Either way, it may be apt to say that the character of perplexity is situated in relation to how the problem for explanation is formulated.

In this article, I suggest this variable positioning of perplexity can be said to characterise the responses of the empirical sciences to COVID-19. The complex and highly variable 'symptoms' and 'disease effects' of infection have been and continue to perplex the biosciences. Whereas achieving COVID-19 immunity has been, to a degree, successful. However, it has sharpened the empirical

focus on familiar terrain. At the forefront of a vast field of inquiry is the question of how to harness the promise of COVID-19 antibodies through the time-old method of vaccination (Jenner 1909; Waldmann 2003). The evidence-making means of establishing 'proof' of vaccination is integral to the rise of the biosciences, the concept of immunity, and, no less, the primacy of natural science logic. This logic postulates distinct morphological substances as the ultimate reference for explanation (Stengers 2011, 144).

For the speculative philosopher of organism, Alfred North Whitehead, morphological substances are abstractions of 'simple location' apart in their existence 'from any essential reference of the relations of that matter to other regions of space and to other regions of time' (1967, 58). As such, they cannot, in themselves, explain the dynamic process of transition witnessed of bodily infection and immunity. This reliance on abstractions does not refute the realness of degrees of immunity achieved by vaccination. Nevertheless, what makes degrees of immunity real for an empirically grounded positivist science, is a method that relies not on an explanation of transition but observable correlations attributed to substances (Huang *et al.* 2020; Lau *et al.* 2021). For example, proof of the cause of COVID-19 infection is established by showing it statistically correlates with the virus SARS-CoV-2 (identified by shape). Proof of the immune potential of vaccines is established by showing they statistically correlate with the generation of specific antibodies (identified by shape) and a reduction of the number of infections or severity of infection across a population group (Corum and Zimmer 2021). It is in the absence of an explanation that metaphors become instructive.

The role of metaphor in immunological discourse has attracted and continues to attract attention in social sciences, medical humanities and philosophy (see Cohen 2010; Esposito 2011; Haraway 1991; Jamieson 2017; Martin 1990; Mitchell 2017). Of those who have devoted much of their life work to the topic, it is difficult to go past Alfred Tauber's rich contribution to understanding the historical development of immunology. Notably, the problematic metaphor of self/non-self in immunology that, in his words, 'omits the deeper perplexities of the science that remain largely unstated and thus ignored' (Tauber 2018, 3). These perplexities arise from what he rightly sees as presupposing a stable organism, counter to allowing for a lifelong dynamic



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**To cite:** Rosengarten M. *Med Humanit* Epub ahead of print: [please include Day Month Year]. doi:10.1136/medhum-2021-012343

process whereby the organism evolves ‘in the face of internal and external challenges’ (Tauber 2018, 3). Even so, Tauber recognises that metaphor suffices in the absence of a better-articulated conception of immunity (Tauber 1997, 10).

In a manner, this paper could be said to take as its point of departure Tauber’s reference to George Lakoff and Mark Johnson’s work on metaphor, on the basis of which he says: ‘Metaphor unites reason and imagination ... offering a tool to comprehend partially what cannot be conceived by other means’ (Tauber 1997, 138). Indeed, I have wondered when writing this article, in line with Lakoff and Johnson, whether the distinction made of metaphor as merely a ‘rhetorical flourish’ is adequate to the challenge of conceiving infection and immunity. Alternatively, all conceptual thinking ‘is fundamentally metaphorical in nature’ (Lakoff and Johnson 2003:3). Even if the latter is correct, it remains relevant to consider the character of those employed. For reasons that pertain to the relationship between the medical humanities and the life sciences discussed below, I attend to those currently used in COVID-19 vaccine research to explain the achievement of protective antibodies. Although they do not depart from a concept of self/non-self, they infer a cognitive body that, arguably, tallies with what I offer of Whitehead’s processual ontology.<sup>1</sup> In a review of critical contributions on immunological discourse, Andrew Goffey takes the view that metaphors typically work to skew explanations towards historically partial and culturally particular understandings of sickness’ (Goffey 2015, 8). However, his primary intention is to redress what Stengers (2000, 65) raises of the judgement that has been made of science for its use of metaphor and other cultural concepts—‘as if no different to any other social practice’. This judgement leads Goffey to take up Stengers’ proposal that a ‘shared perplexity’ arises from the inevitable partiality of knowledge across the disciplines. Stengers suggests that this ‘shared perplexity’ places us all in the same boat. In effect, it equalises the tussle between the natural sciences and those in the medical humanities and social sciences who have sought to challenge the biosciences’ privileged claim on the body. Significantly, she comes to this view when discussing the notion of an event. Although we can never know an event in its entirety, we can know that it singularly signifies for those who ‘are situated in the space it has opened’ (Stengers 2000, 65). This situatedness requires specifying the relative positions of scientists and their interpreters. However, it also requires avoiding ‘any way of describing them which implies that scientists have a privileged knowledge of what this difference that singularises them *signifies*’ (Stengers 2000, 7). For Goffey, this repositioning of disciplinary differences requires attention to the partiality of our modes of knowledge-making. In his conclusion, he states: ‘the kinds of conceptual “shortcuts” one takes in generating one’s close analysis of the discourses of immunity as a practice like any other, obviate the need to tackle what it is that one might not know oneself’ (Goffey 2015, 13).

While departing from his claim that metaphors typically skew understanding, his claim of obviation has led me to consider whether scholars—on either side of the disciplinary divide—may be too quick to dismiss what they see as the signifying role of metaphor. Bearing in mind his Stengerian approach to the fractious relationship that has developed between the biosciences and the medical humanities and that the character of perplexity depends on what is respectively signified for the various actors engaged in an event, I revisit the critique of metaphor. While, in part, my argument builds on early critiques of the self/non-self distinction, it also diverges in its attempt to

recuperate metaphor as necessary in response to a scientific logic that proceeds on what Whitehead says of the mode of abstraction.

To focus on the problematic of abstraction is not unusual. Warwick Anderson argues that COVID-19 epidemiological modelling relies on abstractions of the ‘r’ rate of infection to decide policy but leaves aside a vastly more complex assemblage of factors (Anderson 2017). Nonetheless, in the absence of an explication of what he intends by the term abstraction, we might be mistaken in believing that abstractions can be avoided. Indeed, given what I have said above on the problematic of morphological substance, we might mistakenly assume that, as an abstraction, it should be jettisoned. But Whitehead was a realist and firmly engaged with the possibilities that abstractions afford. Contrary to opposing the mode of abstraction, he proposed it as a necessary feature of existence. For instance, plants abstract water from the soil for nutrients. So, too, does thought abstract from a situation, thus ‘exhibiting itself as an element in nature’ (Whitehead 1927). Indeed, Rosengarten and Savransky (2018) point out, creatively so. Hence, the problem is not with abstraction per se, but when, as Whitehead says, our abstractions are mistaken for concreteness. As if, to reiterate, morphological substances exist *prior* to their connection with other matter in space and time.

Although Ed Cohen does not engage with Whitehead’s philosophy of organism and the work of abstraction, his challenge to biomedical conceptions of autoimmunity is not only illustrative of the problematic of ‘self/non-self’ distinction taken up by Tauber. It chimes with Whitehead’s notion of process. Describing his own experience as a young boy diagnosed with autoimmune disease, Cohen says:

First one doctor told me: “Your immune system is attacking the lining of your small intestine. It’s as if your body is rejecting part of itself.” My face must have shown that I didn’t get the concept, so another added: “Well, autoimmunity is like being allergic to yourself”. Despite this clarification I was still adrift, so they tossed one more. “It’s as if you’re eating yourself alive,” they said... No doubt, the doctors who gave me these memorable images offered them as gifts of understanding... It is just that their metaphors were not particularly safe for a thirteen year old’s imagination. Or anyone’s imagination as far as I am concerned (Cohen 2004, 7).

Cohen suggests that his doctors were well intentioned, even if their metaphors were unpalatable or downright scary. However, what I take from his account is not that his doctors sought recourse to metaphor because their scientific explanation would have eluded him. Rather, they did so because their logic has no other way of explaining how morphological substances produce an effect. Having since come upon ‘radical thinking scientists’ who find the distinction of self/non-self insufficient to explain autoimmunity, Cohen proposes that the concept of immunity can be understood as a spatiotemporal process that challenges the notion of a bounded autonomous body (2004, 10). This proposition resonates with the view expressed by Jaeger and Monk (2015) when drawing on the process philosophy of Whitehead and others, including William James and John Dewey, that reality is processual: it is achieved by ‘interconnected occurrences or events’. Events that are the antecedents for the becoming of new events or, in Whitehead’s own words: ‘In some sense or other, ... each happening is a factor in the nature of every other happening’ (Whitehead 1934, 87). However, due to the legacy of mechanistic thought traceable to the likes of René Descartes and Isaac Newton and from which modern scientific logic has developed, ‘substance is taken to be fundamental and processes

are mere epiphenomena or derived properties of things' (Jaeger and Monk 2015, 1064).

### VACCINE ANTIBODIES AND THE ROLE OF METAPHOR

While it is not my intention in this article to weigh the efficacy of COVID-19 vaccines, a little further on we will see that this has primacy for those engaged in their development. Even so, no scientist would venture to guarantee that the method of vaccination will be 100% efficacious (Lacerda and Bargieri 2022, 1; Stengers 2018, 117). It is also possible that it will not surprise scientists that much of their language reflects cultural concepts and metaphors. Notably, when it comes to explaining the potential that precipitates the generation and 'inhibiting' action of COVID-19 antibodies, notions of cellular 'recognition' and 'memory' are employed. However, unlike those who claim that metaphors and various cultural concepts skew access to the materiality of the body, scientists might say that their use of metaphor is merely a 'placeholder' for an explanation still to be sought (Riskin 2018, 5). As if to signify what is difficult to perceive, but there is sufficient evidence to warrant intervention while grappling with perplexity about the nature of the event itself.

Further, it is also possible that specialists in immunology would not regard notions of 'memory', 'recognition' and 'misrecognition' as unusual to characterise the process of change central to thwarting or arresting an infection such as COVID-19. Indeed, they might be startled that we should fix on their language when, from their perspective, what matters is the 'material' difference achieved irrespective of the language. Nevertheless, it is here that I want to pause: might there be something that should make us curious about characterising mechanistically interacting morphological entities in the manner usually held to be the preserve of human thought?<sup>2</sup>

It is not necessary to rehearse the complex and chequered history of contemporary immunology to underscore what has emerged as a morphological conception of immunity. Even so, it may be helpful to note key recorded events and some of their celebrated figures. Paul Ehrlich is said to be responsible for the concept of immunity. In the late nineteenth century, he fed increasing quantities of toxin that rendered animals immune against an otherwise lethal dose. Based on his observations of correlations of cause/effect, he proposed that alongside a nucleus of activity, side chains in the form of receptors existing in the 'protoplasm' were able to specifically bind distinct toxins. According to Winau *et al.*: 'Released into the blood, these receptors represented antitoxins or antibodies' (Winau, Westphal, and Winau 2004). This perception of antibodies and antigens as morphological substances, whose function arises from their shape, cohered with the hypothesis of a mechanistic 'lock and key model' proposed, according to historical accounts, by Emil Fischer in 1894 (Behr 2008). However, it was not until 1959 that Gerald Edelman and Rodney Porter published on the molecular structure of antibodies, for which they were later jointly awarded the Nobel Prize in 1972.

Although scientific knowledge has become considerably more complex since the classical mechanistic conception of life that emerged in the late seventeenth century and, indeed, since Whitehead's description of modern science, the idea of antibodies whose *shape* can inhibit other substances remains. The morphological structure of antibodies is described as 'Y' shaped. The form is understood to bind and, thus, 'neutralise' antigens that sit on the surface of infectious agents such as viruses, bacteria, fungi (Burton and Wilson 2007). The 'Y', if shaped

appropriately, is also known within the biosciences to bind and, thus, inhibit cancerous cells (Little 2021).<sup>3</sup>

In contrast to what is known of autoimmune disease and several other communicable infections, such as HIV and dengue fever discussed later, the achievement of COVID-19 vaccine research may appear relatively straightforward. Even so, the scientific question of how to achieve adequate immunity is by no means resolved. Despite what is now evident of degrees of vaccine efficacy, COVID-19 keeps on *giving*. From the current perspective of bioscience, not all bodies generate sufficient immunity from antibodies to prevent the infection and its spread (Luchsinger *et al.* 2020). More critically, the morphological shape of the virus is mutating into new strains, which may not be 'inhibited' or 'neutralised' by antibodies generated by current vaccines (Bhandari, Khanna, and Kuhad 2021; Kirby 2021). At the time of writing, questions abound about the potential of antibody longevity and the match of laboratory-generated antibodies in response to new viral strains. Associatively, there is the question of whether there might be a more sparing use of existing vaccines to speed up the inoculation of large numbers of individuals. This is regarded as crucial to thwarting the spread of potentially disabling or fatal infection and intercede in viral mutation by inhibiting, if not eliminating, the viability of the virus.

These questions are addressed in an article in the journal *Nature*, titled 'Is one vaccine dose enough if you've had COVID-19? What the science says' by Dolgin (2021). I have selected it from numerous others, appearing while writing this article, not only because the piece provides a relatively succinct illustration of the use of metaphor but, more so, because the metaphors explain what is not available from the scientific studies cited. Studies focused on static morphological, molecular structures. As the following passage indicates, the aim was to evaluate the evidence from laboratory and clinical studies on whether a second jab of the specific design of mRNA vaccines currently being deployed is necessary. Referring to a scientific study by Wang *et al.* (2021), Dolgin states:

The researchers analysed participants' levels of 'neutralising' antibodies, potent immune molecules that can block the virus from entering cells. At the moment, the quantity and vigour of a person's neutralising antibodies are the best markers for assessing whether that person is protected from infection and illness — although scientists are still working to confirm that antibody levels can serve as a realistic stand-in for immune protection.

It is clear from the above that 'markers' are a surrogate or, as the article states, a 'stand-in' for a happening established by correlations between, as Whitehead would say, 'the simple location' of 'things'. It is not clear why the mention of 'neutralising' requires quote marks, although we might assume that it underscores the action required of antibodies. As the article proceeds to introduce another component of the immune system, it is explicit in its use of metaphor and what could be argued as colloquial or 'cultural' terminology:

The team also assessed participants' levels of memory B cells, which *remember* pathogens and can quickly *crank out* targeted antibodies if they encounter an infectious agent that *they've seen before*. Within a month or two of vaccination, study participants' levels of *memory B cells* had risen, on average, nearly 10-fold and their 'titres', or levels, of neutralising antibodies had shot up around 50-fold. Those gains were apparent in previously infected participants whether they'd received one shot or two... In the 12 months after participants were infected, their memory B cells had not been *static*. Instead, those cells spent the entire year evolving, which left them *able to craft anti-*

bodies even more potent and versatile than those that they produced immediately after infection. (my emphasis) .

If we were to read these passages as merely indicating that the language of metaphors and certain colloquial phrasing is a convenient way to explain the desired process of inoculation by vaccination, we might ask: in what manner is the language problematic? Is it necessarily distorting the actuality of the event of the body or, on the contrary, gesturing to what Whitehead 1938 states is ‘the fact’ of transition that is core to the possibility of nature? Here I want to detour to one Elgin’s sources. All refer to molecular structures, including those of proteins involved in antibody ‘neutralising’. One source, in particular, describes cellular ‘memory’ as a chemical ‘reaction’ that ‘boots’ change (Ebinger *et al.* 2021, cited in Dolgin 2021). The description is based on visualisations of the molecular structure of B cells. However, it is difficult to explain how a structure creates change. Even when we refer to ‘institutional memory’, we do not imagine it is a feature of the structure itself. Rather, we think of it residing in the experience of individuals involved in its historical process. Dolgin’s metaphors and colloquial expressions provide an explanation that is absent from his sources. However, this returns me to the curious use of a language more usually associated with the notion of thinking subject.

Dolgin’s choice of metaphor infers that the living and endangered body is involved in a process. It is not the kind of process we would imagine of morphological substances functioning as part of an animate mechanistic process. It is a process that involves remembering, recognising novelty and a mode of crafting with ingenuity. It leads me to consider whether his metaphors, within a prestigious science journal, speak to an unacknowledged awareness by scientists of something more than their methods can explain.

### PERPLEXING ANTIBODIES AND THE ROLE OF METAPHOR

Here I turn to Alex Nading’s piece in an earlier issue of this journal on dengue fever and include an explicit discussion of antibodies. The aim was to provide a practical illustration of Goffey’s claim that natural scientists and medical humanities scholars experience ‘shared perplexity’. In contrast with what I have included on COVID-19 antibodies, dengue fever antibodies stand in the way of a widespread mode of vaccination. This view is illustrated in the following account replete with metaphors:

In a phenomenon known to immunology as “original antigenic sin”, bodies exposed to a single serotype (eg, to Dengue 1) develop antibodies and immunological “memory” of the antigens dominant in that particular serotype. Problems arise when the same body confronts another serotype (say, Dengue 2). Dengue two may contain some of the same antigens as Dengue 1, but the antigens that were dominant in Dengue one are recessive in Dengue 2. An immune system already familiar with Dengue one can thus select antibodies that bind to receptors on the Dengue two viral monocytes, helping the virus replicate more quickly than it otherwise would (Nading 2015, 14).

Nading continues, ‘[b]odies pay a hefty price for this. Secondary dengue infections can result in what is clinically called “severe dengue”, marked by internal plasma leakage and dangerously high fever. In short, as frontline health workers often say, “Dengue makes you sick the first time, but it can kill you the second”’ (2015:14) . Not surprisingly, Nading finds it necessary to address the metaphorical claim that renders the immune system capable of ‘sinning’. As he points out, it raises ‘both technical/scientific and ethical/

political perplexities’ (2015:14). In order to address this, he introduces a difference in thought on this issue within the biosciences. Allowing for diversity within science and, by doing so, breaking from what Goffey rightly says of the risk of generalisation, Nading states: ‘For starters, agreement among scientists about original antigenic sin theory has never been uniform. Some suggest that the immune system’s “misrecognition” of antigens may sometimes be protective. Not everyone who is exposed to multiple serotypes develops severe dengue’ (2015:14). From this angle, similar in this respect to what Cohen has offered on contrasting conceptions of the body in studies of autoimmunity, Nading underscores how scientists, themselves, engage in differing modes of thought within the scientific paradigm. However, the metaphors themselves are most relevant to my proposition that they are instructive of unacknowledged awareness by scientists of something more than their methods can explain.

Dengue fever’s tragic consequences are said to arise from what is explained as the body ‘*misrecognising*’ the relevant antigen. While this leads Nading (2015, 14) to conclude: ‘They (scientists) are perplexed, and we (medical humanities scholars) are perplexed’, he is not attributing this perplexity to the metaphors but to a body engaged in an endangering process. It is not that the metaphors skew conceptions of the body; rather, they suggest, again, that scientists cannot rest with the idea of an essentially bounded and, thus, stable immune system. While the metaphors signify perplexity, they are also employed as a tool for unravelling it. Another way of saying this is that metaphors expose efforts to reconceptualise infection and immunity. While it is unlikely that anyone, on either side of the disciplinary divide, would refute the centrality of the body to research on infectious disease or that its capacity to generate antibodies relies on other elements, its participation is paradoxically nulled when regarded as implicitly ‘dull’ morphological substance. Indeed, we can ask: are what I am referring to as ‘metaphors’ merely a ‘place holder’ for something that cannot be explained by ‘dull’ substance as the ultimate reference? Or, alternatively, might we reconsider the view that they necessarily skew conceptions of the body and look to them as more telling than a first order of substance permits?

### CONCLUSION: A GESTURE TO AN ‘AFTER’ PERPLEXITY

My decision to revisit critiques of the use of metaphor in immunological discourse has been fuelled by what I have found to result in a type of cul-de-sac in thought (to use my own metaphor), when we too quickly dismiss or gloss what others call on to gain purchase on the world. When it comes to illness and disease, this dismissal risks eliding the difference that science makes. More pointedly, it elides the creative function of difference achieved by events (Whitehead 1920). Based on what I have been able to include in this article, I am inclined to suggest that the scientific use of metaphors of ‘memory’, ‘recognition’ and ‘misrecognition’ hints at an implicit awareness that there is something sidelined by the familiar logic of scientific materialism.

When surpassing an imagined first-order reality of morphological substances, metaphors offer an answer to the warranted but perplexing question of how ‘to characterise the something which thus emerges?’ (Whitehead 1967, 93). A question that arises when explanation can no longer be deferred or ‘blackboxed’ by probabilistic correlations to decide an exclusive relation of cause and effect. Indeed, when

gesturing to the processual nature of infection and immunity, we might consider metaphors as ‘thought events’ that invite a new terrain of possibility. A terrain where those who call on metaphors to decipher the body *and* those who have argued they are problematic, might develop an appreciation for what it ‘is’ that they lay claim to when contending with the realised potential of infection and immunity. While we can agree with Cohen that his doctors resorted to crude metaphor (his body ‘eating itself alive’), we can also say that they were provoked by the perplexing logic of a mode of scientific materialism that cannot explain aberrant change (‘intent’). The same can be said of the metaphors used to describe the action of COVID-19 antibodies and those of dengue fever, arguably attuned to what Whitehead proposes as a process of creative transition.

This returns me to the question of might there be something that should make us curious about characterising mechanistically interacting morphological entities in the manner usually held to be the preserve of human thought? Insofar as some metaphors infer that bodily events are creative in a manner more usually held as the preserve of the human mind, they invite us to go beyond the limits of scientific materialism. Indeed, based on the character of the metaphors more usually assigned to a thinking self or subject, we might entertain the speculative pluralist panpsychist proposition, developed by Martin Savransky from Whitehead’s philosophy and also that of William James, that the body ‘thinks’ (Savransky 2019): it shares a mode of consciousness that has been conceptually partitioned with the differentiating of disciplines. Further, it engages in its own creative diagnosis of infection (Rosengarten 2021). To be sure, as is eminently clear from the tragic loss of life from COVID-19, dengue fever, and a host of other diseases, including autoimmune disease, a thinking body involved in making decisions does not always lead to what is necessary to endurance. Nevertheless, it does suggest that concern about the notion of a self/non-self distinction might also be revisited.

Rather than settle for a ‘shared perplexity’, as proposed by Goffey and taken up by Nading, I conclude with the speculative proposition that our shared metaphors might be a starting point for unravelling what situates perplexity. Although some metaphors may skew what ‘is’, others, nonetheless developed on their basis—such as ‘self/non-self’—may serve as a speculative gesture to the realisation of an immanent potentiality, as Whitehead proposed, in the situated connectedness of all things.

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**Contributors** MR is the sole author of this paper.

**Funding** Funded by Australian Research Council Award Number: DP210101604.

**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Ethics approval** Not applicable.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data sharing is not applicable as no data sets were generated and/or analysed for this study.

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## NOTES

1. On this score, my approach differs from a deconstructive approach to the concept of immunity (see Jamieson 2017; Kirby 2017; Mitchell 2017).
2. Mechanistic conceptions of infection and immunity are commonplace in scientific publications, for example: Charles *et al.* (2001); Velikova *et al.* (2020); Waldmann (2003).
3. Antibodies are also known as immunoglobulins, composed of glycoprotein molecules produced within the body by B cells (leucocytes). The viral envelope of the SARS-CoV-2 virus held responsible for COVID-19 infection, projects spike proteins (S proteins) composed of two subunits (S1 and S2), which facilitate viral entry into the host cell by attachment to host cell receptors (Bhandari, Khanna, and Kuhad 2021; Monpara, Sodha, and Gupta 2020).

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