Multiscale and Rare Events in Physiology

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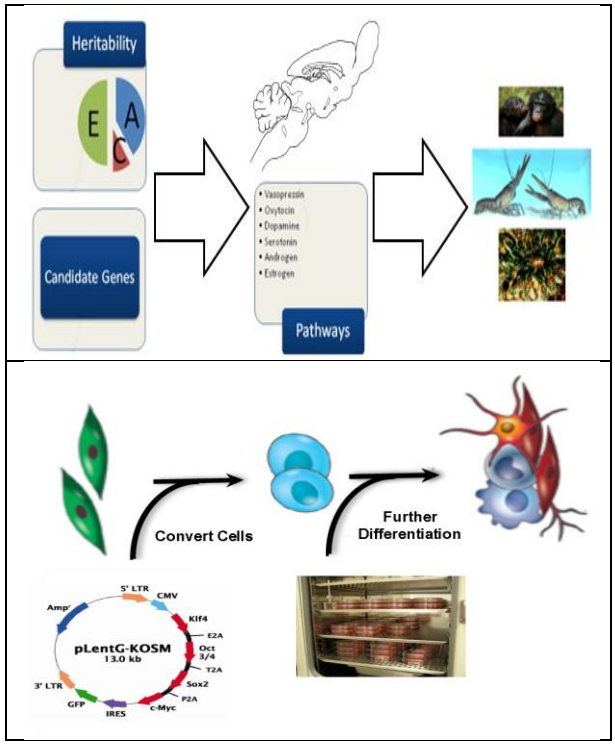
Physiological processes are complex and often hard to characterize quantitatively. Not only are there a potentially large number of variables and interactions, but a large number of unknown factors as well. In addition, there are many rare events that occur in only a few individuals or very infrequently in time. From a modeling standpoint, these potential drawbacks (complexity, rarity) may serve as opportunities for future advances.



We will explore current challenges and observations in the context of two physiological processes: transformation from genes to phenotype/behavior and engineered changes in cellular state (e.g. cellular reprogramming). In the former case, understanding the genetic and cellular bases of phenotype/behavior is widely considered to be a hard problem with many interacting components. For the latter, the reprogramming of cells from one phenotype to another produces many rare events and non-uniformly distributed phenomena.

Figure 1. TOP: commonly studied pathway from gene expression to behavior (partially from Figure 1, Neuron, 65(6), 831-844. 2010). BOTTOM: conversion of cells from somatic to pluripotent and back again (partially from Rossi Lab Website, Harvard).

In the case of the mapping between processes (genes to phenotype/behavior), there are many open problems that could be solved by a multiscalar model. In this presentation, we will consider how to formalize relevant physiological questions as a multiscalar phenomenon. In the case of inducing cells to a new phenotypic state, some of the same “vertical” issues apply, but empirical rare events define the outcome of this process. This talk will conclude by placing these examples of multiscale and rare events into the broader context of biological complexity and systems biology.