Review on Eric Davidson's book **"The Regulatory Genome: Gene Regulatory Networks in Development and Evolution"** Academic Press 2006 (part of it printed on the book back cover)

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The foremost experimentalist of regulatory genomics, Eric Davidson, with his new book, "The Regulatory Genome," is delivering a compelling proof that after the availability of the Human Genome in 2001, the next major event in Molecular Biology has been the availability of the developmental gene regulatory networks. Like his mentor Max Delbruck, and with the *sea urchin* genome in hand, Eric Davidson is today the leading liberator of *quantitative principles* of cell regulation, trapped in the qualitative, descriptive world of biology without genomic sequence.

With the notorious elegance of his writing, Davidson forcefully reminds us that in the scientific method *causality* is everything; all other approaches are just distractions. Such "posterior Biology" approaches, too impatiently employed today – "measure first" expression of thousands of genes, "and then, computationally infer Biology," receive in the book, by contrast, a devastating criticism. The luminaries of mathematical statistics of the last century taught us in no uncertain terms that causality cannot be inferred from statistical tables. Aligned with them, Davidson adds to the argument a practical dose of reality. The exquisite regulatory mechanisms, locked down by evolution, can only be revealed through systematic experimental perturbations. In the absence of the ocean deep "prior Biology" knowledge, no amount of clustering statistics, or other skinny deep dives, would be able infer "Biology."

Having the First Gene, *endo16*, and the First Network, the *Endomesoderm* Network as its flagship, the book presents the state-of-the-art understanding of genomic regulatory systems and networks of animal complexity -- derived through the extraordinary decade-long work on sea urchin and fruit fly -- and prepares us for the breadth-taking goal of the next decade of research. *"The time is almost upon us when we will be able to build cis-regulatory modules and network subcircuits in the laboratory and test their developmental operation in living systems."* With such an *engineering* mission in mind, it is not surprising that the chapters of the book would appear familiar to computer scientists and engineers. Eric Davidson is presenting to us, for the first time, the "Biological computer" of cell regulation. The first four chapter themes read as in a computer systems textbook: regulatory information processor I/O, designs of processors, regulatory state and regulatory time and space, and networks of processors. Chapter five concludes the book by delivering a paradigm-shift revision of evolutionary theory, an information processing -- survival of the computational most fit, paradigm. *"Considering evolution of body plans in terms of network circuitry, as a history of assembly of grades of network organization, is to transform this vexed subject into a prospectus for laboratory research."*

In the post genome-sequence era, this is an epoch making book marking the change of tide to principled, quantitative biology reality. As the first biology textbook grounded in causality-focused and genomics-based systems, and with its symbiosis of insights from experimental biology, biochemistry, physics, computers science, logic, and mathematics, *The Regulatory Genome* is poised to become the definitive text for most popular biology, engineering, and computational biology courses. Our teacher and mentor, Eric Davidson, is bringing all of us together biologists, physicists, biochemists, engineers, and computer scientists, like in his CalTech Laboratory, in a research renaissance movement towards the quest for the functional meaning of DNA. From such research will ultimately come, by experimental demonstration, the revelation of the much searched laws of regulatory Biology. The sea urchin genome, the First Genome of cell regulation, is indeed *The Regulatory Genome.*