The free energy principle induces compartmentalization

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Abstract: Living systems at all scales are compartmentalized into interacting subsystems. This paper reviews a mechanism that drives compartmentalization in generic quantum systems. It first discusses three symmetries of generic physical interactions, then shows that if one of these, a permutation symmetry on the inter-system boundary, is spontaneously broken, the symmetry breaking is amplified by the Free Energy Principle (FEP). It then shows how compartmentalization generically results from permutation symmetry breaking under the FEP. It finally notes that the FEP asymptotically restores the broken symmetry, showing that the FEP can be regarded as a theory of fluctuations away from a permutation-symmetric boundary, and hence from an entangled joint state of the interacting systems.

Keywords: Active inference; Contextuality; Free energy principle; Multicellularity; Multiscale competency architecture; Spontaneous symmetry breaking

Abbreviations used: FEP: Free Energy Principle; HP: Holographic Principle; MB: Markov Blanket; MCA: Multi-scale Competency Architecture; QRF: Quantum Reference Frame; VFE: Variational Free Energy

1. Introduction

The Free Energy Principle (FEP) states that any system that persists through time will behave in a way that preserves the integrity of the boundary that separates it from its environment [1]. Systems accomplish this by engaging in active inference, a combination of 1) learning to better predict, and therefore anticipate, the environment's behavior, and 2) acting on the environment to change its state, and hence its behavior, to fit predictions [2,3,4,5]. The criterion of success in both cases is decreased prediction error over the long term, which can be framed formally, following [6], as long-term decrease in a variational free energy (VFE). Hence the FEP can be stated more formally as the claim that any system that persists through time will behave in a way that decreases, over the long term, the VFE measured at the boundary that separates it from its environment.

Recent work on the FEP has further formalized its statistical foundations [7], developed a classical path-integral formulation [8], and re-expressed the FEP in the formalism of quantum information theory, where it emerges as a classical limit of the Principle of Unitarity [9]; see [10] for a thorough comparison of the classical and quantum formalisms. It has also been shown that the FEP induces

hierarchical structure whenever VFE at the boundary has multiple characteristic temporal scales [11,12]. The FEP has been widely applied in neuroscience (see [13, 14, 15, 16] for recent work) and related fields; most relevant for the present purposes are applications in evolutionary and developmental biology, which from the perspective of the FEP describe a single process operating at multiple spatiotemporal scales [17,18,19,20,21,22,23,24].

The present paper reviews the FEP in its quantum information-theoretic formulation, which is both more general than the classical formulation and explicitly scale-free. It first, in §2, describes generic physical interactions in terms of three symmetries. It then shows, in §3, how the FEP describes the restoration of the last of these symmetries following events in which it is locally spontaneously broken. Hence the FEP can be thought of as a theory of fluctuations from a particular symmetry of generic physical interactions, a view consistent with its fundamentally statistical nature when formulated classically. As we will see, these fluctuations effectively convert entanglement entropy – a measure of the departure of a state from purity – to thermodynamic entropy and vice-versa. The consequences of this local symmetry breaking for a generic quantum system are considered in §4, which shows how the FEP generically amplifies fluctuations and induces compartmentalized, hierarchical structures in systems with sufficient degrees of freedom. These considerations are applied to biological cells in §5, which shows how the generic tendency of the FEP to induce organizational complexity is amplified by restrictions on the availability of thermodynamic free energy. Multicellular organization is considered as a second example in §6, which also suggests general conclusions for systems characterized by multiscale competency architectures (MCAs [25,26,27]).

2. Three symmetries of system - environment interactions

Consider a generic, isolated, finite-dimensional quantum system U that can be decomposed as $U = AB$, i.e. the joint Hilbert space $\mathcal{H}_U = \mathcal{H}_A \otimes \mathcal{H}_B$. The assumption that U is isolated implies that B is the complement of A, i.e. $B = \bar{A}$. Let $\mathcal{B}$ be the decompositional boundary between A and B. We can write the interaction between A and B as a Hamiltonian operator $H_{AB} = H_U - (H_A + H_B)$, where H_U, H_A, and H_B are the internal or "self" interactions of the joint system U and the components A and B, respectively. This interaction H_{AB} is, clearly, defined at the decompositional boundary $\mathcal{B}$. We will be interested in the symmetries of this interaction, which can also be thought of as symmetries of $\mathcal{B}$.

2.1 Symmetry #1: A-B exchange, universality of the FEP

The first evident symmetry of H_{AB}, or equivalently, of $\mathcal{B}$, is the symmetry of the "complement of" relation, i.e. if B is the complement of A, A must be the complement of B. Hence the labels `$A$' and `B' can be exchanged in Fig. 1 below without altering the definition of H_{AB}.

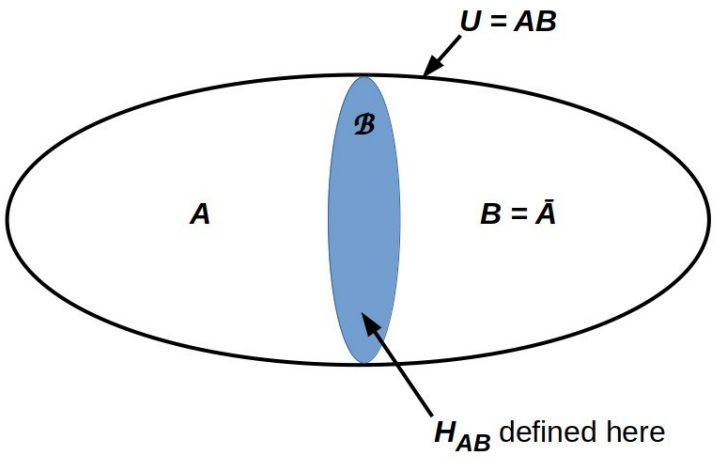

Fig. 1: A bipartite decomposition of "everything" U into a system A and its complement $B = \bar{A}$ induces a boundary $\mathcal{B}$ in the state space of the joint system $U = AB$ and an interaction $H_{AB} = H_U - (H_A + H_B)$ defined at $\mathcal{B}$. Both the boundary and the interaction are invariant under exchanges of the labels `$A$' and `B'.

This seemingly-obvious statement has an important consequence for the FEP. If A is considered the "system of interest" and B is its total physical "environment," i.e. everything that is not A, then the FEP requires A to act so as to minimize the VFE measured at $\mathcal{B}$. Exchanging the labels `$A$' and `B' is then equivalent to noting that A is the total physical environment of B, so that the FEP also requires B to act so as to minimize the VFE measured at $\mathcal{B}$. Symmetry #1 is, therefore, the statement that the FEP is universal: it applies equally on both sides of any decomposition of an isolated "universe" U into a system A and its total physical environment B [9,24].

2.2 Symmetry #2: Conservation of information

The second symmetry follows from the first: if the labels `$A$' and `B' can be exchanged, then $H_{AB} = H_{BA}$. This is, in fact, just the requirement that H_{AB} is mathematically well-defined at $\mathcal{B}$, or equivalently, that H_U is well defined on U.

Symmetry #2 becomes powerful when combined with the Holographic Principle (HP), the claim that any boundary $\mathcal{B}$ crossed by a physical interaction H_{AB} can be characterized by a thermodynamic entropy $S(\mathcal{B})$ equal to the maximum quantity of (classical) information about B obtainable by A or vice-versa [27,28,29,30,31]. We can, in fact, say precisely what information $\mathcal{B}$ encodes: at any instant, $\mathcal{B}$ encodes the eigenvalue of H_{AB} at that instant [30,31]. If the dimension $\dim(H_{AB}) = 2^N$ bits, i.e. any eigenvalue of H_{AB} can be encoded by an N-bit string, then we can write $S(\mathcal{B}) = \dim(\mathcal{B}) = N$ and represent $\mathcal{B}$ by an ancillary array of N mutually-noninteracting qubits (i.e. quantum bits [32]) as shown in Fig. 2 [9,10,30,31]. In this case, we can assign $\mathcal{B}$ a Hilbert space $\mathcal{H}_{\mathcal{B}}$ with dimension 2^N, noting that this Hilbert space is completely ancillary to U, i.e. $\mathcal{H}_{\mathcal{B}} \cap \mathcal{H}_U = \varnothing$.

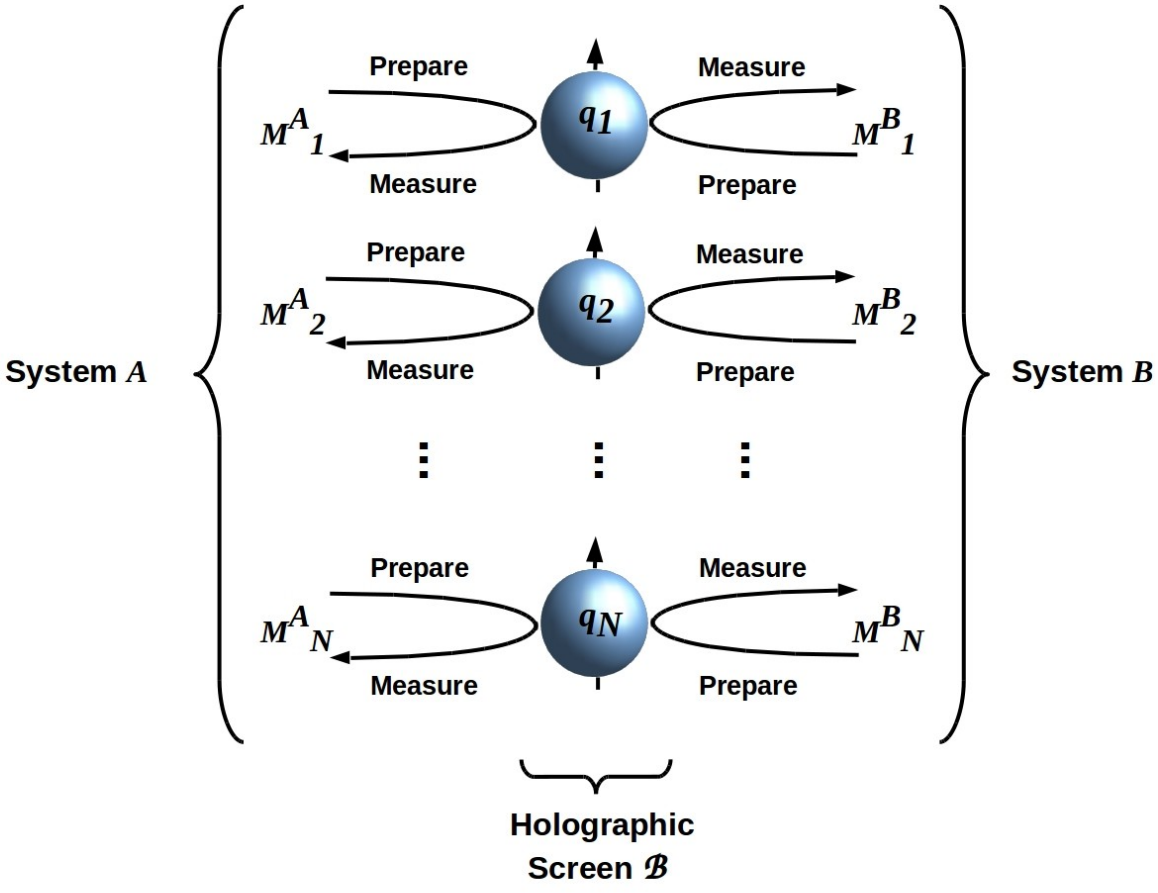

Fig. 2: Any boundary $\mathcal{B}$ compliant with the Holographic Principle can be represented as an array of N mutually non-interacting qubits, with $N = \log_2(\dim(\mathcal{B})) = S(\mathcal{B})$. Adapted with permission from [33].

By equating $S(\mathcal{B})$ with the maximum quantity of (classical) information about B obtainable by A or vice-versa, the HP imposes informational symmetry on $\mathcal{B}$ and hence conservation of information on H_{AB}. When combined with the assumption that U is isolated, and hence prevented from gaining or losing information, conservation of information by H_{AB} for every decomposition $U = AB$ imposes conservation of information on U as a whole. The principle that information is conserved is just the Principle of Unitarity, the fundamental principle of quantum theory [34]. It is the Principle of Unitarity that fundamentally licenses the interpretation of any interaction between generic quantum systems as bidirectional information exchange.

2.3 Symmetry #3: Choice of basis, qubit permutation on $\mathcal{B}$

To be well-defined, physical interactions must be independent of how they are described; hence the interaction Hamiltonian $H_{AB} = H_U - (H_A + H_B)$ must be invariant under changes of basis for the joint system $U = AB$. The eigenvalues of H_{AB} encode the energy exchanged between A and B; changing the basis in which H_{AB} is expressed is, therefore, just changing the effective zero point of the total energy scale. Such a change in how the system is described has no physical consequences.

The basis independence of H_{AB} induces a permutation symmetry on the boundary $\mathcal{B}$: if $\mathcal{B}$ is represented as a qubit array as in Fig. 2, it is invariant under actions of the permutation group S_N on the qubit array [33]. If each qubit is regarded as encoding a single bit, $\mathcal{B}$ is invariant under actions of S_N on this bit array. Since these bits encode eigenvalues of H_{AB}, permutations of the bit array are permutations of eigenvalues of H_{AB}. These reflect scaling of the effective zero point of energy as discussed above.

2.4 Comparison between holographic screens and classical Markov blankets

We will see in §3 below that while all of the above symmetries of H_{AB} are all globally exact, the permutation symmetry of $\mathcal{B}$ can be spontaneously broken locally. Before examining this, however, it is useful to review some differences between the characterization of physical interactions employed here and the classical characterization that results when the holographic boundary $\mathcal{B}$ is replaced by a classical Markov blanket [35,36], as employed in classical formulations of the FEP [1,2,3,4,5].

In a classical causal, and therefore directed, network, the Markov blanket (MB) around some connected subnetwork X is, by definition, the subnetwork comprising parent nodes of X, child nodes of X, and parent nodes not in X of child nodes of X [35]. The MB surrounding X is, therefore, part of the same

network that X is part of, as illustrated in Fig. 3. Thus while a classical MB has the same function as a holographic boundary – both encode all information about the environment that is available to X, and vice versa – they have different structures; an MB is part of the joint system-environment state space, while a holographic boundary is ancillary to this state space. Indeed Friston et al. [1,8] refer to the joint states of a system X and its MB as the "particular" states of X, i.e. the states that characterize X's behavior as a "particle" of matter.

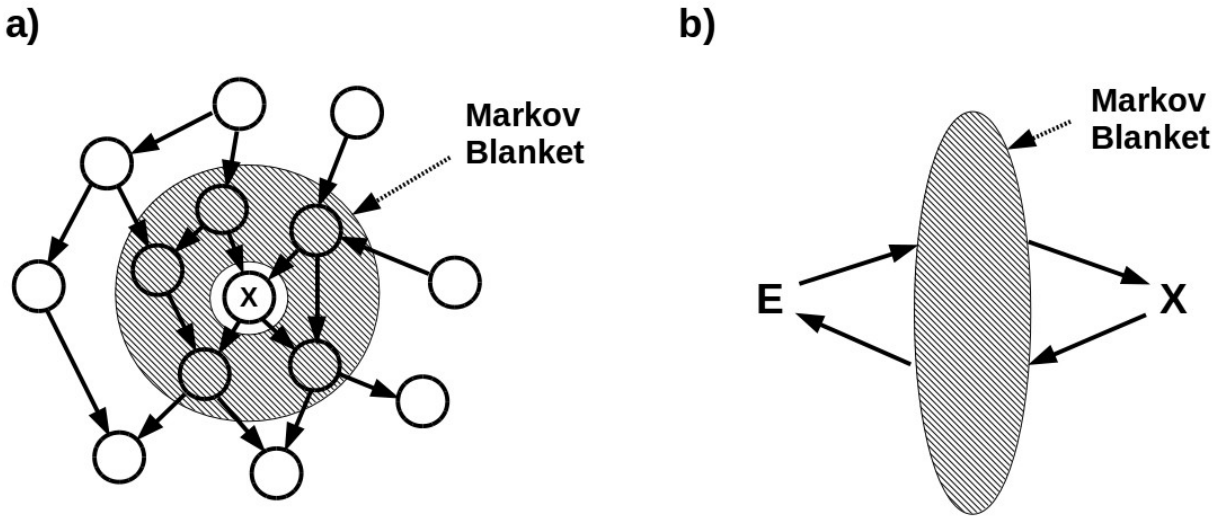

Fig. 3: a) The Markov blanket around a subsystem X within causal network comprises the parent nodes of X, the child nodes of X, and parent nodes not in X of child nodes of X. b) A Markov blanket can always be represented as a boundary between X and the subsystem E that is external to the blanket. Adapted with permission from [37].

Given its function, a classical MB satisfies Symmetry #1 above; the system inside the MB is the "environment" of the system outside the MB. The FEP is, therefore, universal in a classical setting [1]. To the extent that the idea of causal "influence" can be replaced by the more mathematically straightforward notion of force, Symmetry #2 takes the form of Newton's 3rd Law, the law of equal reactions to imposed forces. Classical MBs do not, however, respect Symmetry #3; re-arranging the nodes is a causal network disrupts the dynamics of the network and leads to a new and distinct physical situation. We will see in §3.4 below that breaking Symmetry #3 is a "mark of classicality" in an otherwise quantum system, consistent with the lack of permutation symmetry in classical MBs.

3. Local breaking and restoration of permutation symmetry on the boundary

Spontaneous symmetry breaking is ubiquitous in physics, with phase transitions being a familiar example and the distinction (at low energies) between the weak and electromagnetic interactions a

more arcane one. Understanding a symmetry breaking requires understanding the relevant interaction(s) and the parameters that govern their qualitative behavior. In the present case, it is the strength of the interaction between A and B – effectively, the Hilbert-space dimension N of the boundary $\mathcal{B}$ – that determines whether and how permutation symmetry is broken.

3.1 Weak interaction as a requirement for conditional independence

Everything said so far is consistent with a physical situation in which the state $|U\rangle$ or state density $\rho_U = |U\rangle\langle U|$ is pure or nearly pure, i.e. it is highly entangled and therefore has a von Neumann entropy $\mathcal{S}(U) \sim 0$. We can now ask what happens as this condition is relaxed toward separability across the boundary $\mathcal{B}$, i.e. factorizability as $|U\rangle = |A\rangle|B\rangle$ or $\rho_U = \rho_A \rho_B$. Note that if $|U\rangle$ is entangled, i.e. $|U\rangle \neq |A\rangle|B\rangle$, A and B cannot be considered conditionally independent; hence it is only the separable case that satisfies the classical criteria for the FEP. In particular, separability across $\mathcal{B}$, and hence conditionally independent states $|A\rangle$ and $|B\rangle$, is required if A and B are to be considered to be agents that measure the states of and act upon each other.

In this separable case, the interaction Hamiltonian H_{AB} can be written in the form:

$$H_{AB} = \beta_k \, k_B \, T_k \sum_{i=1}^{N} \alpha_i^k \; M^k{}_i$$

where $k = A$ or B, $\beta_k \geq \ln 2$ is an inverse measure of system k's thermodynamic efficiency, k_B is Boltzmann's constant, T_k is (effective) temperature, the α_i^k are coefficients that sum to unity, and the $M^k{}_i$ are N orthonormal Hermitian operators with eigenvalues in $\{1, -1\}$. Each of the $M^k{}_i$ can be regarded as independently measuring or, dually [38], preparing the state of the i^{th} qubit, q_i, on $\mathcal{B}$; see [9,10,30,31,33] for further details and discussion. Measuring q_i with $M^k{}_i$ yields an outcome, +1 or -1, that can be represented as a classical bit value; preparing q_i with $M^k{}_i$ encodes one of these two possible classical values. The $M^k{}_i$ thus implement the exchange, for system k, between quantum (qubit-encoded) and classical (bit-encoded) information, as illustrated in Fig. 2.

Separability requires a "weak" or low-dimensional (small N, small eigenvalues) interaction between A and B; in particular, it requires $N << \dim(\mathcal{H}_A), \dim(\mathcal{H}_B)$. This allows A and B to have "internal" states not directly involved in the interaction. The existence of such internal states is required to define the classical VFE on which the FEP is based. Intuitively, the internal states provide a computational resource for building a predictive model of the environment's actions on $\mathcal{B}$. It is accuracy of this predictive model that the process of active inference progressively increases.

The requirement of a weak interaction to maintain separability, and hence conditional independence from the physical environment, imposes a tradeoff on all active inference systems. Maintaining a low boundary dimension N, and hence a low bandwidth for information exchange, keeps the interaction H_{AB} weak. A low informational bandwidth, however, limits the informational access needed to build a

high-quality predictive model of the environment. "Inert" systems such as rocks exemplify weak interaction and low bandwidth [1]. Organisms interact more strongly with their environments, but constantly face the threat of interaction strength spirally out of control, disrupting the integrity of the boundary and leading to loss of separability. This is a "death" outcome in which the organism becomes indistinguishable from its environment. It is the need to constantly maintain an interaction with the environment that is strong enough to yield sufficient information but weak enough to preserve the integrity of the boundary that renders the situation of living systems "precarious."

3.2 Quantum reference frames for measurement and state preparation

As each of the M^k_i acts on a single qubit and has eigenvalues in {1,-1}, they can be considered "copies" of the *z*-spin operator s_z; Fig. 2 illustrates this interpretation. This immediately raises the questions of what defines the *z* axis, and whether it is the same for every qubit. The *z* axis for qubit q_i is a reference frame that defines the "up" (+*z*) direction for q_i; when physically implemented, it is a quantum system and hence a *quantum reference frame* (QRF [39,40]) for q_i.

Consider now how *A* uses the M^A_i to obtain information about *B*. What information A can obtain is precisely specified: it is the result of *B*'s most recent preparation of the states of the q_i. To obtain this information, *A* must implement a local *z* axis – a directional QRF – for each of the M^A_i. These local QRFs are physical systems, so can only be components of *A*. If we think of *A* as an information-processing system, i.e. as executing a quantum computation, then each of these local QRFs executes a component of that computation.

The same local QRFs that enable measurement also implement state preparation. Each action with the M^A_i on $\mathcal{B}$ encodes *N* classical bits onto the *N* qubits composing $\mathcal{B}$. Compliance with Landauer's Principle requires an expenditure of thermodynamic free energy obtained from *B*, or equivalently, dissipation of waste heat into *B*, of at least $N(\ln 2)k_BT$ [41,42,43]. This thermodynamic flow induces thermal disequilibrium, but must preserve the informational equilibrium imposed by Symmetry #2. As discussed in [9,33], this requirement for a thermodynamic free energy flow that preserves informational symmetry requires designation of a sector of $\mathcal{B}$, which we will label *F*, dedicated to thermodynamic exchange and hence unavailable for "informative" measurement. A dedicated component of the internal dynamics H_A is required to allocate the thermodynamic free energy obtained through *F* to the information actions, i.e. encoding of bit values, carried out by *A*. Let N_F designate the number of qubits dedicated to *F*. In this case, $N - N_F = N_E$ qubits are available for information processing; the sector *E* thus defined is the observable or *informational* environment of A. The job of any active inference agent is to become a good regulator [44] of the behavior of its physical environment *B* by building a good predictive model of *B*'s actions on its informational environment *E*.

The free energy cost of encoding classical bits on $\mathcal{B}$ thus imposes a second tradeoff on active inference agents. For a given thermodynamic sector dimension N_F, increased thermodynamic efficiency, i.e. smaller β_k, enables more information processing and hence larger N_E, larger total bandwidth *N*, and hence a stronger interaction H_{AB}. In the limit as $N_F/N \rightarrow 0$, however, the energy density on N_F

diverges. Organisms avoid this outcome by avoiding "fuels" with overly-high energy density; breathing pure oxygen, for example, can be fatal. Becoming a more efficient heat engine, in other words, increases predictive power, but also increases the risk of runaway interaction, boundary collapse, and death.

3.3 Identification of "systems" in the informational environment E

Predicting the next state of *E* requires implementing a model of *B*'s actions on *E*, and hence sufficient internal computational resources to support such a model. Testing such a model, and tracking its convergence toward being a good model, requires a memory not just for the model, but also for the state of *E*; at minimum, it requires sufficient memory to record previous measurements of VFE on *E*. These previous-state data are classical, and hence require a classical encoding, i.e. an encoding on $\mathcal{B}$. As writing classical memories on $\mathcal{B}$ is writing them on *E*, these memories are by definition stigmergic [45]: they are modifications of the observable environment that can be "read" as indicators of past states. Pheromone trails and written records are canonical examples.

The fundamental requirement for stigmergic memory is a time-persistent external substrate. In physical terms, this is an external system *Y* that has some number of distinguishable states $|y_i\rangle$. As discussed in [9,10,31,33], identifying such a system *Y* and measuring its state requires two QRFs, one that measures a "reference state" $|y_R\rangle$ of *Y* that does not change in time, and one that measures the time-varying "pointer" states $|y_i\rangle$. As *A*'s QRFs are all collections of operators $M^A{}_i$ that act on $\mathcal{B}$, this system *Y* is a sector of $\mathcal{B}$, a collection of qubits that have mutually-correlated states. Writing a memory on Y is preparing some specific state $|y_i\rangle$.

This situation generalizes: any external system *X* identifiable and measurable by *A* corresponds to a sector *X* of *A*'s boundary $\mathcal{B}$ that is acted upon by two QRFs, one that performs system identification and one that performs time-varying (i.e. informative) state measurement as well as state preparation or manipulation. All such systems and their states are, clearly, defined relative to *A* [46,47,48].

We can, therefore, represent a system *A* that measures the state of some external system *X*, i.e. the state of some sector *X* of its boundary, and then records its measurement on some external memory *Y* as in Fig. 4. As this process takes time, it defines an internal time QRF; see [31,33] for discussion. Systems at this level of complexity experience "differences that make a difference" to behavior [49], and therefore create "meaning" in the sense of semantic significance [45,50].

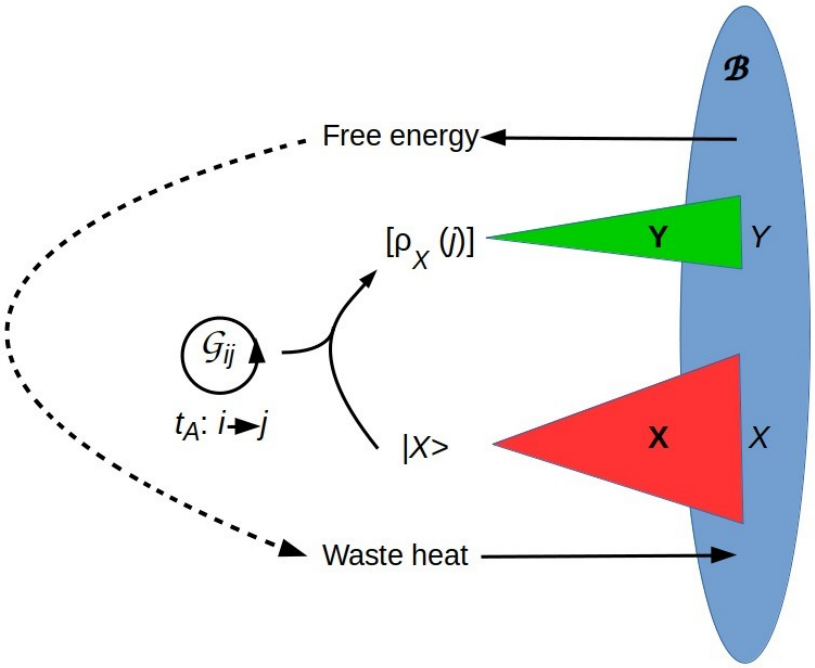

Fig. 4: Cartoon representation of a system A that deploys a QRF **X** (red triangle) to measure the state of an external system X in its informational environment (i.e. a sector X of its boundary $\mathcal{B}$), and then deploys a second QRF **Y** (green triangle) to write the outcome to a memory sector Y. This process induces one "tick" of an internal clock $\mathcal{G}_{ij}$ that defines an internal elapsed time t_A. The process is powered by a thermodynamic loop from (free energy in) and back to (waste heat out) the physical environment B. Adapted with permission from [31].

3.4 Active inference locally breaks permutation symmetry on $\mathcal{B}$

Defining functionally-distinct sectors on $\mathcal{B}$ breaks Symmetry #3, the qubit-permutation symmetry on $\mathcal{B}$. As active inference requires a functional distinction between the thermodynamic exchange sector *F* and the informational environment *E*, active inference generically breaks permutation symmetry by assigning different functional roles to different qubits. The identification of external systems, including stigmergic memories, in *E* further breaks this symmetry. The FEP drives systems with sufficient computational power toward the identification of external systems, since doing so modularizes, and therefore simplifies, the problem of predicting the behavior of the environment. Hence the FEP

amplifies permutation symmetry breaking on $\mathcal{B}$ as a means of achieving better predictions and thereby lowering measured VFE.

This symmetry breaking is relative to the agent *A* and hence is local with respect to the joint system *U*. As notes in §2.4, Symmetry #3 is exact for *U*. The symmetry is broken locally by *A* writing classical data on $\mathcal{B}$, i.e. by *A* acting in some specific, thermodynamically-irreversible way. Hence local breaking of Symmetrry #3 is associated with classicality, and can be considered a criterial for classicality.

This association between local permutation-symmetry breaking and classicality is fundamental to quantum theory. If systems *A* and *B* are separable, i.e. $|U\rangle = |A\rangle|B\rangle$, both *A* and *B* can be considered to have "free choice" of basis for defining the operators M^k_i. As illustrated in Fig. 2, free choice of basis corresponds to free choice of the local *z*-axis for each qubit on $\mathcal{B}$. The opposite of free choice, in this case, is superdeterminism: if A and B are entangled, a basis choice for *U* fixes the basis for both *A* and *B*, and hence for both the M^A_i and the M^B_i. This is, clearly, just a way of stating in quantum language that *A* and *B* are not conditionally independent if they are not separable.

3.5 The FEP asymptotically restores permutation symmetry on $\mathcal{B}$

As shown in [9], the FEP drives interacting systems toward entanglement, and hence toward a restored permutation symmetry on $\mathcal{B}$. Intuitively, the FEP drives systems toward perfect mutual predictability. The limit of perfect predictability entails shared QRFs on all of $\mathcal{B}$. The condition of perfectly shared QRFs, however, entails loss of free choice of QRFs, i.e. entanglement [33]; see [51] for an alternative proof and further discussion. Perfect prediction of the environment requires a perfect model of the environment, one that is indistinguishable from the environment itself.

We can see the FEP, therefore, as both amplifying separation between *A* and *B* by driving an increase in thermodynamic exchange, and a corresponding increase in model complexity and variety of deployed QRFs as the systems strive to become better mutual predictors, and then destroying separability as *A* and *B* "lock in" to shared QRFs that assure maximum predictive power. As the asymptotic state of any isolated quantum system is entanglement, we can thus see the FEP as a theory of fluctuations away from entanglement, i.e. toward separability, as shown in Fig. 5.

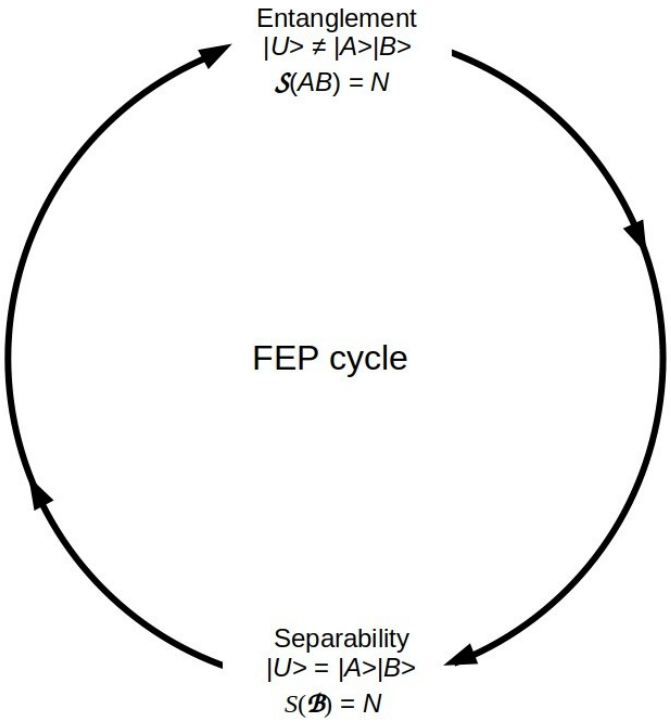

Fig. 5: Cycle between entangled and separable states driven by the FEP.

The cycle shown in Fig. 5 can be viewed as a cycle between the two forms of entropy that characterize $\mathcal{B}$, both of which have maximum values of $\dim(\mathcal{B}) = N$. When A and B are separable, the classical entropy $S(\mathcal{B}) = N$ as required by the HP. When A and B are fully entangled across a fixed $\mathcal{B}$, the entanglement entropy across $\mathcal{B}$ reaches its maximum value of N. If the constraint of a fixed $\mathcal{B}$, and hence fixed N, is relaxed, the maximum entanglement entropy $\mathcal{S}(AB) = \max(\dim(\mathcal{H}_A), \dim(\mathcal{H}_B))$, violating the requirement that the boundary dimension $N << \dim(\mathcal{H}_A), \dim(\mathcal{H}_B)$ that enables separability. Allowing the boundary dimension N to become "large," in other words, incorporates the previously "internal" states of the smaller of A and B into the boundary, again a "death" condition that renders the smaller system indistinguishable from its larger environment. Entanglement is precisely this condition of indistinguishability.

4. Non-commuting operators induce compartmentalization

With the background of §3, we are in a position to see how the FEP induces compartmentalization in generic quantum systems under well-defined circumstances. In brief, this happens whenever a system implements QRFs that cannot be deployed simultaneously. There are two circumstances in which this occurs: when the operators in question are intrinsically non-commutative, and when insufficient thermodynamic resources prevent their joint deployment.

4.1 Intrinsically non-commuting QRFs

Heisenberg's uncertainty principle formulated, in the early days of quantum theory, the fact that certain pairs of measurements could not be performed simultaneously. Most well-known is the uncertainty principle for position and momentum, usually written $\Delta\mathbf{x}\Delta\mathbf{p} > \hbar/2$, where **x** and **p** are measurement operators for position and momentum, respectively. An intuitive explanation was given by Heisenberg: measuring the position of a particle requires interacting with it – e.g. shining light on it – which alters its momentum.

Mathematically, the uncertainty principle encodes an effect of operator non-commutativity, which in the present context can be extended to QRF non-commutativity. Let Q_1 and Q_2 be QRFs. If the commutator $[Q_1 , Q_2] = Q_1Q_2 – Q_2Q_1 = 0$, Q_1 and Q_2 commute; otherwise they do not. Many pairs of QRFs do not commute; examples include position and momentum, energy (i.e. the Hamiltonian) and time, and vertical (*z*) and horizontal (*x*) spin or polarization.

As any QRF acts on some subset of the qubits on a boundary B, the component operations that together compose the QRF must be simultaneously deployable, and therefore must commute. This allows QRFs to be represented as hierarchies of operators in which the apex operator is both the category-theoretic limit and colimit of the operators below it [33]; see [52] for a fully-general proof. The conditions for commutativity can then be formulated very simply: Q_1 and Q_2 commute if and only if the corresponding operator hierarchies (cone-cocone diagrams or CCCDs) themselves commute, i.e. there is some operator that is their common limit and colimit. Commuting QRFs can, in other words, be combined to form a single QRF.

As an example, consider a QRF X_R that identifies the reference state $|x_R\rangle$ of some system *X* and the QRF X_P that measures its current "pointer" state $|x_i\rangle$. Clearly X_R and X_P must commute; otherwise identifying the system would change its state, and worse, measuring the state would alter the identity – i.e. disrupt the persistence through time – of the system. The system X may, however, have distinct sets of pointer states – e.g. position states and momentum states – that do not mutually commute, although both must commute with the reference measurement X_R if *X* is to remain identifiable as a system.

4.2 Thermodynamic limitations on co-deployability

Non-commutativity of measurements arises in classical physics whenever measurements have finite resolution, i.e. in all physically-realistic settings [53]. Finite resolution can be considered a thermodynamic effect: it is the lack of infinite thermodynamic resources that forces all actual measurements to have finite precision. Finite resolution effectively coarse-grains measurement outcomes. A measurement context appears "classical" if all outcomes obtained in that setting are sufficiently coarse-grained that non-commutativity can be safely ignored.

Thermodynamic restrictions can, however, prevent even coarse-grained measurements from being performed simultaneously. Whenever the combined energetic cost of two measurements exceeds the free energy – or other free-energy dependent resources such as memory or processing power – that is available, the measurements must be performed in series, not in parallel. Typical human beings, for example, have fairly strict limitations on cognitive multitasking, and must deploy an attention system to serialize complex tasks. Any measurements, or dually, actions, that cannot be performed simultaneously due to resource restrictions are effectively non co-deployable. In any such cases, measuring or acting with Q_1 can perturb the physical environment *B* sufficiently that subsequent measurements or actions with Q_2 do not have the same outcomes or effects that they would have had if Q_1 had not been deployed first. In any such case, Q_1 and Q_2 do not commute.

4.3 Failures of commutativity induce compartmentalization

As noted above, commuting QRFs can be combined to form a single, composite QRF. Any single QRF can be represented as a single quantum process acting on a pure state [52]. Any single QRF can, therefore, be implemented by a single quantum system, with all classical information read from or written to its boundary as required by the HP.

Any collection of QRFs that do not mutually commute cannot be combined to form a single, composite QRF, and cannot be represented as a single quantum process. They cannot, therefore, be implemented by a single quantum system with no internal boundaries. Any such collection must, instead, be implemented by a separable (i.e. factorizable) system having at least two components separated by an internal boundary.

Non-commutative QRFs can only, therefore, be implemented by compartmentalized systems. Any requirement for differential thermodynamic free energy allocation to compartments implementing distinct QRFs induces further compartmentalization, as the allocation process requires access to a classical representation of each compartment's state. Differential free energy allocation thus requires a "controller" compartment that takes compartmental state information as input and provides free energy as output. This further level of compartmentalization is induced whenever distinct QRFs are required to model behaviors of the physical environment at different time scales [11], but may also also required if non-commuting QRFs operate at the same or similar time scales.

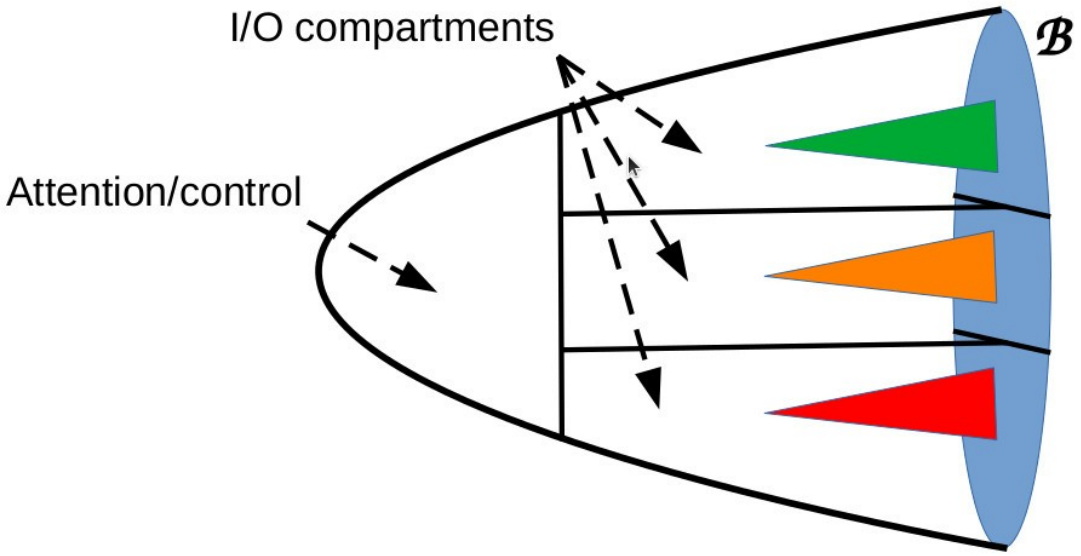

Fig. 6: Cartoon representation of a system A that deploys three pairwise non-commuting QRFs (colored triangles) that induce internal compartmentalization into three "input/output" (I/O) compartments and one attention/control compartment.

4.4 Compartmentalization reflects contextuality

Dependence of the outcomes of one measurement on what other measurements are performed simultaneously is termed intrinsic or quantum contextuality [54,55,56], and is distinct from causal dependence of an outcome on what other measurements have been performed previously. While contextuality was originally considered a exclusively microscopic "quantum" phenomenon, it has since been shown to characterize classical systems [57], including human decision making [58,59]. Statistical tests for contextuality detect failures of conditional independence between distinct, *prima facie* unrelated measurement outcomes; hence they detect failures of separability of joint states characterized by the measured degrees of freedom. Measures of contextuality are, therefore, measures of non-classicality in the same way that measurements of entanglement are [56].

Not surprisingly, non-commutative QRFs induce contextuality [60,61]. In any compartmentalized system, therefore, what one compartment measures defines a context for what other compartments measure, inducing a context dependence that may or may not be detectable in the short-term statistics of the joint measurements. If *A* is the compartmentalized agent, these context effects are mediated by the dynamics H_B of *A*'s physical environment *B*, dynamics to which *A* has access only via their effects on the boundary $\mathcal{B}$. Contextuality can, therefore, be regarded as a prediction problem: the problem of predicting the side effects of actions. In this form, it is closely related to the Frame Problem in

artificial intelligence [62], which is known to be Turing non-computable [63]. One can, therefore, summarize the situation by saying that all compartmentalized systems experience the Frame Problem.

5. Cells as conpartmentalized active-inference agents

Biological cells have been recognized as exemplars of active inference since the early days of the FEP [2,3]. It is natural to regard the cell membrane as physically implementing a classical MB, and to view transmembrane receptors and effectors (e.g. ion channels, secretory systems, and structures such as flagella) as implementing sensation and action, respectively, at the cellular level. Relatively simple, well-characterized biochemical mechanisms such as bacterial chemotaxis [64] can then be recast as encoding VFE-minimizing models of the cellular environment. This characterization is conceptually powerful, and extends quite naturally to complex cells such as neurons and to networks of interacting neurons as mentioned previously [13,14,15].

Eukaryotic cells are, by definition, compartmentalized systems. Even bacterial cells are, however, functionally compartmentalized, with subsystems such as DNA replication, gene expression, metabolism, and motility implemented by distinct, albeit mutually cross-modulating, molecular pathways. While the genome has long been recognized as a memory system that cells access to retrieve instructions for making particular proteins, the cytoplasm, cytoskeleton, and membrane also serve as memory structures that store state information at different spatial and temporal scales [37]. It seems reasonable, therefore, to consider functional subsystems within cells as active inference agents that measure and act on their local environments, exchange information with other subsystems via well-defined interfaces, and write and read memories at multiple scales. The MBs of such systems may not be physically implemented by membranes or other structures, but instead be purely informational boundaries.

As an example, consider the interactions between the chemotaxis pathway and the gene expression, protein degradation, and metabolic pathways shown in Fig. 7. Chemotaxis provides fuel for metabolism, while relying on metabolism for ATP, gene expression for replacement proteins, and degradation for removal of excess or nonfunctional components. Communication between pathways relies on molecular signalling, i.e. the “reading” of molecular concentrations in localized areas of the cell. Communication also requires short-term memory, e.g. as implemented by enzyme activation, for the states of targeted pathways. It is enabled over the lifetime of cell, and indeed over generations, by the long-term memory for protein sequence implemented by the genome and by the intermediate-term memories for small-molecule concentrations, cell shape, and receptor/effector organization implemented by the cytoplasm, cytoskeleton, and membrane, respectively. Memory at the pathway level has now been demonstrated by simulation studies of multiple well-characterized molecular pathways [65,66].

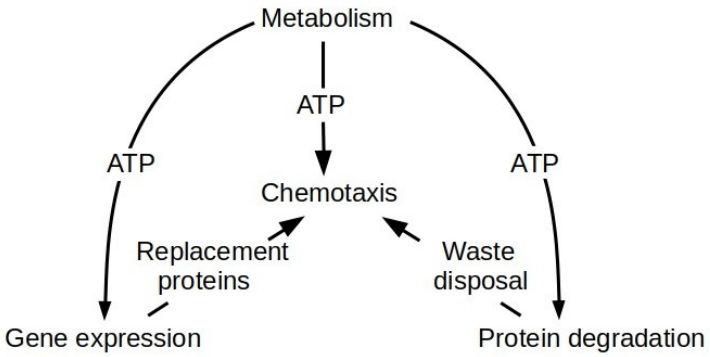

Fig. 7: Resource flows to the chemotaxis pathway from neighboring pathways. The activity of the chemotaxis pathway provides fuel, in the form of sugars, to the metabolic pathway.

Molecular pathways and their interactions are standardly represented as completely classical. Cells, however, process information by altering molecular structures and conformations. The free energy budgets, measured calorimetrically, of both prokaryotic and eukaryotic cells are orders of magnitude too small to support fully-classical changes in protein conformation alone, neglecting all other computational processes [67]; see [68] for a similar argument focused on energy usage by human brains. This suggests that cells reserve their limited free energy for funding classical communication between pathway components that employ quantum coherence as a computational resource and hence must be regarded as intrinsically quantum processes. As seen in §3 above, such classical information exchange effectively implements an MB.

Characterizing pathways as active inference agents immediately raises the question of where pathways come from. The structure of the last universal common ancestor (LUCA) remains unresolved, but it seems safe to assume both that LUCA's molecular architecture was significantly simpler than that of typical bacteria, and that it included functional pathways for at least metabolism and reproduction. From this point, the most natural mechanism for generating new pathways is duplication followed by diversification. As gene duplication can act on entire operons in bacteria, a duplication followed by diversification mechanism could be expected to generate alternate pathways particularly efficiently in a bacterial setting [70].

Treating intracellular pathways or pathway components as encapsulated by MBs also raises the questions of 1) characterizing the informational environments of such components, and 2) characterizing the QRFs that they employ to read from and write on their informational environments.

Answering these questions amounts, effectively, to characterizing an application programming interface (API) in molecular terms. An ability to characterize such interfaces from available biochemical and cell-physiological data would enable a modularized approach to natural, engineered, and even fully synthetic cells.

6. Conclusion: Compartmentalization as a scale-free outcome of FEP-driven dynamics

From microbial mats to humans, multicellular systems, even if only facultative, are compartmentalized. Division of labor at the cellular level, which is evident even in microbial mats [71], indicates different cellular capabilities and hence different QRFs. Coordination of cellular activity requires intercellular signaling, either via the intercellular space between cell membranes, or via membrane-bound structures such as adhesion molecules or gap junctions. Detecting and generating such signals requires further specialized pathways, all of which must be supported by gene expression, protein degradation, and metabolism.

The FEP induces multicellularity by enabling individual cells to mitigate environmental challenges by associating with other cells that can serve as buffers [19,24]. Centrally-located, and hence maximally buffered, cells in such associations serve a coordinating, and hence nervous-system like role even in aneural sponges [72]. Totipotent cells, whether they are somatic stem cells or reproductive cells, are typically also protected by internalization. It is worth noting that all known multicellular systems include microbial components [73,74,75]; hence division of labor in such systems includes cross-species division of labor.

Larger-scale structures, from social-insect colonies to human societies to ecosystems, similarly exhibit compartmentalization, division of labor, and specialized inter-agent communication systems. While it becomes increasingly difficult at larger scales to characterize such systems as agents measuring the states of and interacting with a well-defined environment – in other words, to describe them in cognitive terms – they remain physical systems and there is no evident reason why the FEP should not apply to them [18,21,76].

Hierarchical multi-component structures in which components at each scale have their own, scale-appropriate competencies have been termed multi-scale competency architectures (MCAs [25,26,27]). The FEP generates systems of increasing complexity by driving MCA components at one scale to form functional agents at the next higher scale [24]. These agents survive to the extent that they maintain the integrity of their boundaries, and can be considered intelligent (or cognitive [77]) to the extent that they manage to survive. We have seen here that this process is driven by fundamental physics. The FEP, in particular, amplifies permutation symmetry breaking on holographic boundaries whenever such symmetries are spontaneously broken, i.e. whenever interacting systems fluctuate away from entanglement. As interaction partners approach the limit of perfect mutual predictability, however, they “collapse” back to an entangled joint state. We can, therefore, view the FEP as a theory of spontaneous fluctuations away from entangled pure states, suggesting a connection to other areas of fundamental physics in which quantum fluctuations play an important role.

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Conflict of interest

The author declares no conflict of interest.

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