Emergent Natural Selection for Engineering Living Systems
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INTRODUCTION
Motivating Question:
Can we focus on the role of natural selective forces in the construction of complex organisms and living systems?

* perhaps, if we treat a complex organism as an emergent, hierarchical directed graph with control properties.

Must rely on the following:
A) fundamental unit: a volume that serves as a minimal description of biological function at the cellular level.

* at cellular population level, this can be a single cell.

B) Free energy (e.g. Gibbs, Landau de Gennes [1,2]) = information, natural selection = constraint.

* framework for self-assembly at single spatial scale [3].


* also a tenet of complex adaptive systems (CAS) approaches [5] to emergence

* makes approach amenable to fault-tolerance, robustness.
Abstraction:
1) organism is a hierarchy of “fundamental units” [6].
   * fundamental units in hierarchy can be connected in various modes. Provide modular and structural organization.
   * connections are pruned when selection exceeds free energy input.

Focus is on organizational complexity, trophic complexity of cellular populations.
   * fundamental units are replicators that exhibit diversity embodied in a genotypic representation.

2) Metrics for characterizing hierarchical natural selection. For more details, see end of poster and [6].
   * describe both selection and information.
   * scope (S), transformity (T) [see 1], and connectivity (C) variables contribute to the magnitude of selection in a relative manner.
   * pervasiveness and relative embodied energy contribute to fitness in an additive fashion.

3) basic set of relations.

![Figure 1: Example of relations between fundamental units, different hierarchical levels.](image-url)
To achieve the types of tissues seen in Figure 2, a geometric component must be added to this model.

* Flows added to model, act externally to network (have an aggregate effect on entire structure).

* Laminar field (Figure 3) can act upon connectivity, replication ability of units.

* Structures result from flows, which are constrained by minimization of energy. Consistent with constructal theory [8].

* Complex flow fields (composite flows) might be able to structure units at a single scale to mimic modularity [see 9] in multicellular organisms.

* Tissues and structures at single scales can also form structural networks [10] in response to local mechanical conditions.
In Figure A, fundamental units can be treated as either “black boxes” (Organ and Tissue A in Figure 1) or groups of units in an array (cell populations, Figure 1)).

**System Behavior:**
The goal of these networks is not to imitate a neural network or to simulate the evolution of organisms, but to approximate the dynamical behavior of self-assembled systems.

Connections between fundamental units are critical to determining the hierarchical nature of these evolutionary systems:

1) Information: acts as a support mechanism for parental units.

Biological analogue: trophic and tropic signaling.

Examples:
* diffusion (stochastic and directional).
* one-to-one chemical signaling.

2) Selection: acts as a constraint on child units.

Determined by rules such as logical functions, simple relational equations [11].

Examples:
* helps to maintain function modules composed of child units.
* feedback mechanism for determining which cell populations, biological components are needed to form a functional organ.

3) Aggregate selection: acts on all units in a single module or at a specific scale. Governed by force fields and flow fields.

Approximates physical aspects of development and tissue self-assembly [12].

Examples:
* cell sorting in development based on chemotactic signals [13].
* local cyclic stresses determine cell fate in stem cells [14].
Natural selection acts on populations recursively.

A: selection imposed at lower level of hierarchy, small magnitude of effect.

B: selection imposed at higher level of hierarchy, little to no effect.

C: selection imposed at lower level of hierarchy, small magnitude of effect.

D: selection imposed at higher level of hierarchy, large magnitude of effect.

Examples from neural evolution/development:

Parcellation theory (left) [15] and population matching (right) [16].

Displacement hypothesis and developmental plasticity (right) [16, 17].

Figure 4: Four versions of connectivity.
Potential application domains.
There are many potential applications of this theoretical framework, from tissue engineering to biological analysis. Below are two key areas for further study.

Nanoassembly.
At the micro- and nano-scale, self- and human-assisted assembly of synthetic elements is impacted greatly forces and stochastic processes. One way to do this is to directly implement a genetic algorithm [18]. However, the method proposed here might be a more open-ended way to approach the problem.

Biomimetic Control.
Knowing which units and modules lead to higher-level structures requires the implementation of a biological control policy. This control policy could be loosely based on hierarchical natural selection.

Variables and Definitions:

Scope. \[ S = \frac{U_{ns}}{U_{lms}} \]
\( U_{ns} \) = # of units at 10\(^{-n}\) under selection.
\( U_{lms} \) = # of units at 10\(^{-n}\) not under selection.

Connectivity. \[ C = 1 - \sum \frac{U_n}{C_u} \]
\( U_n \) = single unit at 10\(^{-n}\).
\( C_u \) = # connections to units at other levels.

Transformity. Scaling factor between hierarchical levels [1].

Energy. \[ E = G_n + B_n \]
\[ E_f = \frac{E_n - E_{min}}{E_{max} - E_{min}} \]
\( G_n \) = free energy, \( B_n \) = bond energy. \( \text{max, min} \) = maximum, minimum energy across hierarchy.

Pervasiveness. \[ P = 0.5 \left[ \frac{C}{C_{max}} \right] \]
\( C_{max} \) = maximum connectivity across hierarchy.

References: