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Reply to comment

Variational neuroethology: Answering further questions Reply to comments on "Answering Schrödinger's question: A free-energy formulation" ☆

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First and foremost, we sincerely thank our commentators for their incisive and thought-provoking responses [1–14] to our metatheory of living systems; namely, variational neuroethology (VNE) [15]. We appreciated the critical insights, questions, suggestions, and proposals for future research. We were also pleased to see signs of a fruitful dialectic between different perspectives – unexpectedly, some of our commentators addressed others' questions and concerns; suggesting that VNE might enable productive scientific discourse and inspire new, multidisciplinary research questions. There were also friendly critics, who helpfully questioned the coherence and validity of VNE, and motivated us to revisit key issues.

Given the space constraints of this Response, we cannot attend to each commentary with the level of attention it deserves. Instead, we have addressed the commentaries collectively, by organising our Response into themes. Our critiques tended to fall within two broad domains: those that questioned the formal ontology of VNE, and those that questioned VNE as a research heuristic. This was unsurprising, since as a metatheory, VNE comprises: (1) a new way of modelling the structure and dynamics of living systems (i.e., a formal ontology of life based on nested Markov

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blankets), and (2) a new approach to studying them (i.e., a multidisciplinary heuristic for theorising and research). To begin, we revisit our key terms and concepts. We then address the criticisms aimed at these two aspects of VNE. Finally, we address issues pertaining to the constructs that we borrow from information theory, which question VNE, and indeed, the free-energy principle (FEP) itself.

1. What's in a name?

Bruineberg and Hesp [4] make the lucid point that, given our choice of words, VNE should only apply to the behaviour of animals with a central nervous system (CNS). Clearly, however, the scope of our metatheory ought to extend beyond this limited domain – indeed, to any living system in general.

We consider the term "variational neuroethology" to be not altogether inappropriate. VNE is a synthesis of a variational formulation of the function, structure, and dynamics of the nervous system (i.e., the FEP) and Tinbergen's [16] seminal approach to animal behaviour. Our framework is within the purview of ethology, since VNE, with its emphasis on *active inference*, explains the *behaviour* of living systems. Indeed, under the FEP, *neural structures* function essentially as *behavioural control structures*. Hence, a metatheory derived from the FEP must comprise (neuro)ethology. This pragmatist emphasis on *adaptive action* that mediates and enables self-organisation aligns VNE with *enactive* and *autopoietic* models of cognition – an issue discussed by Bitbol and Gallagher [3], which deserves further consideration. We also drew on the suggestion by Sengupta and colleagues [17] to recast theoretical neuroethology under the FEP. We understand *neuroethology* as the study of the dynamics and coevolution of (generally neural) control systems and (typically animal) behaviour. Because VNE concerns precisely such phenomena, the term we chose seems justified. Furthermore, applying our metatheory to species with a brain does not mean that it cannot be extended to those without one. Indeed, although it originated as a global theory of the brain, the FEP has already been successfully extended beyond animals with a CNS; e.g., to plant life [18], single celled organisms [19], and morphogenesis [20]. We were encouraged to see that Pezzulo and Levin [11] clearly acknowledged the fundamental similarities between neural and somatic processes, and appreciated how the FEP can be leveraged to study biological phenomena beyond the brain, such as anatomical traits and homeostasis. Similarly, Campbell [5] emphasises the applicability of Tinbergen's four questions to phenomena beyond animal behaviour, from microscale dynamics (i.e., genes) to macroscale ones (i.e., culture). Van de Cruys [13] also provides a compelling application of VNE to explain preferences about sensory inputs, leveraging the FEP to account for this phenomenon at each of Tinbergen's four levels of analysis. We are most grateful for these commentaries, which illustrate the promise of synthesising the FEP and Tinbergen's nested levels under VNE.

Still, the point that we need to choose our words carefully is well taken: we are working on two complementary metatheories that extend VNE to phenomena beyond animal behaviour. These are the *variational approach to niche construction* (VANC) and *variational ecology* (VE). The VANC concerns those lasting, self-generated, adaptive changes to the ecological niche that are imposed by the dynamics of living organisms, whereby physical states of the niche come to participate in self-evidencing dynamics [21]. Similarly, VE addresses higher-order Markov blankets by proposing a model for recursively nested organism-niche dynamics, providing a more general framework for the study of biological systems that share a niche [22]. VE leverages the skilled intentionality framework (SIF) developed by Bruineberg & Rietveld [23], especially its reinterpreted notion of *affordances*. These are possibilities for engagement through action and perception that are offered to an organism. Under the SIF, affordances are cast as free-energy gradients that can be resolved through active inference. VE draws the surface of higher-order Markov blankets as the field of affordances (i.e., free-energy gradients) that emerge from dynamics at these higher scales: their closure is the closure of actions afforded at those scales. Since living systems instantiate a single generative model, there is – for any living system (or system of systems) – one global free-energy gradient, constituted by partial gradients at each scale. Through active inference, the entire ensemble acts to resolve free-energy across scales, underwriting integrated dynamics for multiscale, ecological niche-organism systems. This multiscale integration speaks to the insightful philosophical remark by Tozzi and Peters [12] that VNE affords a conception of *living* as a *belonging-together*, as an integrated dynamical system with integrated dynamics. Collectively, these variational models can be said to constitute a fully generalisable, scientific metatheory of hierarchically nested living systems – what one might call a *variational biology*, or a physics of sentient systems.

2. VNE as a multiscale, formal ontology of life

A few of the commentaries criticised VNE's formal ontology of nested Markov blankets. The appropriateness of our ontology was questioned by Bruineberg and Hesp [4], Kirchhoff [7], Kirmayer [8], and Bitbol and Gallagher [3]. Bruineberg and Hesp [4] argue that although the Markov blankets for clearly bounded systems (e.g., single cells and organisms) are intuitive, those for larger-scale, higher-order systems are not so clearly drawn. Similarly, Kirmayer [8] suggests that the Markov boundaries of human cultural systems are more like flags and tents than they are like blankets, in that their limits are transient, fluctuating, and sometimes intentionally laid out, to symbolically mark aspects of the environment as especially relevant, and to channel adaptive behaviour. Kirchhoff [7] raises the issue that on its own, the Markov blanket formalism is insufficient to demarcate *adaptive* living systems from non-living ones; e.g., coupled pendulums have a Markov blanket, but we would not classify them as alive. Bitbol and Gallagher [3] criticise the statistical separation of internal and external states entailed by the Markov blanket formalism, and frame the idea that organisms model their worlds (entailed by the FEP) as suspect and representationalist.

These concerns present a fascinating challenge to VNE. As discussed above, VE will directly address the issues raised by Bruineberg and Hesp [4]. Kirchhoff's [7] commentary prompts the useful clarification that active inference is a *special case of* (and not simply equivalent to) generalised synchrony. Coupled pendulums do synchronise, but this is not equivalent to *active inference*, which (as he notes) implies the selection of relevant action policies to counteract entropic weathering and is therefore *necessarily adaptive*. What he calls 'mere' active inference is simply generalised synchrony. Kirmayer's [8] concerns are valid, but we would stress that the point of using the Markov blanket formalism is that it entails *conditional independence* over appropriate temporal and spatial scales. The Markov blanket formalism is apt to formulate the dynamics of systems that assemble and reassemble transiently, and does not imply rigid boundaries and demarcations, or metaphysics. This responds to Bitbol and Gallagher [3] as well: the conditional independence induced by Markov blankets is just part of what it means to *exist as a bounded system at all*. Although VNE emphasises the bidirectional causal relations between organism and niche (as Veissière notes [14]), it also recognises the asymmetry inherent to living dynamics. Here, it is worth mentioning that variational free-energy is only defined in relation to an approximate posterior probability distribution – a (Bayesian) belief about hidden causes in the environment (i.e., those beyond the organism's Markov blanket). In this very limited sense, Bayesian beliefs are quintessentially *intentional* because they are "about" the causes of sensory input. As noted, however, VNE clearly aligns with an enactive conception of cognition and should not be misconstrued as representationalist.

Encouragingly, other commentators recognised that the Markov blanket formalism can be applied just as readily to the "fuzzy" boundaries of groups of organisms and their collective, multiscale dynamics as it can to clearly bounded biological systems [11,12]. Pezzulo and Levin [11], in particular, discuss how one might scale up the formalism to higher-order systems. In short, Markov blankets themselves are statistical constructs that fluctuate at a slower timescale that the internal states that they envelop. A Markov blanket is only in play for as long as the conditional dependencies that define it hold. The key notion here is that (fluctuating) Markov blankets necessarily entail a separation of temporal scales: a Markov blanket endures over a longer time scale than the dynamics that define it.

Some commentators discussed important conceptual issues that we have yet to explore under VNE. Campbell [5] notes our failure to explicitly discuss genes. We refer to genes on three occasions, but only in passing, and we contextualised their effects in terms of "(epi)genetic" processes – a shorthand way to acknowledge both the role of the genome itself, and the epigenetic influences that sculpt its expression. This alludes to similar views in systems biology, according to which inheritance should be recast as the reiterated reconstruction of the individual lifecycle, made possible by leveraging heritable, reliably recurrent units of information transmission (e.g., genes, cells, cytoplasm, and the extracellular environment), rather than genetic transmission alone [24,25]. That said, it would be worthwhile to extend VNE to directly address genetics. Bitbol and Gallagher [3] argue that the FEP does not address the first-person perspective or conscious experience. They suggest that VNE might benefit from contact with enactive and autopoietic approaches, which have been extended to address phenomenology [26–28]. As mentioned, we agree that VNE is compatible with these approaches, but we would also draw their attention to extant applications of the FEP to conscious experience [23,29–36]. Further suggestions that warrant attention include the roles of non-stationary fluctuations of temperature in Markov blankets and the effects of time-reversal asymmetry in biological dynamics [12].

The commentaries by Veissière [14], Leydesdorff [9], and Kirmayer [8] concerned the applicability of VNE and nested Markov blankets to human social and cultural systems. Leydesdorff [9] makes a number of astute observations about the "systems level" constituted by the social world. We agree that this layer is *sui generis*, comprising shared intersubjective expectations that evolve faster than (non-cultural) biological systems and produce technological interventions based on shared expectations. Dynamics at this scale constrain biology by acting on awareness at the individual level, and by serving as phenotypical retention mechanisms at the institutional one. We also appreciated his nuanced point that knowledge-based technologies impact the social world in ways that are markedly different from the ways in which the generation of scientific knowledge does. Moreover, we are grateful for his use of VNE as an example of how a knowledge claim (i.e., a hypothesis) is able to alter previous knowledge states in the cultural evolution of science. We respond to these points with two of our own. First, the processes described by Leydesdorff [9] can be explained under the broader rubric of *cultural affordances*: they can be cast as the mediation of human behaviour through the transmission of shared expectations, and through the development of cultural artefacts that contribute to the free-energy bounding dynamics of the nested Markov blankets of social groups. However, drawing on recent work in cognitive anthropology and cultural psychiatry (e.g., [37–40]), we emphasise that human biology is always a cultural biology, and human culture always reflects biology. Thus, we are reluctant to demarcate biology from culture so strictly. The second, more challenging issue to note is the sheer complexity of modelling free-energy bounding dynamics at sociocultural scales – there are many factors at play here, which raises the question of whether we can track sociocultural dynamics by studying a limited set of mechanisms amenable to computational modelling and empirical scrutiny.

One promising candidate model of cultural free-energy bounding dynamics in *Homo sapiens* is proposed by Veissière [14]. He suggests that the engagement of human agents with their niches is primarily mediated by expectations about other humans' expectations. In other words, the internal states of human agents encode information about the internal states of other humans. This 'veil of Other Minds' is offered as a key mechanism through which shared expectations and cultural affordances shape active inference at the level of the individual agent. Veissière also aligns VNE with the Extended Evolutionary Synthesis [41] – both frameworks assume a dynamic, bidirectional relationship between real-time and ontogenetic process on the one hand, and phylogeny and adaptation on the other, as well as the co-production of organism and ecological niche. We certainly agree with these insights, and would emphasise two points. The first is that the internal states comprising the veil of Other Minds transcend individual psychology and spread into the socio-material environment, e.g., to evolved, adapted behavioural patterns and constructed niches – an issue to be addressed by the VANC [21]. In short, cultural affordances extend beyond individual brains and recursive mindreading into the socio-material fabric itself. Our second, related point is that although internalised shared expectations may do much of the mediating work, there are doubtless many other mechanisms involved here as well. Humans offload relevant information into their environment (e.g., traffic lights, improvised desire paths, shelters on a hiking trail) and learn much of what they know implicitly, by participating in patterned sociocultural practises, and by acting in designed environments that direct their attention and behaviour [21,33]. Such adapted behaviour and constructed niches encode shared expectations as well, but they do not necessarily require explicit inferences about what others expect – consider, for example, human infants, who have yet to develop the ability to explicitly infer the mental states of others, but clearly participate in, and learn from, the social and physical environment. As such, although we accept the importance of the veil of Other Minds, we are disinclined to reduce cultural affordances to any one mechanism.

This brings us to another cautionary note. The commentaries just discussed [8,9,14] emphasised the myriad ways in which sociocultural environments shape their denizens. We certainly agree with this perspective. Still, one must also not neglect the role of biology in shaping the social and cultural world. Since the social environment of humans can be seen as the product of human biology (and *vice versa*), it is important to account for reciprocally causal relationships between the two.

That said, all three of these commentators raise important questions for the future, and highlight the complexities of applying biological principles to sociocultural phenomena. According to VNE, sociocultural phenomena should instantiate free-energy bounding dynamics too, which suggests that they can be modelled computationally. Although we believe that VNE supplies the requisite conceptual apparatus to tackle such complexities, the issue remains as to whether or not they can be accurately measured, allowing us to test our computational models against real-world observations. Indeed, the reason we chose scientometrics as a way to test VNE at the cultural level was because it already affords reliable, empirical means to do so. Other promising avenues are likely to be found in social network analysis [42]. Nevertheless, testing the ways in which sociocultural dynamics bound free-energy at different spatial and temporal scales could well reflect the greatest challenge for VNE in the future.

3. VNE as a multidisciplinary research heuristic

We were encouraged to observe that many commentators could see the promise of VNE as a research heuristic. Here, it is important not to conflate our ontology of nested Markov blankets – a theoretical proposal that might only be confirmed empirically via simulation studies (as noted by Bruineberg & Hesp [4] and Allen [1]) – and the broader, heuristic value of synthesising the FEP with Tinbergen's four questions as a guide to multidisciplinary research. Criticisms of the former should be kept apart from those of the latter.

In their generous commentary, Tozzi and Peters [12] recognised how VNE furnishes general mathematical and physical concepts from which experimentally testable (and falsifiable) hypotheses can be derived, while Daunizeau [6] lauded VNE as an important new direction for evolutionary neuroscience, provided that researchers invest the requisite resources to integrate diverse experimental results with complex computational models. We were also encouraged to see the suggestions by Daunizeau [6] and Van de Cruys [13], who emphasised the utility of inter-species comparisons and phylogenetic comparative methods to identify and predict adaptive phenotypic responses to selection pressures.

Allen's [1] insightful commentary raises the concern that the FEP, and consequently VNE, might not be amenable to *falsification*. This echoes Bruineberg and Hesp's [4] worry that VNE might only be apt to provide *just-so stories*. In our target article [15], we conceded that when evaluated on its own, the explanatory scope of the FEP is limited. As Bitbol and Gallagher point out [3], the FEP is an *a priori* principle; it can be used to derive top–down, 'principle theories' to explain the characteristic features of living systems. Much like Hamilton's principle of least action, the FEP might (or might not) apply to phenomena in the life sciences – it is *not a theory of everything*. However, we disagree with their assertion [3] that VNE neglects bottom–up processes. As we argued in Section 4 of the target article [15], to explain any given species, the FEP needs to be supplemented by an evolutionary (i.e., ultimate) account that considers the path-dependency of species' evolution, and accounts for the specific adaptive solutions that are responsible for producing specific phenotypes and behaviour. By subsuming Tinbergen's four levels of analysis – which are certainly capable of explaining *how* a given biological process or structure is accomplished [43] – applying VNE clearly requires both 'top–down' and 'bottom–up' theorising.

We have already exemplified this heuristic by explaining the embodied, situated, generative models of *Homo sapiens*, as defined by the (formal and substantive) hypothesis of the Hierarchically Mechanistic Mind (HMM) [15,44,45]. The HMM is a first-level hypothesis about the hierarchical function, structure, and dynamics of the human brain that can be leveraged to generate specific, testable predictions. We submit that some of these predictions allow the HMM itself to be potentially *falsified*. Consider, for example, the second-order hypothesis that the brain suppresses prediction error via hierarchical message passing in the brain, which has already been tested directly via exemplary experiments of visual processing (e.g., see [46]).

To some extent, just-so stories are a risk for any metatheory – hopefully, the heuristic benefit of VNE, which supplements the FEP with substantial, evolutionary accounts (e.g., the HMM), is that it minimises this risk. *Theoretically*, the HMM (and other substantive evolutionary systems theories that might be derived from VNE) safeguards against this risk by calling for integrative hypotheses buttressed by empirical data and real-world observations spanning four tried and tested (Tinbergian) levels of scientific inquiry. Such hypotheses are especially reliable when developed in a bottom–up, evidence-driven fashion, drawing from disparate but consonant multidisciplinary evidence, instead of relying purely on top–down theoretical speculations. *Methodologically*, both the FEP and Tinbergen's approach have already proven to be productive approaches to scientific inquiry – certainly, simulation studies are an excellent way to examine multiscale dynamics, but the wealth of experimental applications born from these paradigms to date clearly implies that VNE is not restricted to them. Consequently, both VNE and the HMM are likely to produce plausible, substantive hypotheses, which are not only supported by converging lines of multidisciplinary evidence, but can also be tested in real-world settings, using models and methods that are readily available. In this respect, the HMM is practically equivalent to any other theory of the brain – like the Bayesian brain hypothesis or predictive coding theory – in that it can be used to generate new hypotheses from which more specific, testable predictions can be derived (as we have already shown with depression [47]). Nevertheless, as Allen [1] and Daunizeau [6] point out, the explanatory power of VNE will ultimately depend on the cumulative weight of the hypotheses and evidence it generates. It is also worth reiterating the need to assess the validity of simulation studies of biological dynamics by comparing them against real-world observations and experimental findings. This was appreciated by some commentators (e.g., [6]), but overlooked by others (e.g., [4]). Indeed, to rely solely on simulation studies to test scientific theory makes it difficult to progress beyond just-so stories. Hence, our appeal to first-order hypotheses capable of generating testable predictions (i.e., the HMM).

4. Formal affairs

Bellomo and Elaiw [2], and Martyushev [10] make some excellent points. They speak to the importance of carefully relating information theoretic constructs in the FEP to physics and applied mathematics. This will be necessary for the variational formulation to be taken seriously in the physical sciences – and to engage applied mathematicians in the study biological self-organisation.

We limit ourselves to responding from the perspective of the FEP *per se* (that underwrites VNE). The first thing to articulate is that variational free-energy should not be confused with thermodynamic free-energy – and the FEP should not be conflated with things like the second law. The FEP is only concerned with nonequilibrium steady-state (NESS), whereas much of statistical mechanics is concerned with equilibrium states. Technically, the FEP is formulated in terms of random dynamical systems [48,49]; specifically, those that possess an attracting set (i.e., pullback attractor). The question then is: What would such systems look like when equipped with the sorts of conditional dependencies that induce a Markov blanket, which separates internal from external states? It transpires that, at NESS, the flow of such systems appears to counter the dispersive effects of random fluctuations, thereby giving the system an apparent purpose. In other words, in virtue of their existence, the NESS flow will appear to be attracted to particular regimes of state (or phase) space.

The key move to note here is that the gradient flow of such systems will appear to maximise Bayesian model evidence. This means that for any random dynamical system with an attracting set, there is an equivalent description in terms of self-evidencing [50], in which the system will appear to organise itself according to the prior probabilities entailed by an implicit generative model. Indeed, in the cognitive neurosciences, it is quite typical to speak about the priors in this setting as *prior preferences* that lend dynamical behaviour an apparent goal-directed or purposeful nature [51]. This dynamics rests upon a gradient flow down variational free-energy gradients. This variational free-energy is not just a mathematical nicety. It is used routinely in high-end data analysis and assimilation schemes; e.g., the dynamic causal modelling of coupled dynamical systems [52]. It is also exactly the same objective function used by the next generation of deep learning architectures in machine learning; e.g., variational auto encoders [53]. This suggests an answer to the concerns of Bitbol and Gallagher [3] about representationalism. Active inference is about the *self-organisation of mutual information* between coupled systems. Active inference and the statistical (generative) models that it implies entail only information measures (e.g., variational free-energy, self-information, surprisal, entropy, mutual information or relative entropy, information gain, Bayesian surprise). None of these measures mandates a representational interpretation (i.e., one involving semantic content). This emphasis on *informational dynamics* over representations should satisfy even the hard-line enactivist.

A prescient issue here is how to relate the variational free-energy in NESS systems to thermodynamic free-energy in statistical thermodynamics (and beyond). This is an outstanding challenge. Some provisional attempts have been made by appeal to Landauer's principle and the Jarzynski equality [54]; however, the key role of the Markov blanket has yet to be exploited in this domain. Intuitively, the Markov blanket plays the role of a heat bath or reservoir in stochastic thermodynamics and statistical mechanics. However, the questions addressed by the FEP (and VNE more broadly) go beyond the ensemble dynamics of states internal to the Markov blanket and ask: Where did the Markov blanket (i.e., heat bath) come from? and, How does it self-organise to maintain its statistical integrity (i.e., the conditional dependencies by which it is defined)?

This speaks to some of the challenging and thoughtful questions posed by Bellomo and Elaiw [2]. For example, how does one deal with birth and death processes or Darwinian mutation and selection? The presence of a random dynamical attractor does, to some extent, address replication – in the trivial sense that specific neighbourhoods of phase space will be revisited. This provides a mathematical image of replication; however, to simulate the emergence of Markov blankets (and their subsequent destruction) remains an outstanding challenge (although there is a paper under review on this issue). Furthermore, the relationship with selection has been addressed at one level by associating natural selection with Bayesian model selection, where variational free-energy becomes (negative) adaptive fitness [55]. However, the specific mechanisms entailed by VNE have yet to be properly addressed (through simulations or empirical study).

Finally, the question about whether the dynamics of living systems should be referred to as a specific class of equations is most interesting. The technical work underlying the FEP usually considers random differential (i.e., Langevin) equations. Having said this, there is some interesting modelling work that applies the FEP to discrete state space models (such as Hidden Markov Models and Markov Decision Processes). Which will be most apt for modelling the multiscale systems implicit in VNE remains an open question. Interestingly, provisional attempts to elaborate dynamics and message passing in hybrid models (of discrete and continuous states) are now starting to appear in the computational literature [56].

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