Cliffs & canals in Waddington's landscape

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***Short Abstract* — Mature multicellular organisms reproduce by transmitting genetic information onto progeny, which requires successful parental somatic and germline formation. Different strategies to develop to reproductive maturity exist, yet a common thread is that major developmental events are coordinated in time. Given that multiple cell fates are regulated by one genome, we hypothesize that temporal coordination arises from complex gene regulatory network (GRN) dynamics. To test how GRNs affect coordinated multicellular development, we are using a computer simulation based on a standard model of GRN evolution to examine how dynamics and attractor states evolve with stabilizing selection.**

***Keywords* — Waddington's Canalization, Heterochrony, Cell Fate Acquisition, Attractor Networks, Discrete Dynamical Systems.**

I. Background

IN multicellular organisms, reproduction is ultimately achieved by the transmission of genetic material onto progeny, which depends on the successful somatic and germline development in parent(s).

Although there are many strategies used during the development towards reproductive maturity, multicellular organisms tend to have major life history events which are coordinated in time[1,2]. For example, gonads produce sex hormone in vertebrates in response to long range induction by gonadotropin releasing hormone (GNRH), which is first released by neurons within the hypothalamus[3]. In this case, the capacity for the gonad to respond to GNRH is coordinated in time with the ability of the somatic cell to release GNRH. Despite the prevalence of this pattern, how life has evolved to exhibit temporal coordination during development remains unknown[2,4].

II. Hypothesis

We posit that temporal coordination is a common feature of developmental programs where one genome regulates cell fate acquisition and does so robustly from a single cell zygote across multiple daughter lineages. This is supported by the discovery of a genetic pathway in the roundworm nematode *Caenorhabditis elegans* dedicated to regulating the timing of larval development across multiple tissues and cell types[5-8]. In fact, many *C. elegans* developmental timing genes also participate in the onset of human pubertal timing by regulating the GNRH release[6,9-11].

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III. Results

To test how GRNs and gene expression states affect the development of multiple stable cell types, we are using a computer simulation based on a standard model of GRN evolution[12-14]. This model recapitulates how GRNs become more robust to perturbation (i.e. mutational & environmental) when evolved under a stabilizing selection regime. For our analysis, we select GRNs with multiple stable attractor states and impose the constraint that they stabilize within similar time frames.

Here, we present data on how GRN structure and dynamics evolve under a stabilizing selection regime requiring temporal coordination. Our findings indicate that GRNs increase in robustness when they change to take advantage of new inputs from the state space, sculpting, molding, and canalizing the ancestral GRN basins of attraction.

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