Title: Elucidating the rules of assembly and emergent properties of biological superstructure at multiple scales

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Summary:
Biological superstructures are assembled from diverse components through interactions and feedback with the environment, resulting in significant multi-functionality that often extends beyond their biological scale. We aim to bring together biologists studying diverse systems across scale with physicists, mathematicians, materials scientists, and architects to elucidate common assembly mechanisms and emergent properties for diverse superstructures such as mitotic spindles, spider webs and coral reefs. Identifying these universal rules has diverse implications for developmental biology and medicine, resilience of ecosystem superstructures in the face of climate change, and new materials/technologies for manufacturing and architecture.

What is a "superstructure"?

All biological form is a type of structure. Here we focus upon a special class of structure that we define superstructure that occurs across the hierarchy of life, from molecular to organismal to ecosystem levels. Superstructures share a suite of traits that collectively distinguish them from typical biological structures: 1) they are mechanically solid architectures; 2) that are assembled from multiple components through interactions and feedback with the environment; and 3) from which novel functions and/or properties emerge. As a consequence, superstructures show significant multifunctionality in either their constituent units or the superstructures themselves resulting in properties and function beyond the biological scale of the constituent components. We highlight three broad classes of superstructure:

1. Multi-organism superstructures such as microbial mats, fire-ant bridges, termite mounds, and coral reefs.
2. Organism-scale superstructures such as spider webs, beaver dams and bird nests.
3. Cellular- and subcellular-scale superstructures such as complex photonic structures that produce the vibrant hues of butterfly wings and cytoskeletal assemblies.

Superstructures are distinct from structures because superstructures use components at one scale to build architecture at a higher level with emergent properties.

Investigating mechanisms, models, and manipulation of superstructures

Our vision is to identify common principles of assembly and function of superstructure across biological scales. Fundamental questions must be addressed to understand the generation of superstructures: Can we identify principles for superstructure assembly? Which of these principles are common across scales of biological organization? How do the assembly principles change with scale? How have the assembly principles evolved?

Insight into the fundamental processes of superstructure assembly will enable addressing applied questions such as: Can the assembly principles be manipulated to generate superstructure with novel functionalities/properties? Can the assembly principles be used to improve human-made structures? Can these ideas give new insight into tissue engineering, robot swarms, or the construction of self-forming structures that can grow, repair, and evolve?

What is the interplay of genetic control and physiology and environment on superstructure assembly? We do not expect that the final form of superstructures is directly genetically programmed, but genes do influence the process of feedback and interactions that result in superstructures. This leads to the possibility that both genetic and environmental perturbation could be used to tune or engineer superstructure. This would be most powerful if we could identify common rules that operate across the radically different scales of sub-cellular to organism to ecosystem.

What's the potential impact?

Identifying mechanisms controlling superstructure assembly would have several significant impacts on science and society. Superstructures are key components at both the cellular and ecosystem level, so understanding the mechanisms of assembly could provide new strategies to treat diseases that target sub-cellular superstructures such as amyloid plaque formation and neurodegeneration. Ecosystem resilience in the face of climate change could be improved by preserving key assembly and/or maintenance mechanisms for superstructures such as coral reefs and complex rainforest canopies. We expect many superstructure assembly mechanisms to apply to organism development as well, moving the field away from a reductionist focus on the timing and titer of specific molecular signals to a more holistic approach that could identify commonalities across taxa. There is also great interest in material science and manufacturing for both materials with novel properties that could arise through superstructure and for innovations in assembly mechanism outside of the traditional "top-down" manufacturing paradigm. A clear understanding of the principles of assembly might allow the development of hybrid superstructures incorporating key components or materials from multiple systems for truly novel functionality.

Why now?

We believe that the necessary tools and perspectives to discover universal assembly rules for superstructures exist in disparate fields (e.g. genome/transcriptomics, information theory, materials science etc.), so that it is now time to bring these fields together to tackle the problem. Molecular biology has large -omics datasets on many relevant systems while imaging of physiological processes can allow real time monitoring of decision making and interactions during superstructure assembly. The materials community has the capacity to measure, describe and quantify structures at multiple scales so that we can compare physical feedback in the assembly of coral reefs to spider webs to cellular superstructures like mitotic spindles. While the architectural community is increasingly experimenting with bio-inspired and self-assembled structures. Finally, mathematics and computer science are at a point where feedback loops and information processing of complex processes can be modelled to identify the key mechanisms spanning biological scale. Our aim is to bring these communities together to develop a common language and approach to superstructure assembly at diverse scales to identify assembly rules.

Barriers and challenges

A major challenge in developing a unified view of formation and manipulation of biological superstructure is the need to develop a common language to describe and quantify superstructures that applies across scales and disciplines. Bringing these disciplines together and finding among them common platforms of discussion will be essential for the development of this idea.

An important aspect of such language development includes mathematical and quantitative language: we will need to develop tools that quantify a superstructure--what shape is it? How similar is that shape to a specific structure made in another experiment?--and, importantly, the dynamics of how the superstructures are assembled and remodel over time. This will require attention both to comparing superstructures of the same type, and across types. It is not currently clear whether it is possible to compare the structure of a chromosome to the structure of a coral in a reef; we need tools to describe similarity/differences both of structures and the processes of growth/assembly of those structures.

In trying to find common principles of superstructure assembly, we must confront the fact that our depth of understanding of different biological superstructure-generating systems is highly variable. For some systems, we have a reasonably well-developed idea of the genes, genetic pathways, molecules, and interactions that result in superstructures (for example, the cellular cytoskeleton). For other systems, we have some understanding of important components and interactions, but little-to-no understanding of the genes and genetic pathways important for superstructure assembly (for example, biomineralization in coral reefs, fire-ant bridges). Advancing the search for common principles in superstructure growth and assembly will therefore require investment in understanding multiple systems across biological scales. A related challenge is that currently we have relatively few tools that allow us to study and predict higher-order outcomes of genetic interactions, of the type that underlie superstructures. Development of these tools is one of the challenges for this field to develop, but also an exciting opportunity.

Currently we have relatively little understanding of how the physical properties of components/materials within superstructures influence their possible forms and dynamics. For example, the physical materials used to build the superstructures--the proteins of the cytoskeleton, or the biominerals of a coral reef--put constraints on superstructure design and have likely been influenced by evolution. Our understanding of this material-structure connection is limited. Once we introduce dynamics, we confront another poorly understood question: what influences when superstructures are plastic or easily remodeled, versus more fixed and durable? How is this shaped by biological need (for example, for rapid remodeling of the cytoskeleton versus long-lasting structure for a coral reef) and how does that lead to changes in the materials and/or rules of superstructure assembly?

Achieving these goals requires participation by scientists spanning across levels of biological organization to develop common approaches at molecular, organismal and ecosystem scales. The broadly interdisciplinary nature of the question will integrate these biologists with biophysicists, mathematicians, material scientists and engineers. As a first step, we see great potential to use this vision paper in a conference proposal to convene biologists, physicists, engineers, and information modelers.