DEVELOPMENTAL BIOENGINEERING

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Among the challenges for nature-inspired engineering is how to build synthetic devices capable of emulating the process of development, and its uses in repair and regeneration. Here, I offer a set of principles for designing and building bio-synthetic self-repairing devices based upon nature's process of development.

First, nature's living devices are built by a process of gene and environment regulated self-organization. I illustrate this principle with the process by which nature builds embryos and discuss how bioengineers are using in vitro organoids to model nature's process. Second, devices are inseparable from the micro-environments in which they develop, as illustrated in nature by the micro-environment of stem cells, called niches, as well as by the regulatory interactions between stem cell and niche. Bioengineers leverage the mechanical and chemical properties of the niche to build synthetic organs, via processes such as bio-printing. A challenge in emulating the way that nature builds organs is the incorporation of vasculature. Third, nature builds consortia of heterogeneous parts that exhibit distributed control, evident in the relation between neurons and glial cells during development of the mammalian nervous system, and in communication between gut bacteria and the brain. Research has demonstrated that manipulating the properties of the gut microbiome influences the brain and may actually change behavior. This may provide leverage for bioengineers in promoting healthy behavior of individuals with neuropathology. Fourth, nature repairs worn-out or damaged parts by recapitulating the developmental processes used to build them. For example, nature uses progenitor, or stem cells, both during development and to repair injured organs. However, not all animals have the same capability for repair and regeneration, as evident in the contrast between salamanders that can regrow a lost limb, and humans who cannot. Bioengineers facing the challenge of repairing human spinal cord injury have made great strides in promoting regeneration by emulating the process in other animals, such as axolotls. Fifth, nature's parts and systems may switch from one function to another, depending upon the context of intrinsic regulatory networks and environmental signals. Glial cells, called microglia, are resident central nervous system immune surveillance cells that have multiple functions during development, including synaptic refinement and clearing dead and dying cells. The detection of changes in a cell's microenvironment may switch microglial function from surveillance to clearance. In diseases such as neurodegeneration, synapses may be incorrectly marked as debris, and activate microglia to eliminate them. It may be possible for bioengineers to program swarms of bio-hybrid molecular robots for similar surveillance functions. Sixth, biological regulatory systems allow animals, such as killifish, to enter altered metabolic states under adverse environmental conditions, such as drought. Synthetic biologists are emulating the processes by which nature enables animals to enter different metabolic states. And seventh, biological systems exhibit emergent properties, such as low-dimensional patterns in the vast connectivity of brain networks as well as in behavior. The appearance of these low dimensional patterns in recordings of animal reaching behavior has implications for control of neuro-prosthetic devices.