**Lecture 1: Unresolved issues in evolutionary theory and a wish list for their resolution**

*1.1 Main problems*

Robustness vs. evolvability; changeability vs. complexity; predictability vs. contingency; self-replication vs. change; transient innovation vs. historical persistence; directionality and force in development and evolution.

*1.2. Control theory in biology: goals and definitions*

History and basics; minimal set of controls and their topology; boundary condition; function of controls; temporal and adaptive controllability.

**Lecture 2: Key concepts and insights for evolution and development**

Boundary concept; concept of context; transient controls; construction of controls; external vs. internal control; local feedback and distant synchronization; temporal control of adaptive networks; concept of bias; concept of memory; read-write-rewrite biological systems; concept of critical transition and tipping point.

**Lecture 3: Evolutionary transitions in controls**

*3.1 Control theory as viewed by the founders of evolutionary theory: Evolution is gaining and losing external dependencies*

*3.2. Cycles of control in evolution: theoretical expectations and empirical realization.*

**Lecture 4: Reconciling stability and change**

*4.1. Golden anniversary of two classical approaches:* *global regulatory dynamics and hierarchical regulatory network*

Kauffman vs Britten-Davidson 1969 models; the enduring legacy of Waddington’s landscape of cell differentiation; elements of landscape view of cell differentiation: dynamic stability and attractor states; unidirectional and irreversible development made of multidimensional and reversible states; antagonistic external controls and sizes of attractor states; smoothness of transition between discrete stages; factors behind height of differentiation barriers; pluripotency as a ground stage; positional bias in propensity for reprograming and differentiation; the reason for impossibility of direct transitions between functional states.

*4.2. Lifeline of a cell through the lens of control theory: roadmap to key principles*

“Stem cell” as an evolving principle; empirical progress and associated turnover of definitions; emergent vs. deterministic definitions; individual vs. population level properties; insights into general principles of cell differentiation and competition; combinatorial vs. sequential regulation; ontogenetic vs. evolutionary hierarchies of cell types; context-dependence in juxtaposition of self-renewal and change; activation vs. inhibition of signaling pathways and fate specification; local feedback of transcriptional expression and self-reinforcing circuit of pluripotency; principle of mutual antagonism; phenomena of totipotency; dynamic balance between epigenetic regulation and transcription network; epigenetic memory of lineage specification; comparing pathways of development and reprogramming; hierarchy of controls; control transference and integration into functional context of tissues.

**Lecture 5: Elements of control**

*5.1. Empirical realization of key principles*

Priming for control; elite and stochastic models; two kinds of biases; cell vs organismal fitness; integration of generic and genetic components in controls; neighborhood watch as social control; integration with organismal context; stress induced changes; clonal collapse and aging; lessons from reprograming, CellNet conversions, and implantation studies

*5.2. “How does a molecule become a message?” Principles of transcriptional regulation*

Lamina-associated domains and topologically associated domains in relation to cell fate; TF driven dynamics of chromatin landscape; co-location of genes and synergistic function of TF complexes; superenhancers; pioneer factors; shadow enhancers; generic and physical controls.

**Lecture 6: Copying, activating and recycling controls**

*6.1 Evolutionary contrasts*

Specialization without restricting potential; control activation on demand: seasonal and sex-specific structures; recycling controls in regeneration and wounding; maintenance of control configurations as time keeping; resetting chronological age, but not information

*6.2. Differentiation and proliferation control*

Regulation of on demand proliferation: precise production of a billion cells and not one more; basics of layered and distributed controls, feedback control of growth and differentiation; mechanics of long-distance control; branching as effective control of cell fate and proliferation.

**Lecture 7: The enigma of a “niche”**

The most powerful cell concept on loan from ecologists; temporal integration and aggregation of controls in “stem cell niche”; conceptual justification of the borrowed concept; positional information as controls, island and boundary effects, direct links in niche maintenance; mechanosensing and cell specialization; homeostatic integration; reprograming by occupancy; non-genomic context of a stem cell niche

**Lecture 8: Synthesis I. Implications for ecology and evolution**

Revisiting the wish list: curse of dimensionality; transient innovation vs. historical persistence; reconciling robustness and evolvability; predictability vs. contingency; directionality and force in development and evolution.

**Lecture 9: Synthesis II. Implications for ecology and evolution**

Novel implications to the concepts of homology and evolutionary individuation; reconciling complexity and specialization in evolution; temporal scaling of inheritance. Historical context and future directions.

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