The Phenotype-Genotype-Phenotype (PGP) Map

Nayely Velez-Cruz and Dr. Manfred Laubichler

Overview

1. The role of the genotype to phenotype map in current evolutionary theory
2. Origins of phenotypic variation and the insufficiency of the genotype to phenotype map
3. A novel proposal: phenotype→genotype→phenotype map and how to approach the temporal units of evolution

Temporalities of Evolution

- The continuity of the germ plasm (Weismann and after) and the separation of germ plasm and soma
- Genes as the units of heredity that cross the generational boundary
- Phenotypes are produced anew in each generation
- This continuity of genes is the justification for the formal structure of evolutionary theory based on dynamical models of genetic change

Genotype-Phenotype Map

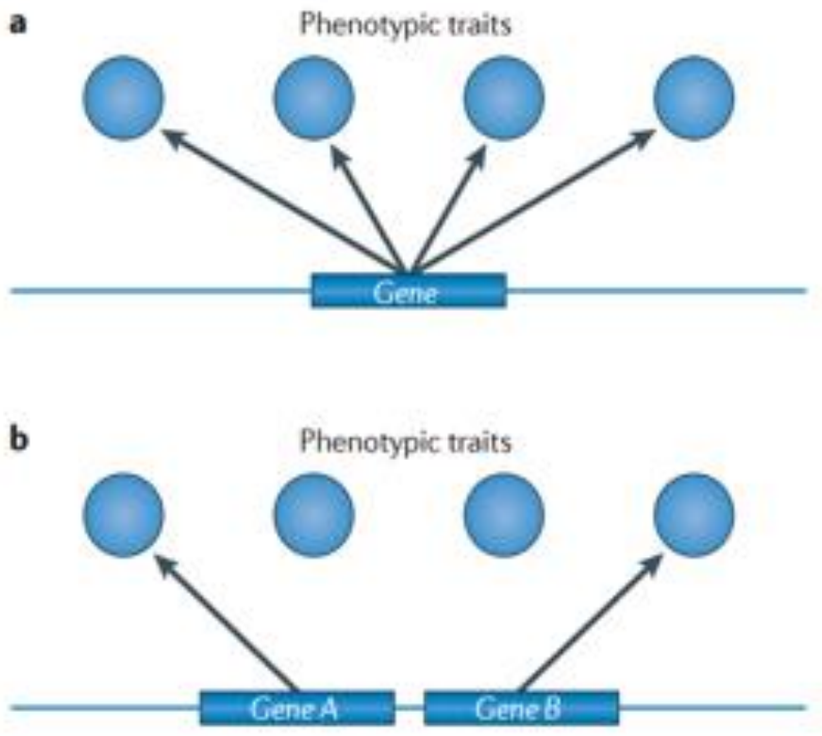

Figure 1. Genotype-phenotype map (Wagner & Zhang, 2011). a) one gene mapped to multiple traits, b) two genes each mapped to one trait

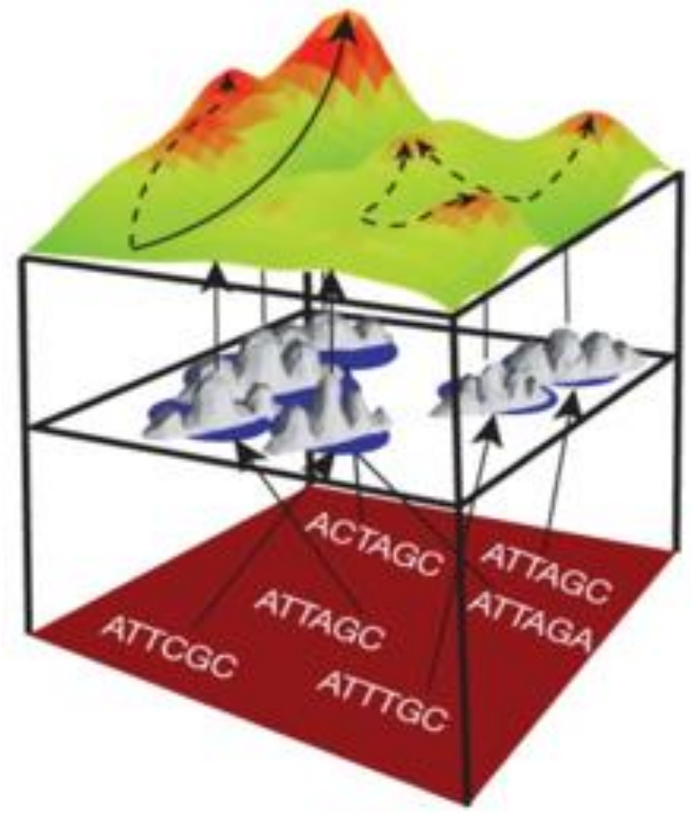

Figure 2. Genotype-phenotype map via the adaptive landscape model (Salazar-Ciudad & Marín-Riera, 2013). From bottom to top layer: genotype space, phenotype space, fitness landscape

Genotype-Phenotype Map in Evolutionary Theory

- Adaptive dynamics as primary explanation for phenotypic evolution
  - Neo-Darwinian assumption: genetic mutation → phenotypic variant → fitness differences → selection
- Developmental mechanisms are secondary; G-P map in each generation

Origins of Phenotypic Variation

LETTER

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Evolution of *Hoxa11* regulation in vertebrates is linked to the pentadactyl state

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Clustering of Tissue-Specific Sub-TADs Accompanies the Regulation of *HoxA* Genes in Developing Limbs

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The origin of Metazoa: a unicellular perspective

Arnau Sebé-Pedrós[1], Bernard M. Degnan[2] and Iñaki Ruiz-Trillo[3–5]

Abstract | The first animals evolved from an unknown single-celled ancestor in the Precambrian period. Recently, the identification and characterization of the genomic and cellular traits of the protists most closely related to animals have shed light on the origin of animals. Comparisons of animals with these unicellular relatives allow us to reconstruct the first evolutionary steps towards animal multicellularity. Here, we review the results of these investigations and discuss their implications for understanding the earliest stages of animal evolution, including the origin of metazoan genes and genome function.

Loss and Re-emergence of Legs in Snakes by Modular Evolution of *Sonic hedgehog* and *HOXD* Enhancers

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A single three-dimensional chromatin compartment in amphioxus indicates a stepwise evolution of vertebrate Hox bimodal regulation

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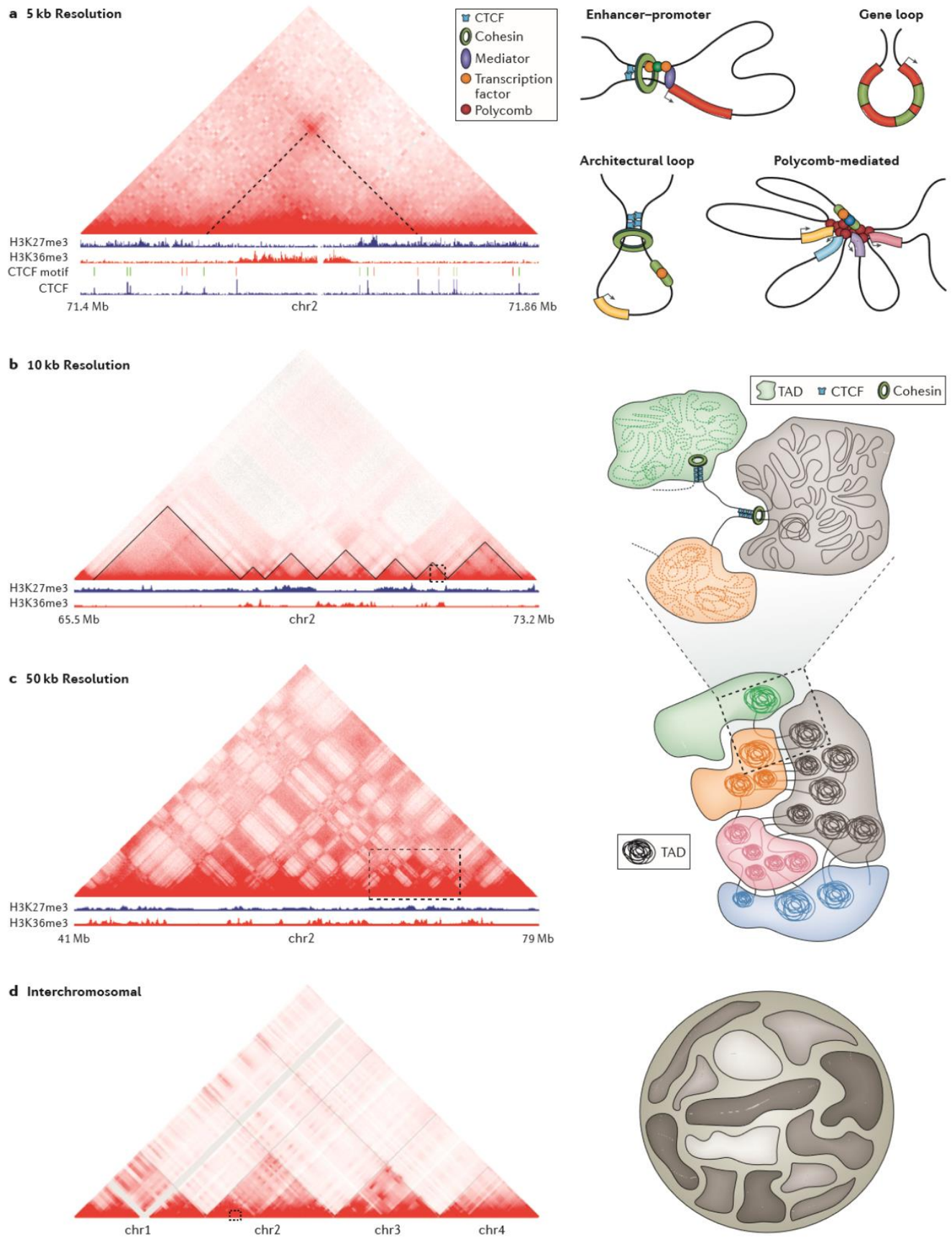
Organization and function of the 3D genome

Boyan Bonev and Giacomo Cavalli

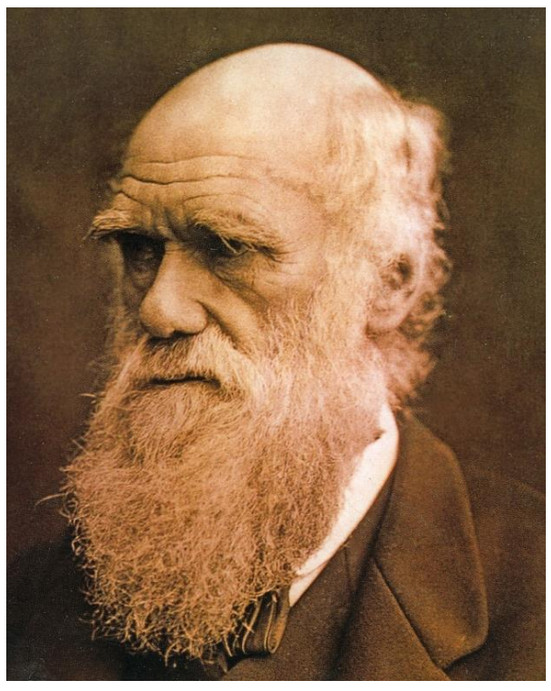
Abstract | Understanding how chromatin is organized within the nucleus and how this 3D architecture influences gene regulation, cell fate decisions and evolution are major questions in cell biology. Despite spectacular progress in this field, we still know remarkably little about the mechanisms underlying chromatin structure and how it can be established, reset and maintained. In this Review, we discuss the insights into chromatin architecture that have been gained through recent technological developments in quantitative biology, genomics and cell and molecular biology approaches and explain how these new concepts have been used to address important biological questions in development and disease.



Life is complicated

Changing our approach…developmental mechanisms primary and adaptive dynamics secondary

How are variant phenotypes constructed? (origins of innovation)



Charles Darwin

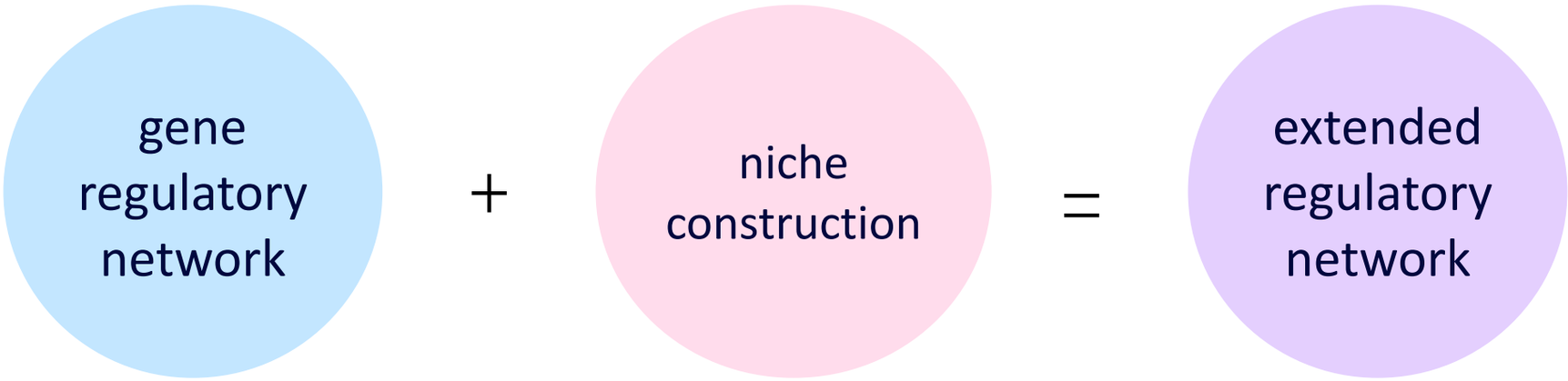
Theodor Boveri

Manfred Laubichler

PGP Map

Theoretical Framework for Phenotypic Evolution

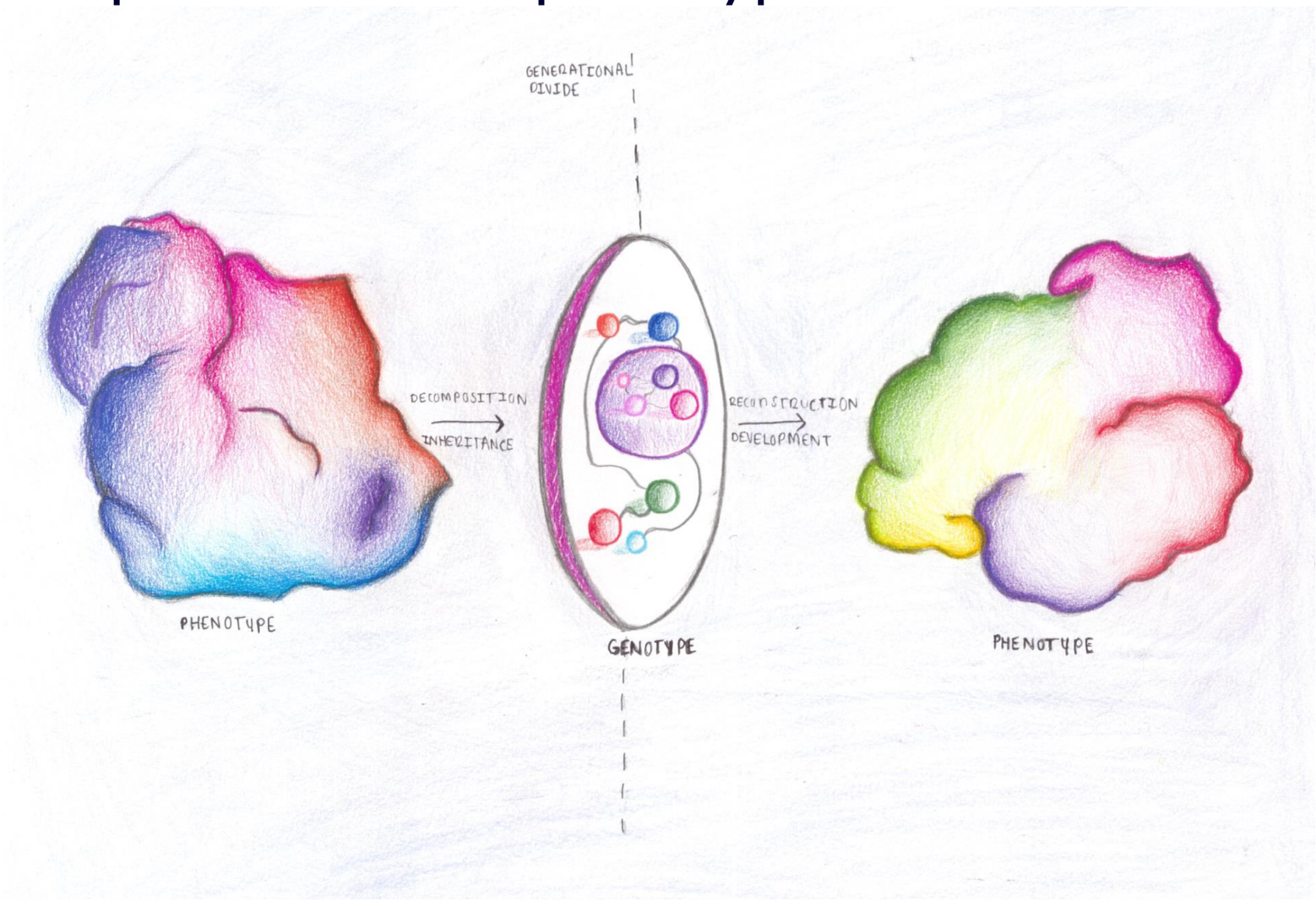
Laubichler, M. D., & Renn, J. (2015). Extended evolution: A conceptual framework for integrating regulatory networks and niche construction. Journal of Experimental Zoology Part B: Molecular and Developmental Evolution, 324(7), 565-577.



- Niche (aspects of environment that causally affect interactions) + internal regulatory network
  - Links between niche and internal regulatory network are causal relations between environmental resources (nodes) and resources of internal network structure (nodes)
  - Information processing: internalization of externally-received information (signals) followed by externalization of internalized information; can capture these dynamics through iterations of the P-G-P map; self-update process
  - Need a multiscale approach

Extending the Life Cycle

- First, a phenotype, as part of its extended life cycle, produces complex units of inheritance
- Units of inheritance combine to form the next generation and interact to produce a new phenotype



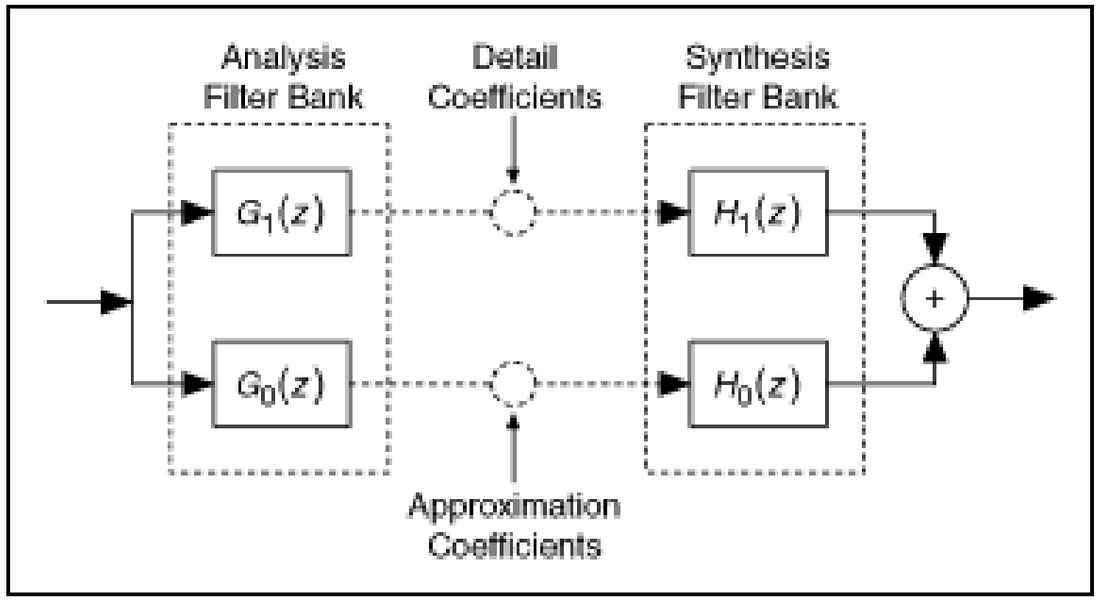
How are units of inheritance formed as part of the extended life cycle?

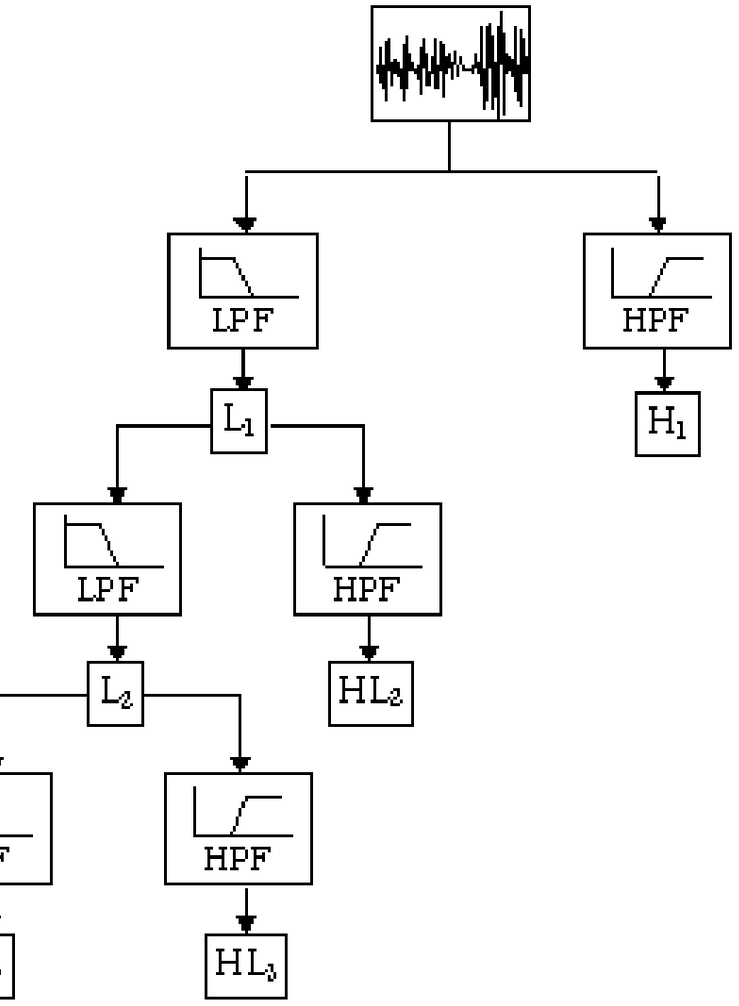
- DNA: molecular mechanisms of copying, mutation and recombination; already have a mathematical framework to model their dynamics
- In case of more complex units of inheritance—look at cytoplasm as source of maternal effects as one of those additional units of inheritance—we are beginning to uncover the developmental mechanisms, oogenesis in this case
- But we have no adequate formal apparatus to analyze the evolutionary dynamics of those

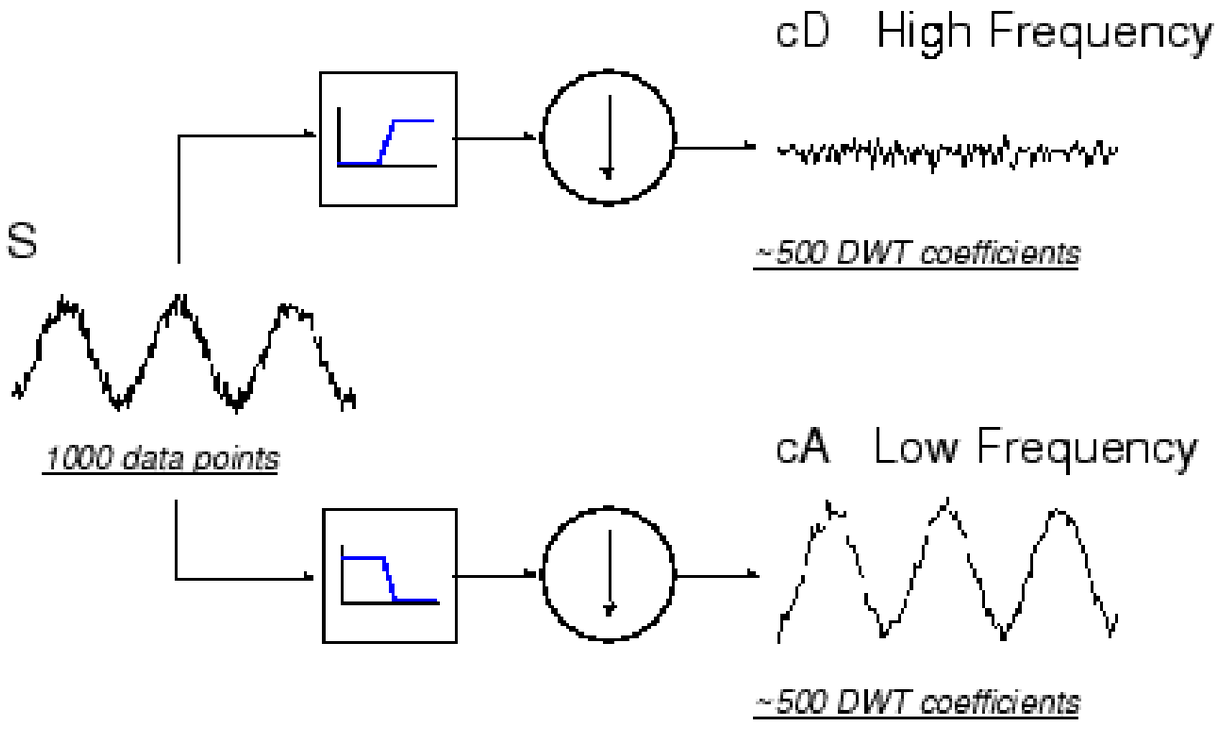
How is the PGP map different from the GP map?

- PGP map introduces a different temporality of evolution
- G-P map exists within a generation; PGP map spans generations
- PGP map, situated within its extended regulatory network, not just genes, as unit of evolution

I/O Maps via Signal Processing



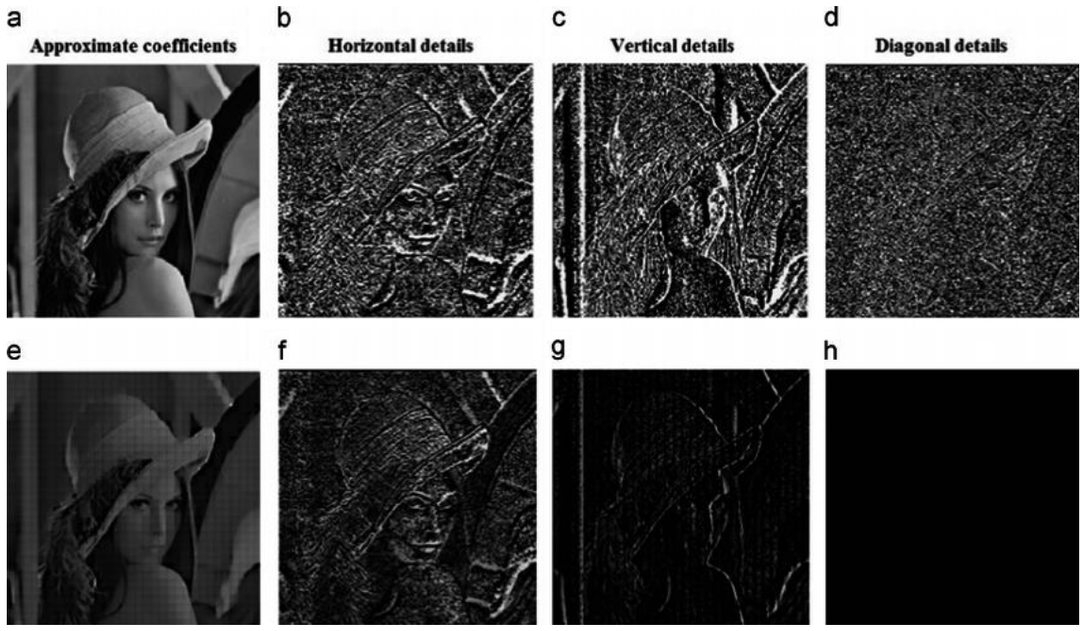


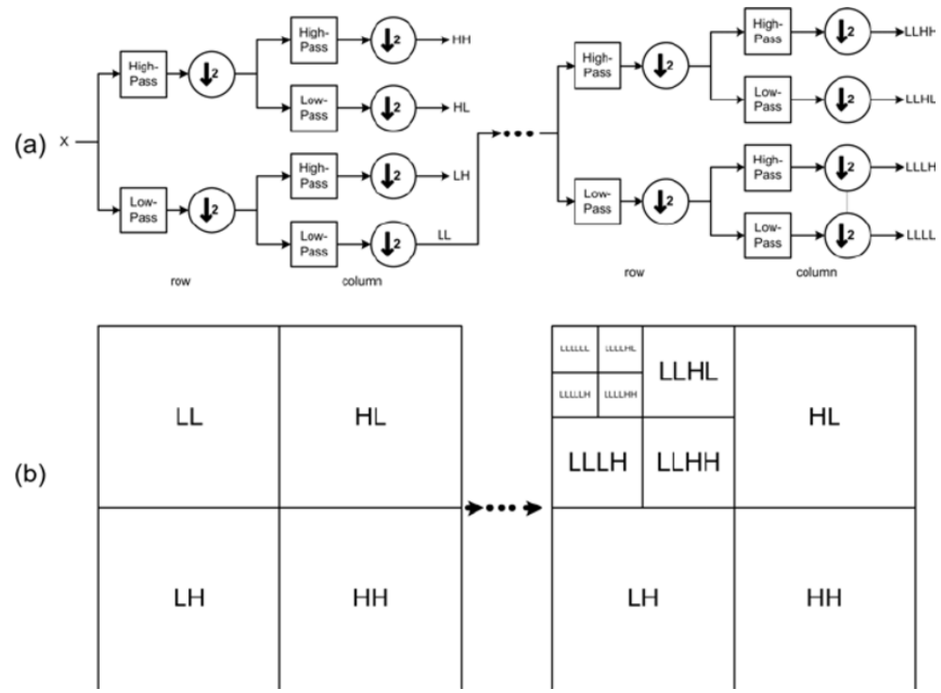


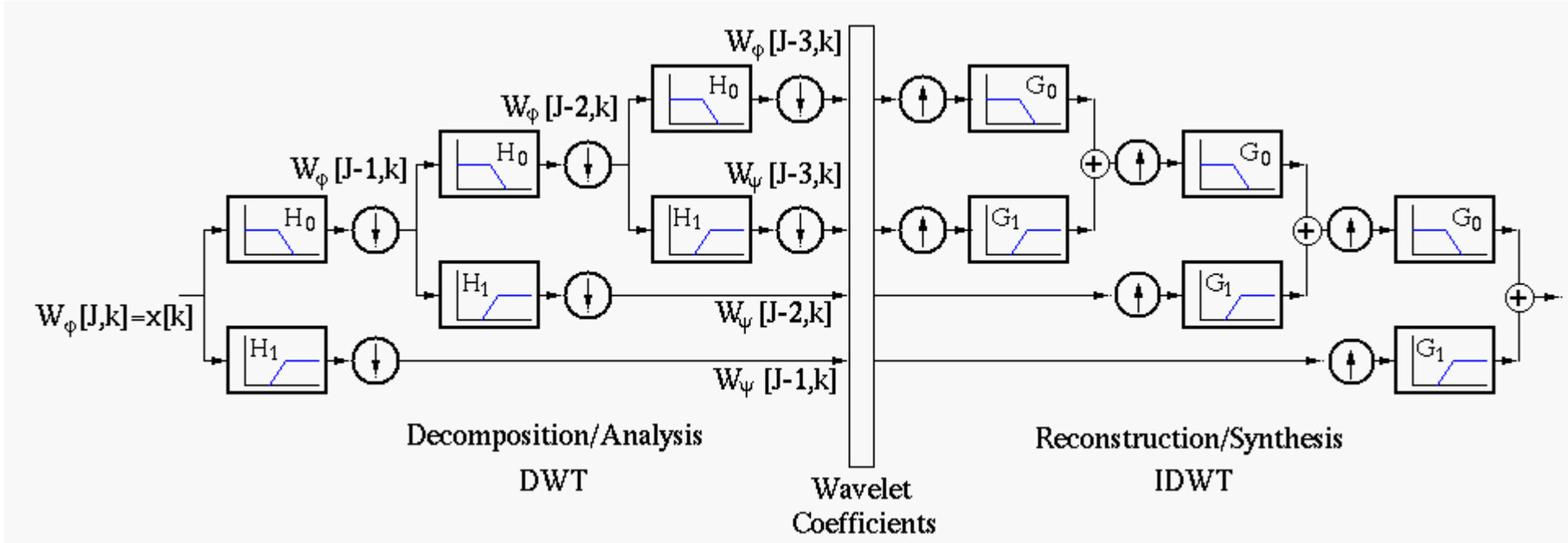
Wavelet

a wave-like oscillation which has its energy concentrated in time or space

Wavelet Multiresolution Analysis







From an extended regulatory network to an extended life cycle

"For now we see that this phenomenon of so-called goal-directedness is not one of life's fundamental characteristics at all. In the life of an amoeba, there is only a cycle, not a goal; there is no special state about which one could say that all other states exist because of it"

-Theodor Boveri, 1906

The EXTENDED Life CYCLE

PHENOTYPE

$f : X \to Y$ DIFFEOMORPHISM!

$f^{-1} : Y \to X$

DECOMPOSITION

n-dimensional manifold at scale j-1

submanifold at scale j

locally homeomorphic to a region in Euclidean space

U, V, p, γ, γ^{-1}, ϕ, ϕ^{-1}

topology $(X, \mathcal{T}_X, \mathcal{A})$

topological space, atlas

$t_1 \dots t_n$, ω_1, ω_2, ω_3, $\gamma(U)$, $\gamma(p)$, Ψ, Ψ^{-1}

$\phi(p)$, $\gamma \circ \phi^{-1}$, $\phi \circ \gamma^{-1}$

GENOTYPE

RECONSTRUCTION

DECOMPOSITION

$(Y, \mathcal{T}_Y, \mathcal{B})$

$\Lambda(Q)$, $\Lambda(d)$, Λ, Λ^{-1}

Q, d, R

$\Omega(d)$, $\Omega(R)$, Ω, Ω^{-1}

$\Lambda \circ \Omega^{-1}$, $\Omega \circ \Lambda^{-1}$

GENOTYPE

RECONSTRUCTION

PHENOTYPE

Thanks ☺