

Introduction to differentiation waves

Part 2. The evo-devo of epigenetic landscapes as differentiation trees

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The differentiation tree as the embodiment of Conrad Waddington's Epigenetic Landscape

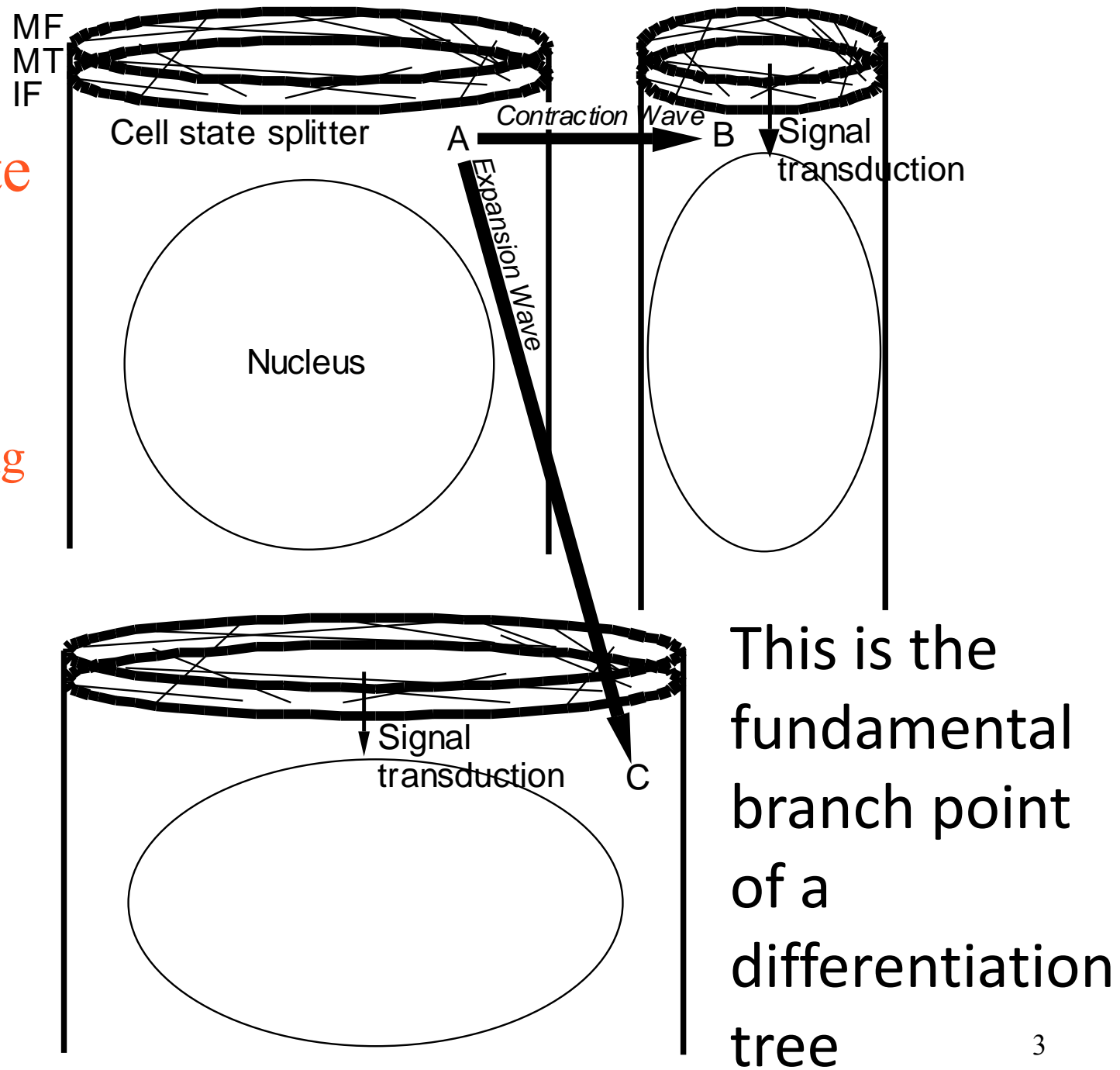
- I decided for this week to follow up on Melinda Fagan's talk last week:
- "Waddington redux: simple abstract models and integrative biological explanations"
- Melinda gave a most detailed exposition of Waddington's model for development
- I will show how it can be made concrete by mapping its features to the differentiation tree

The Cell State Splitter

MF =
microfilament ring

MT =
annular apical
microtubule mat

IF =
intermediate
filament ring



Differentiation waves

- There are two kinds of differentiation waves:
- **Contraction wave**
- **Expansion wave**
- Each tissue appears to be split into two new tissues by a pair of differentiation waves, one of which is a contraction wave, the other an expansion wave

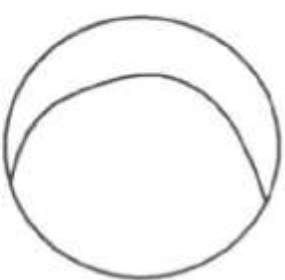
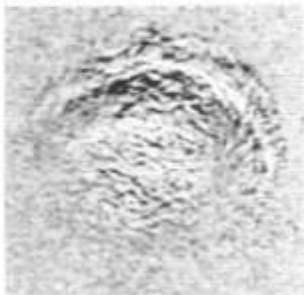
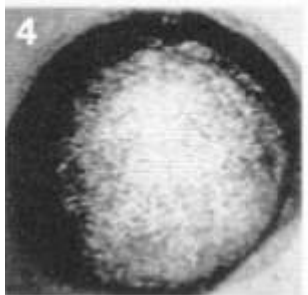
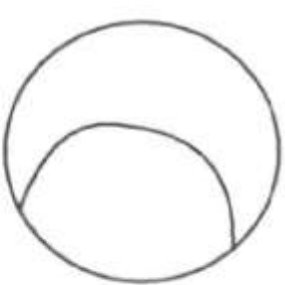
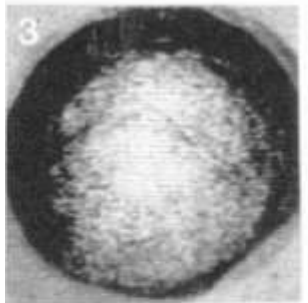
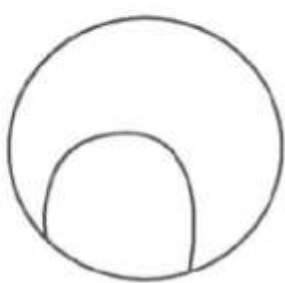
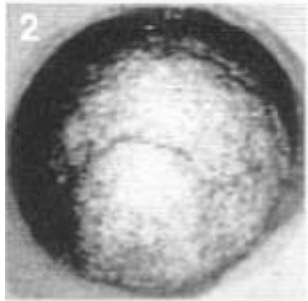
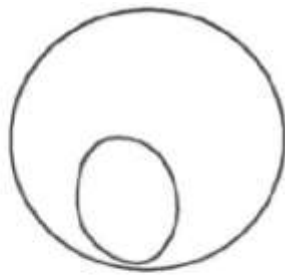
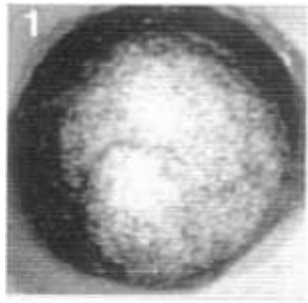


Image Processing
At hourly intervals,
the image was
digitally subtracted
from the one
5 minutes earlier,
showing the moving
ectoderm
contraction wave.

Brodland, G.W., R. Gordon, M.J. Scott, N.K. Björklund, K.B. Luchka, C.C. Martin, C. Matuga, M. Globus, S. Vethamany-Globus & D. Shu (1994).
Furrowing surface contraction wave coincident with primary neural induction in amphibian embryos. *J. Morphol.* **219**(2), 131-142.

Clay model of axolotl
ectoderm contraction wave:

<http://youtu.be/rfiYtwDMr7o>

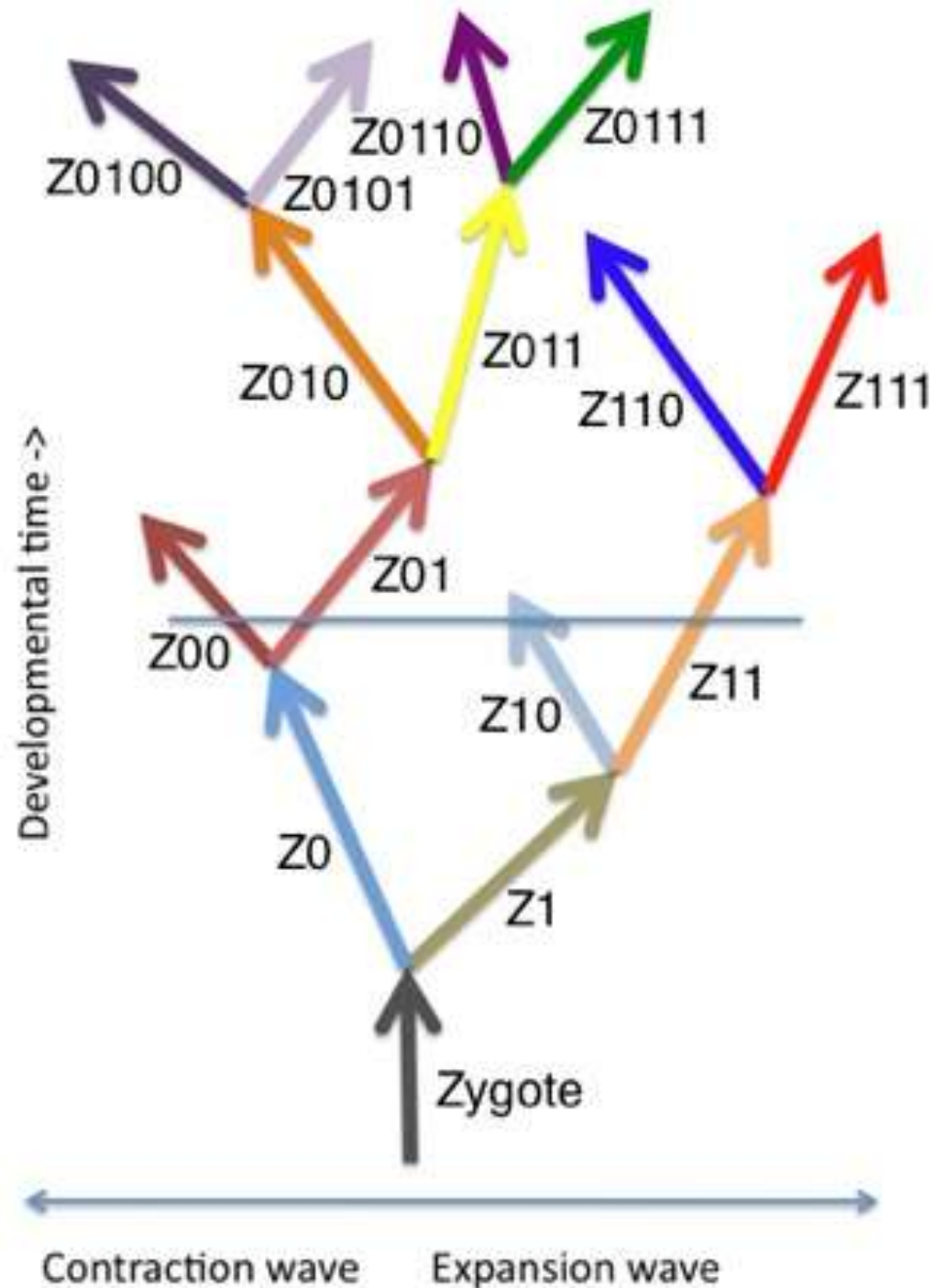
The same model has been rotated to different angles and the contraction wave shown over time. Loop the movie many times to watch each portion and the progression of the wave.

The Differentiation Tree

Each branch represents a distinct cell type

Note binary differentiation code

Natalie K. Gordon & Richard Gordon (2012). Embryogenesis Explained [in preparation]. Singapore: World Scientific Publishing Company.

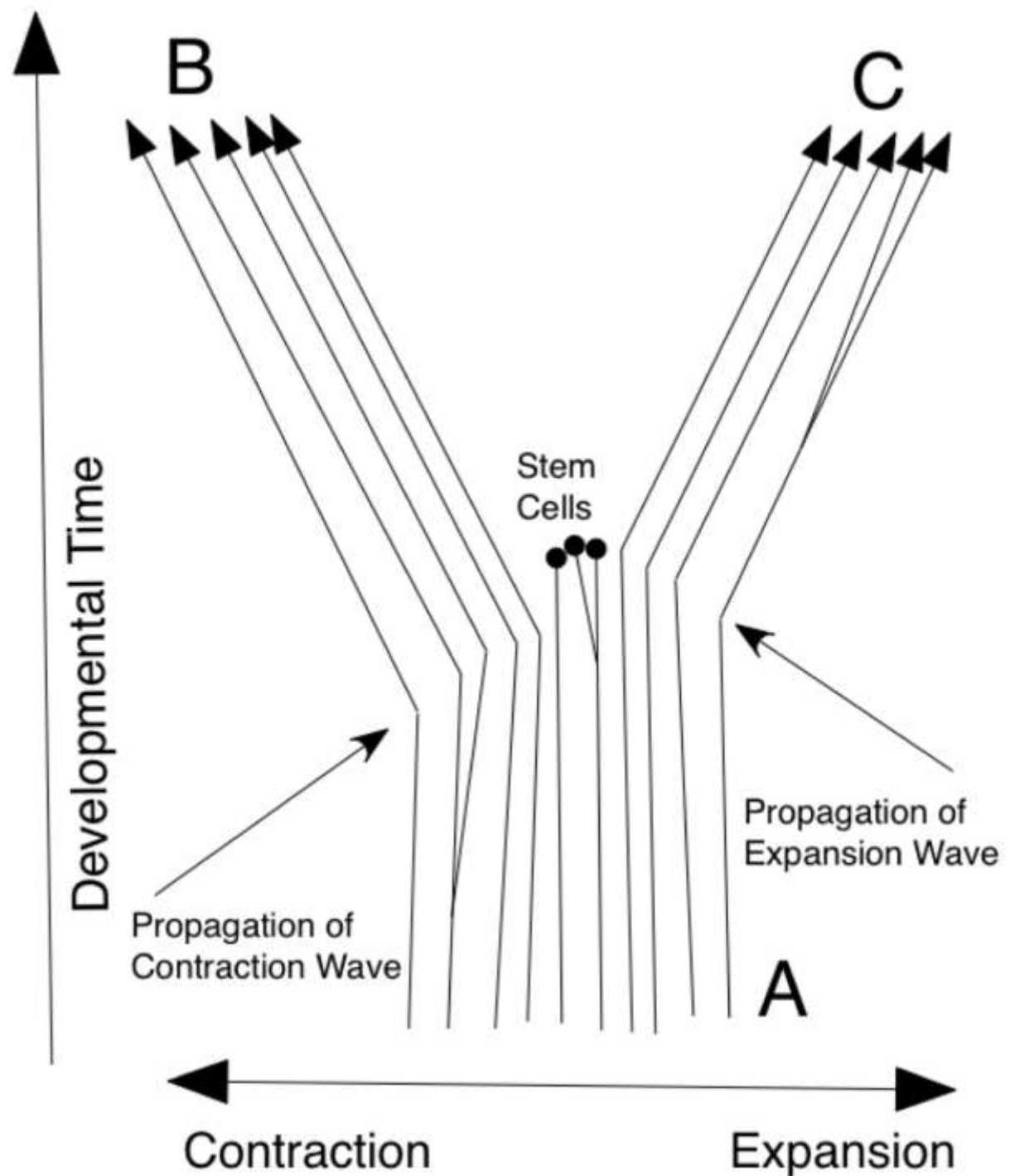


Lineage tree vs Differentiation tree

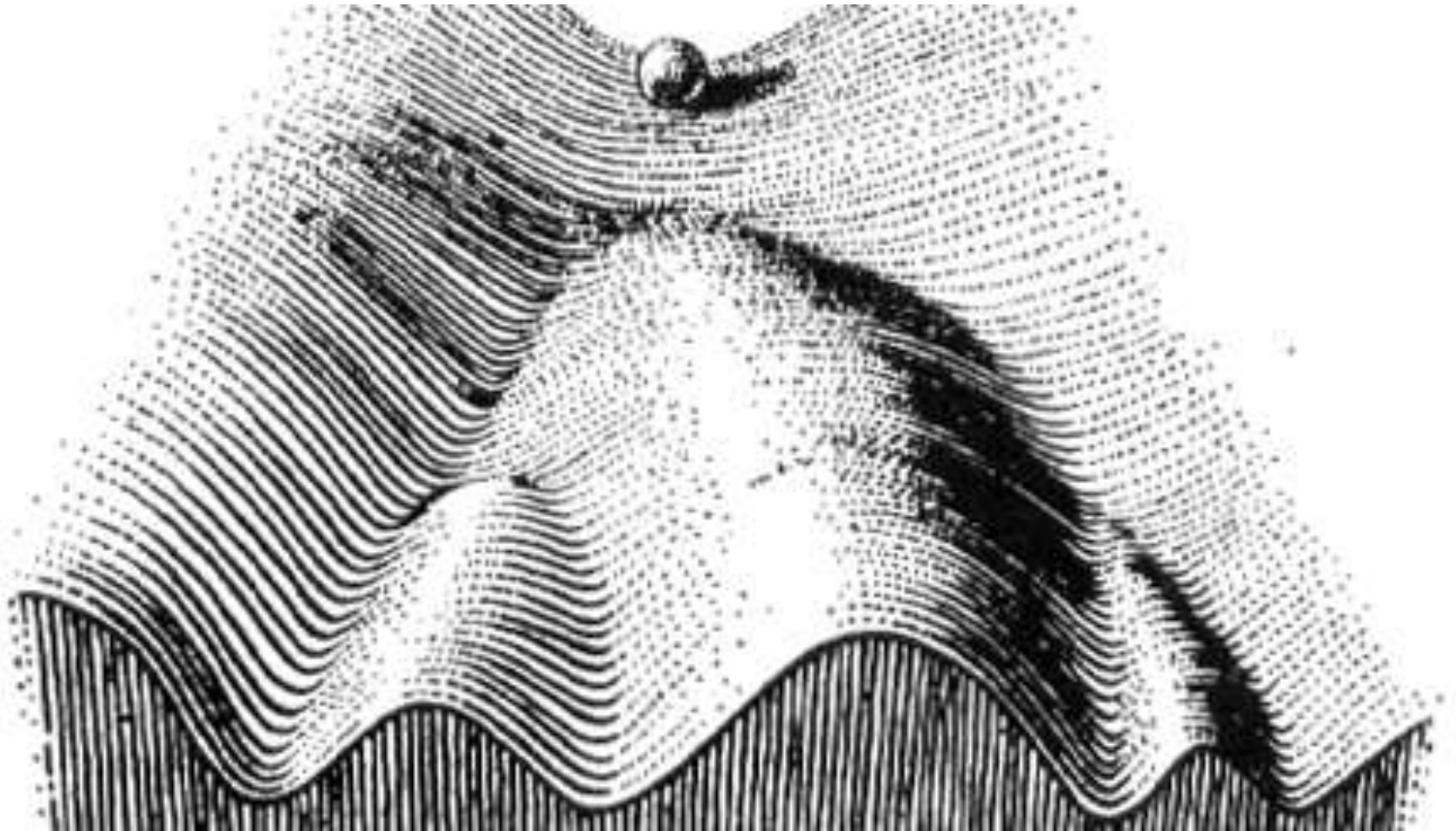
- The lineage tree for an embryo is a tree that shows every cell division and tracks every cell, from zygote to adult
- The differentiation tree “bundles” groups of branches of the lineage tree of the embryo together
- The bundling is according to participation in contraction or expansion waves

A bundle of cells of type A is split into two bundles of cells B and C by a pair of differentiation waves

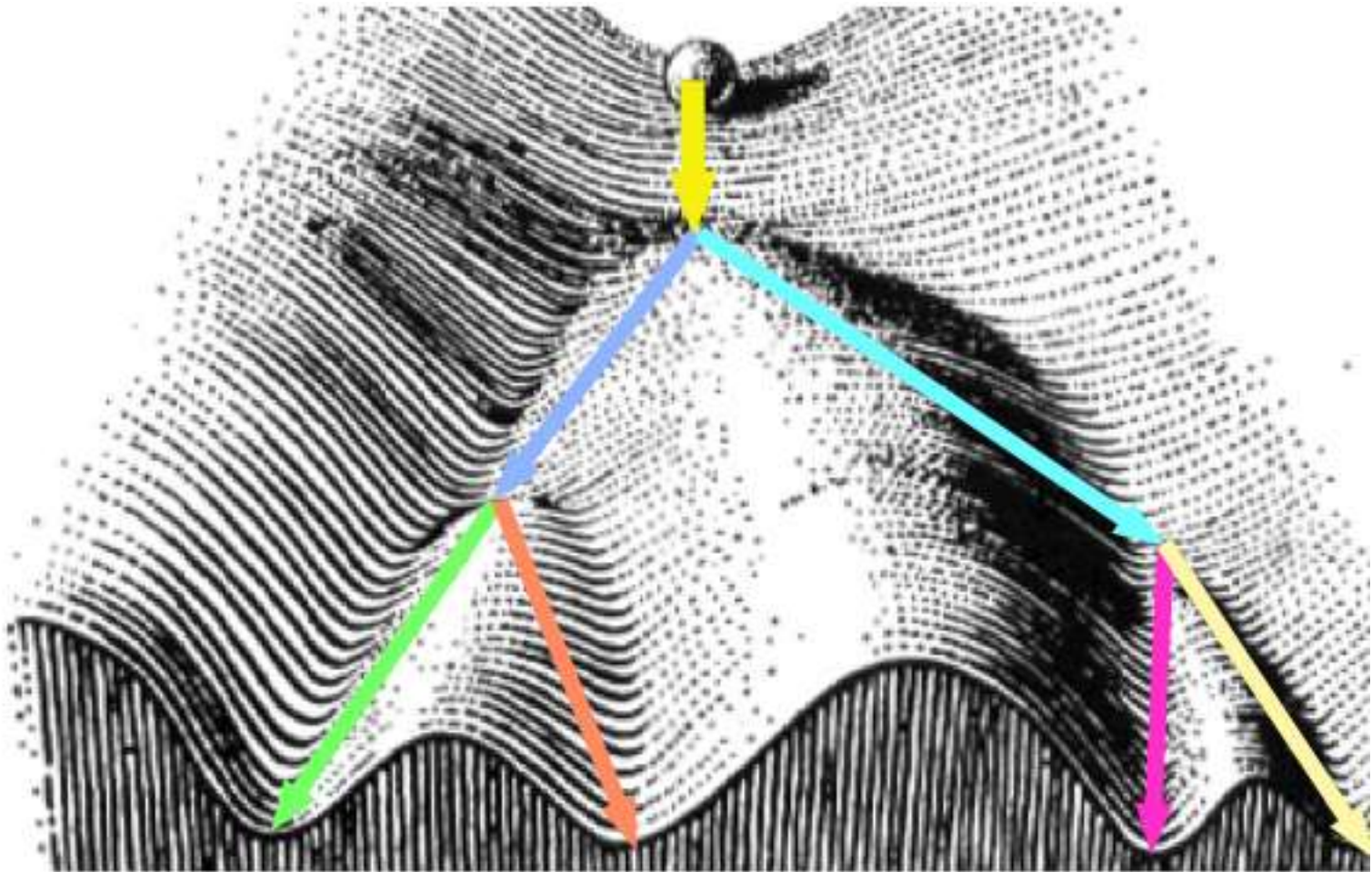
Gordon, R. (2011). Epilogue: the diseased breast lobe in the context of X-chromosome inactivation and differentiation waves. In: *Breast Cancer: A Lobar Disease*. Ed.: T. Tot. London, Springer: 205-210.



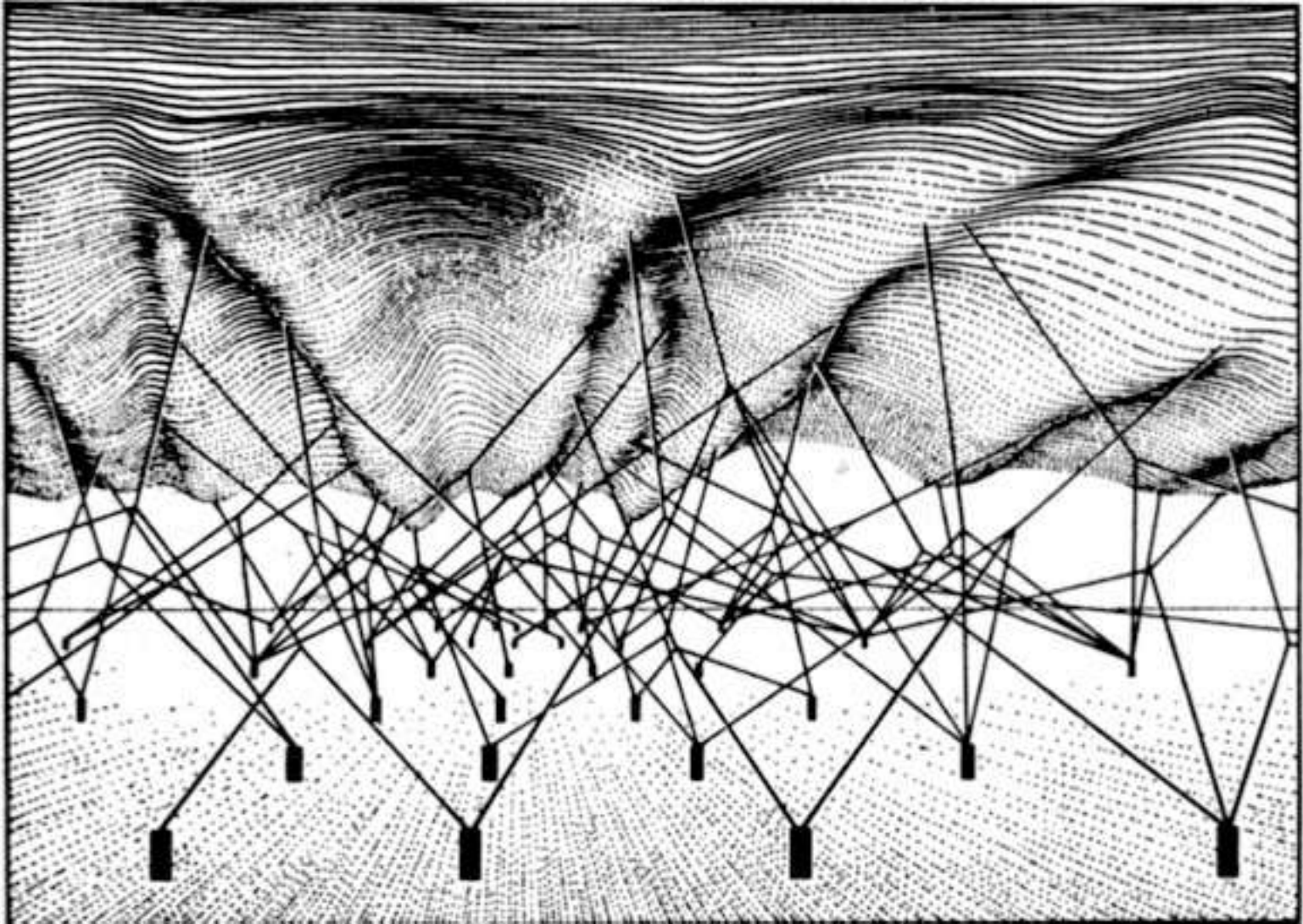
Waddington's Epigenetic Landscape



Epigenetic landscape
overlain with its differentiation tree
<-Contraction:Expansion->



The struts: genetic controls underneath the epigenetic landscape



In the differentiation tree, genes are activated in gene cascades within each edge = cell type

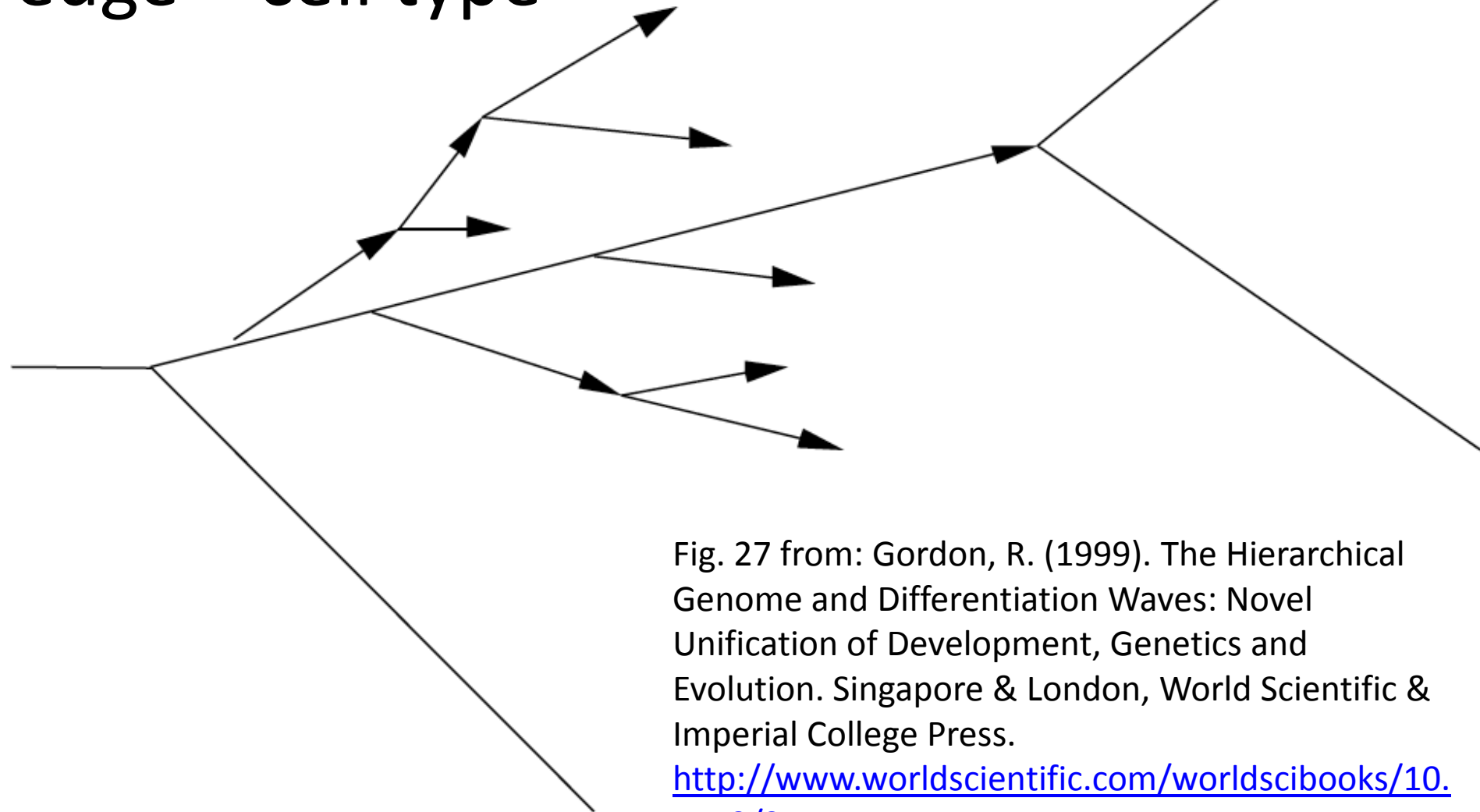
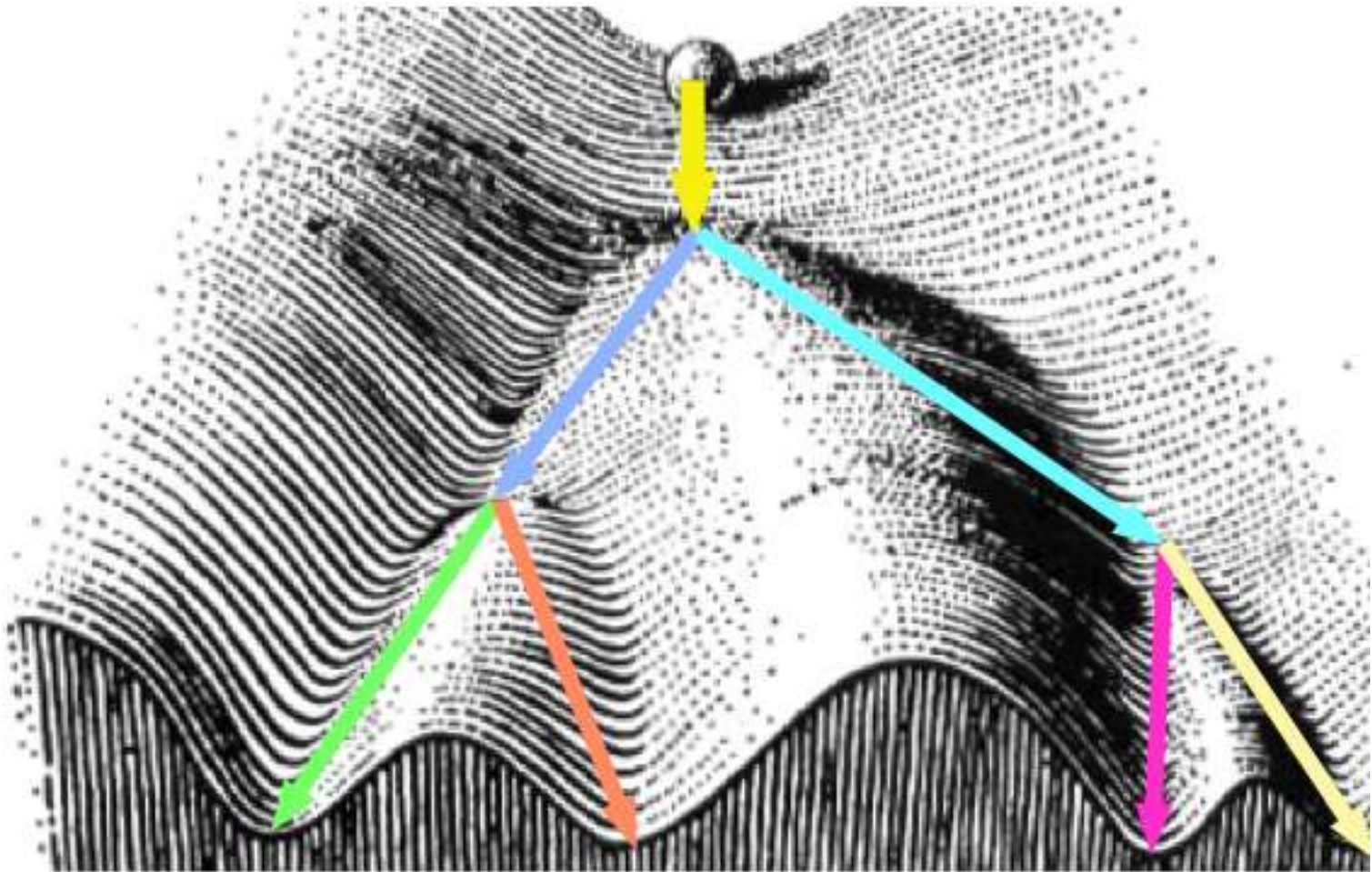
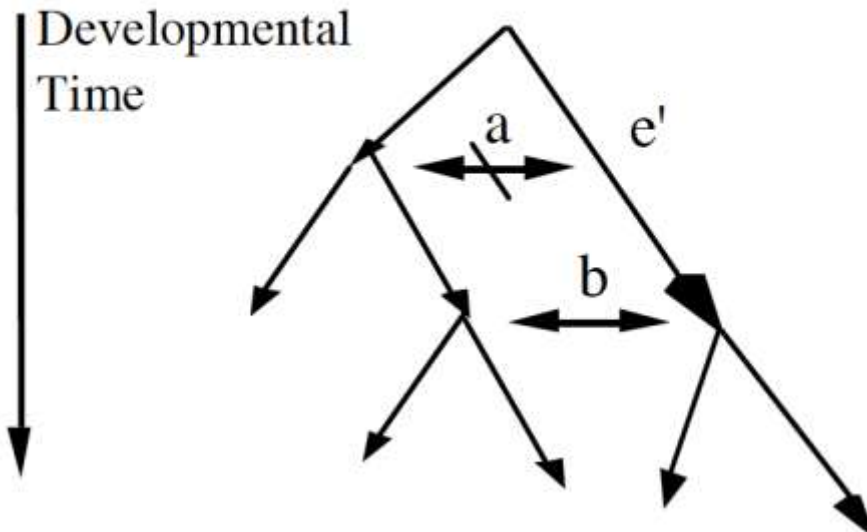
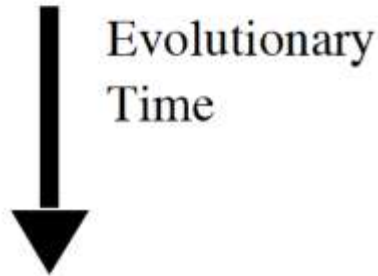
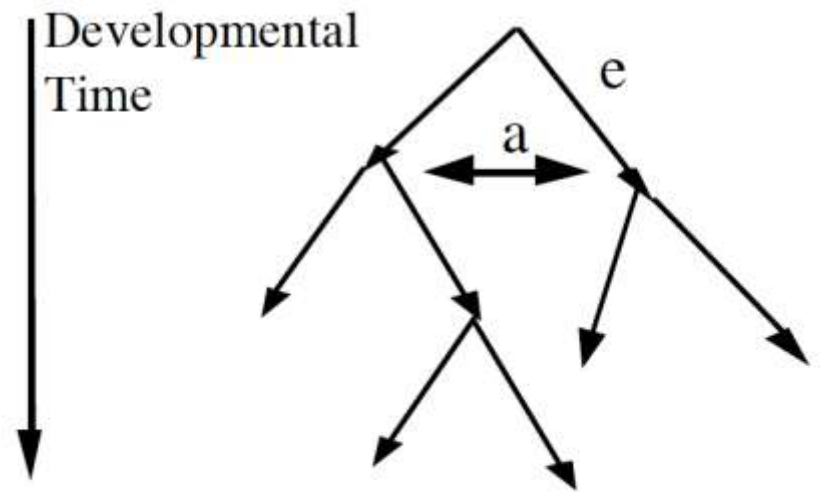


Fig. 27 from: Gordon, R. (1999). The Hierarchical Genome and Differentiation Waves: Novel Unification of Development, Genetics and Evolution. Singapore & London, World Scientific & Imperial College Press.

<http://www.worldscientific.com/worldscibooks/10.1142/2755>

So what changes the hills and valleys of the epigenetic landscape with differentiation trees?





Heterochrony, or timing changes: stretching of one portion of the differentiation tree with respect to another. Inductive relationships can shift

Differences

- Differentiation is not a matter of genes changing the undulations of an overlying surface
- It is rather a matter of two alternative gene cascades being readied for response to differentiation waves
- The parameters of those gene cascades can change

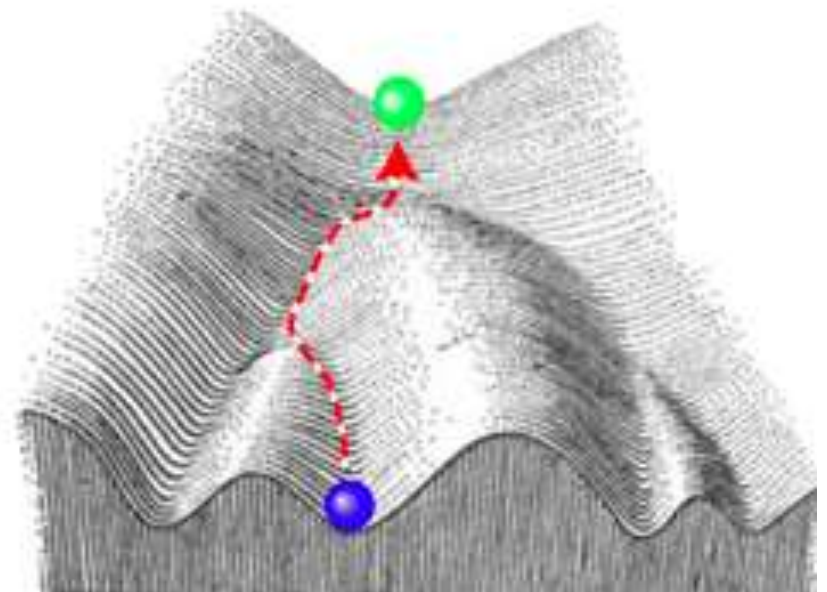
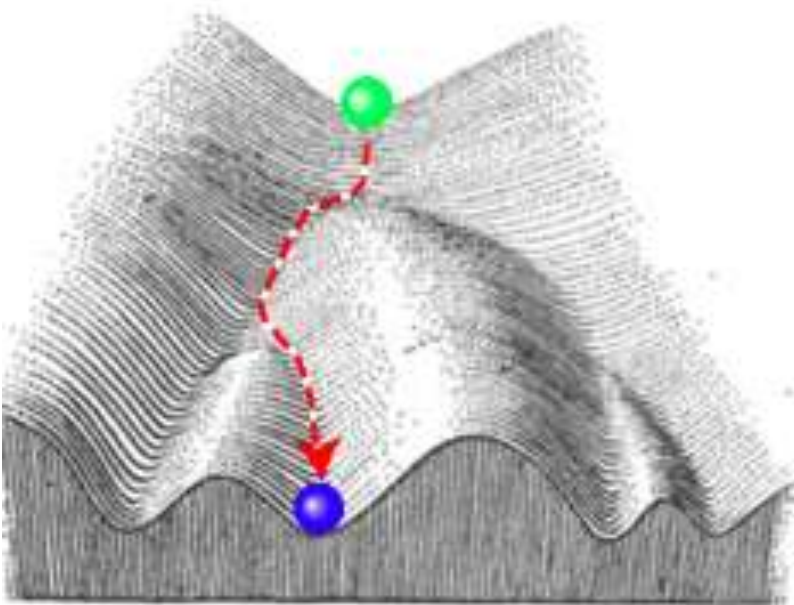
Differentiation Differences

- There is no spatial component to the epigenetic landscape
- In other words, there is nothing in Waddington's model that determines which way a cell goes when it hits a point of bifurcation
- In a differentiation tree, the cell goes one way if it participates in a contraction wave, and the other way if it participates in an expansion wave
- The waves provide the spatial aspect of differentiation

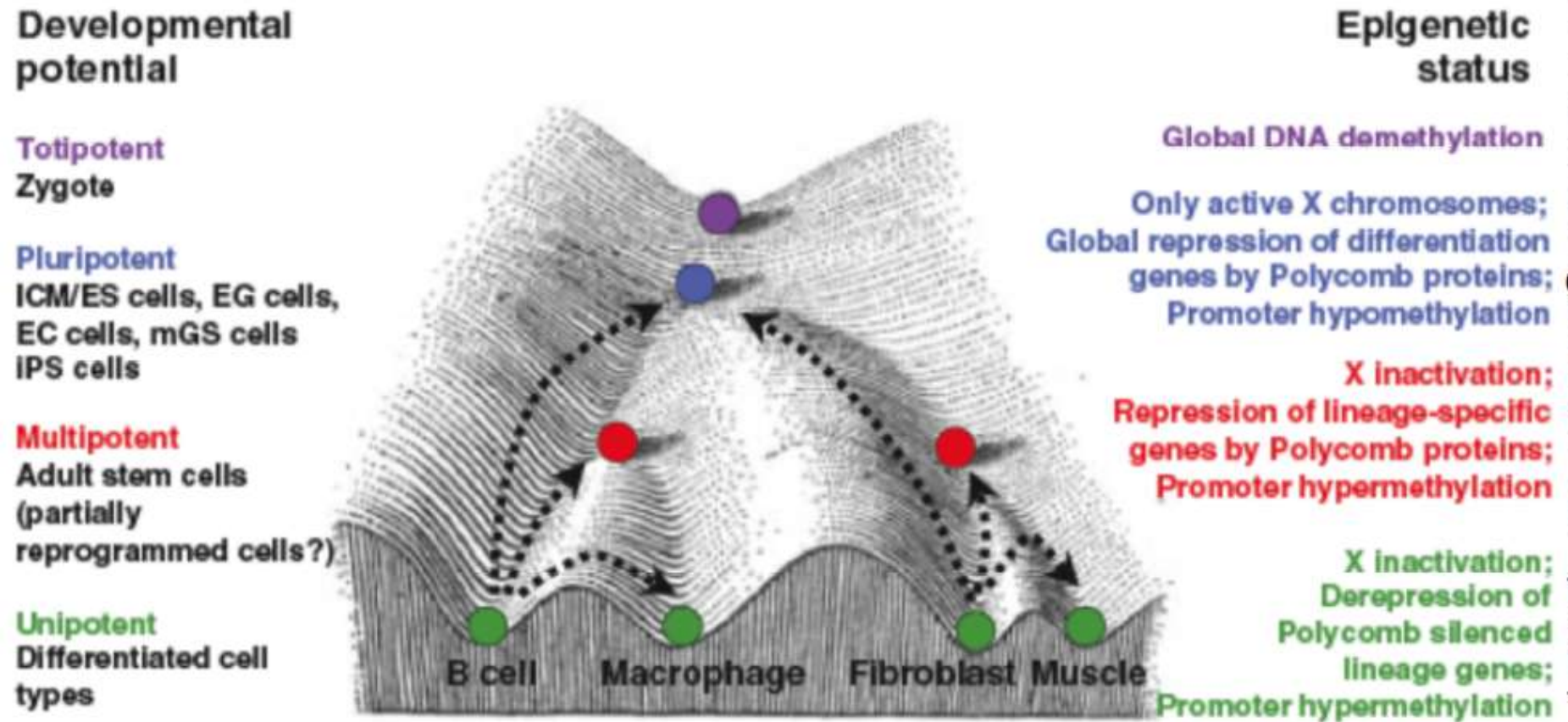
Dedifferentiation

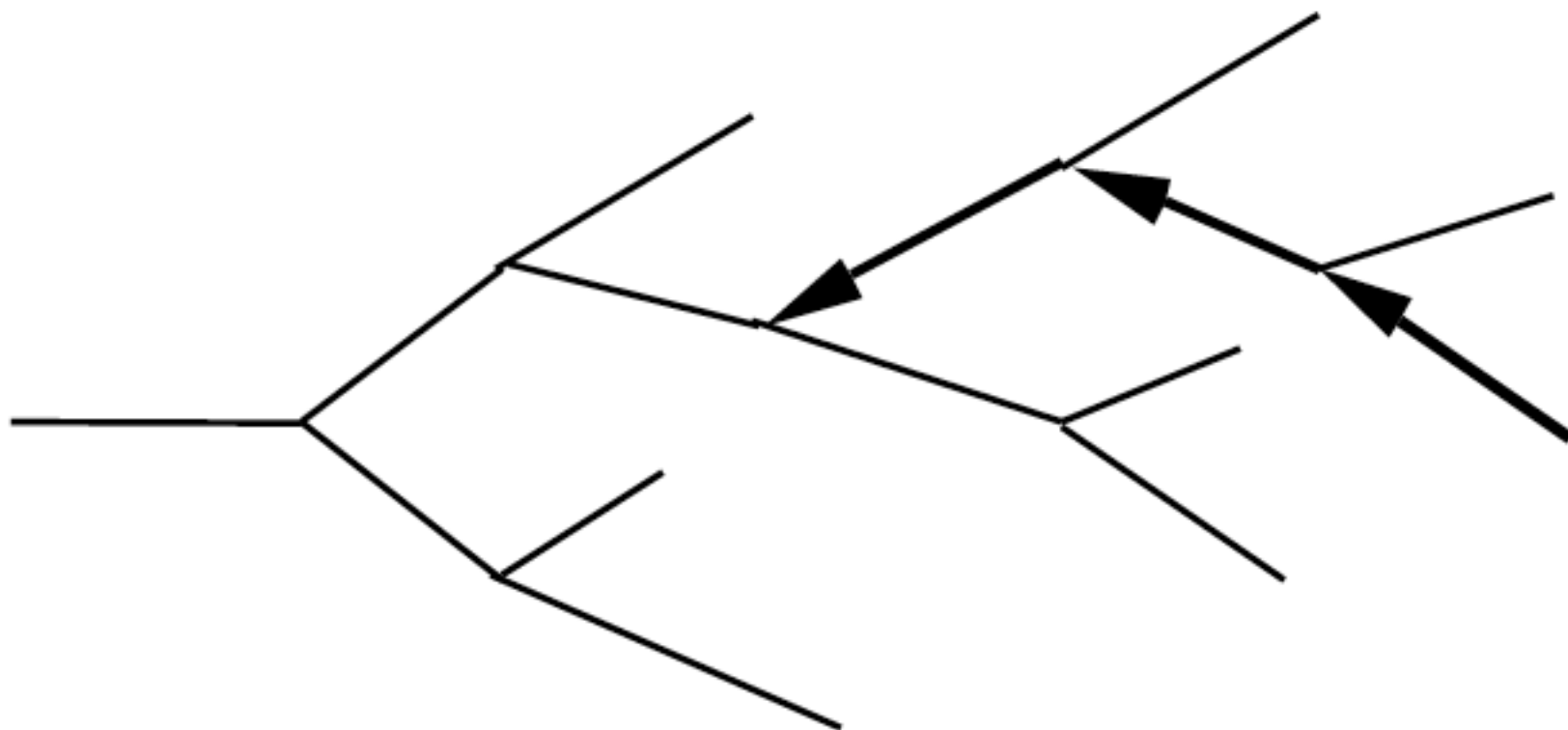
Development

Pluripotent reprogramming
(SCNT, iPS)

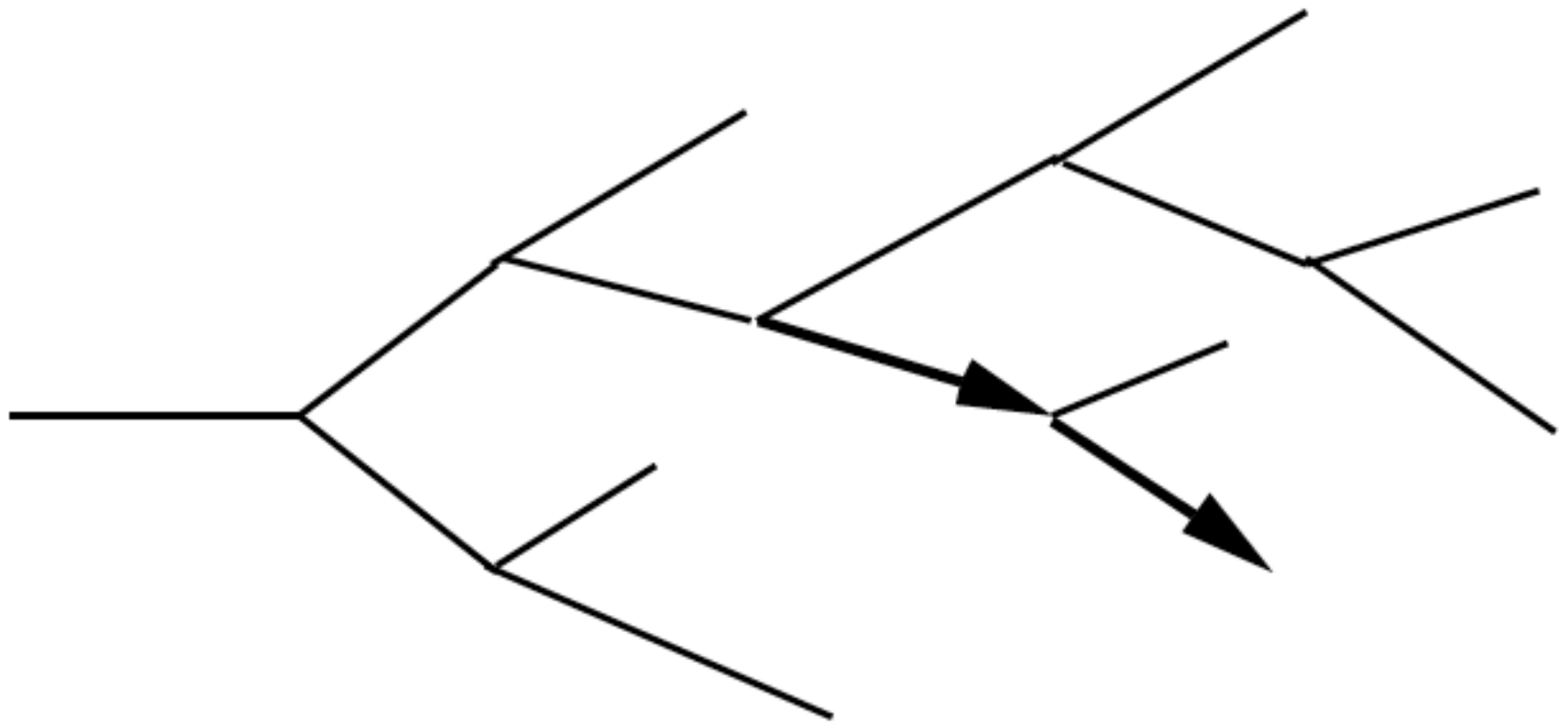


Dedifferentiation and Transdifferentiation



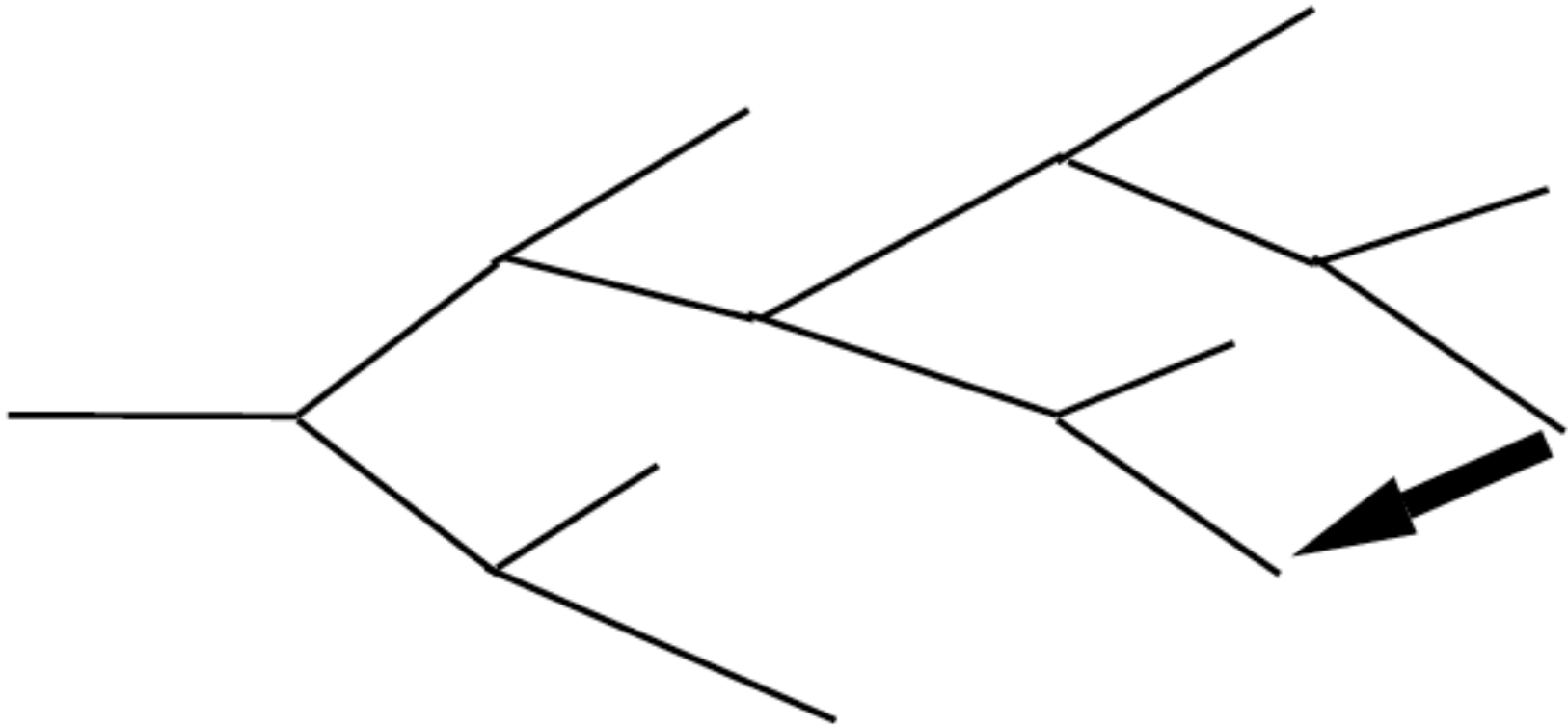


Dedifferentiation



Followed by Redifferentiation

Transdifferentiation



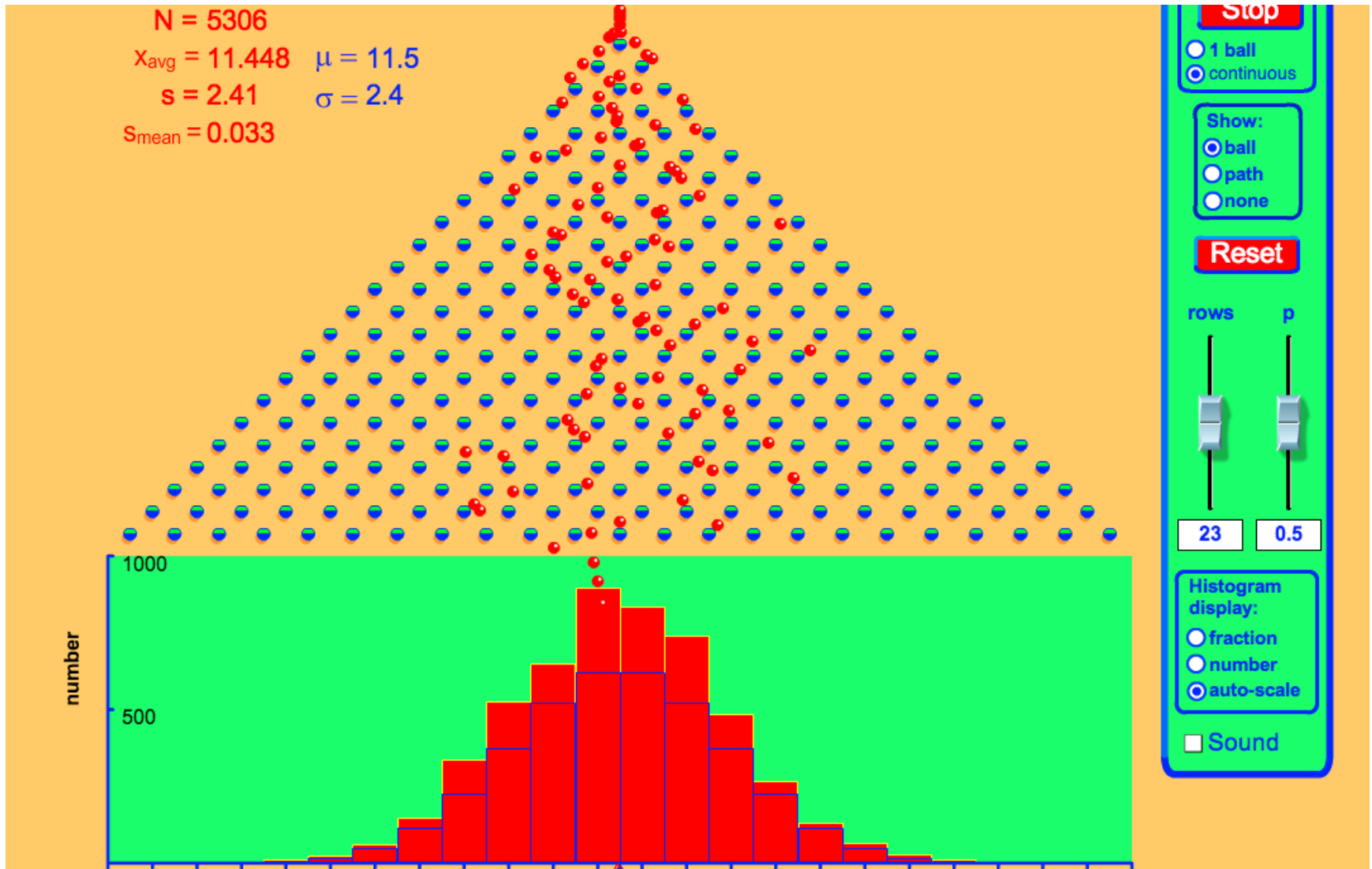
An Alternative:

Jumping across the Differentiation Tree

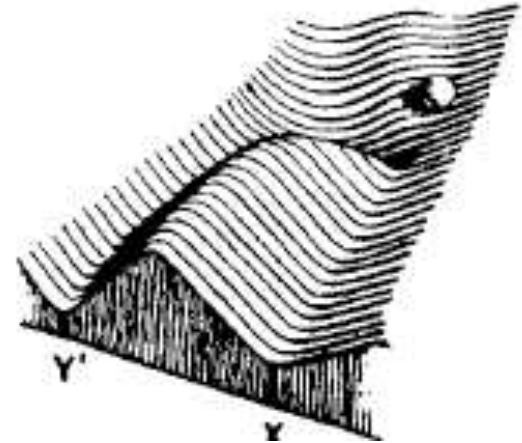
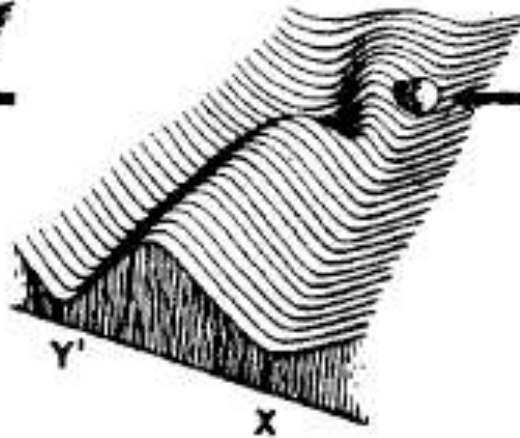
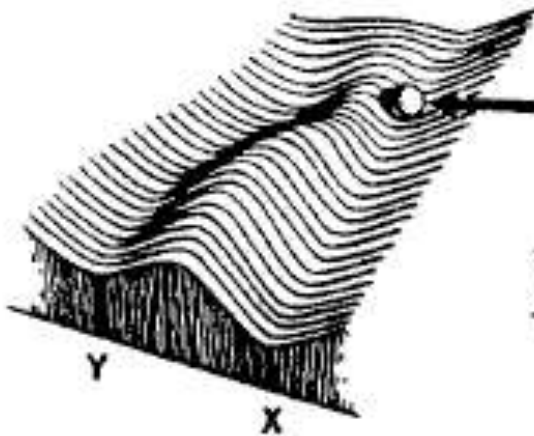
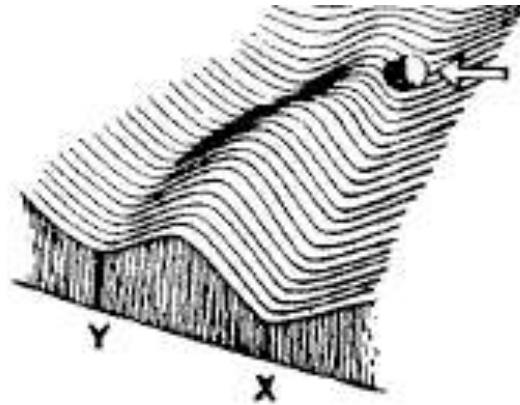
What is the Ball?

- I have never been able to understand what, in an embryo, the rolling ball represents
- After all, in a real embryo, some cells have to go down each bifurcating pathway
- If the paths of each “ball” were independent of one another, we would have something akin to the Plinko probability game:
- http://phet.colorado.edu/sims/plinko-probability/plinko-probability_en.html
- There is NO BUNDLING of neighboring cells in Waddington’s model

Plinko Balls



Generation of Novelty via the Struts



Canalization and Determination

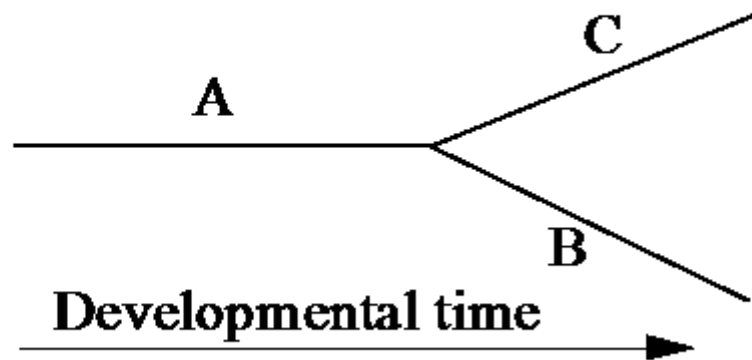
- The hills on that surface of an epigenetic landscape are the enforcers of “canalization”, i.e., determination of the cell types
- These are now understood as involving various epigenetic mechanisms from histone modifications to whole chromosome and perhaps whole genome changes
- Determination is thus part of the mechanism of cell differentiation

Generation of Novelty via Gene cascade Duplication followed by Genetic Drift

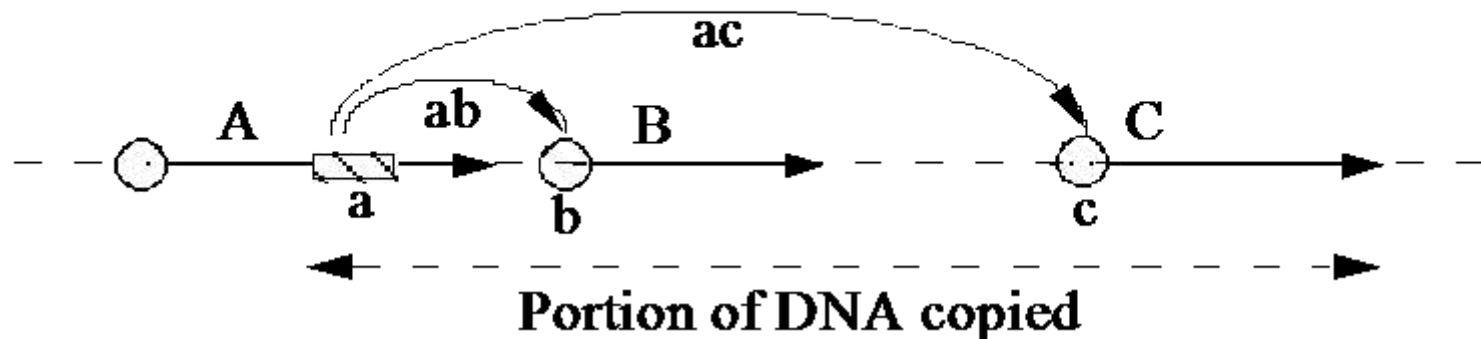
- The only mechanism in the epigenetic landscape is complexification of the folds of the surface
- Differentiation trees allow a relatively simple model based on duplication of portions of DNA

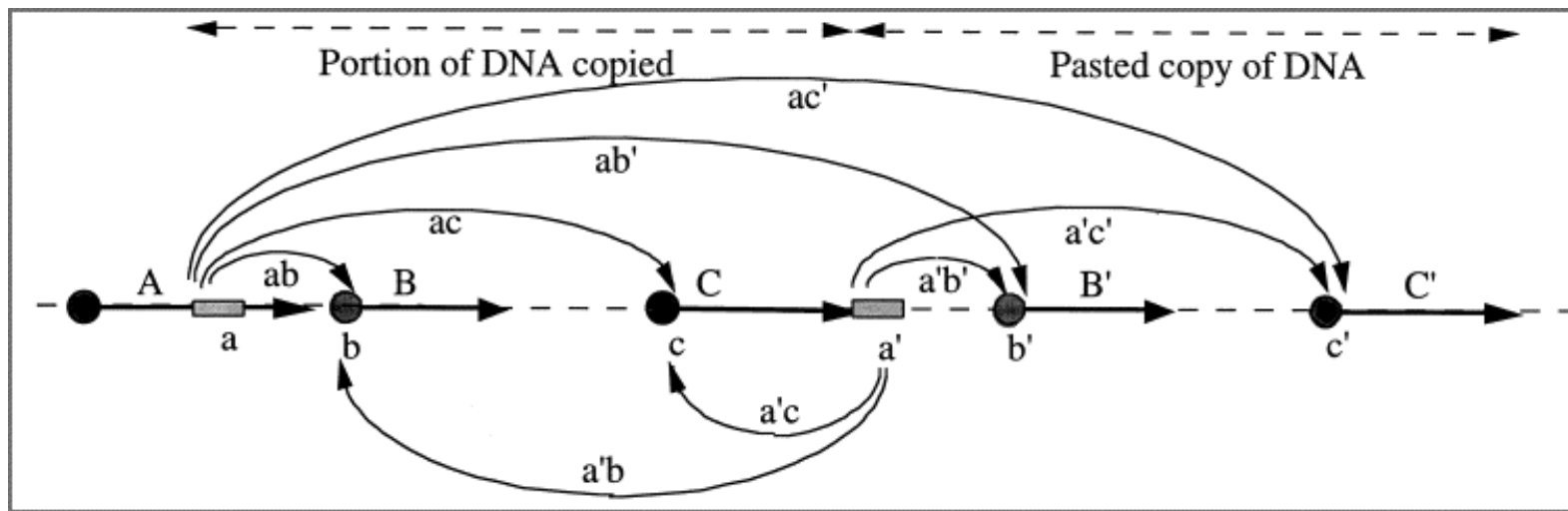
Macroevolution Duplicating a Branch of the Differentiation Tree could involve Cut, Copy & Paste at the DNA Level

Terminal branch of a differentiation tree

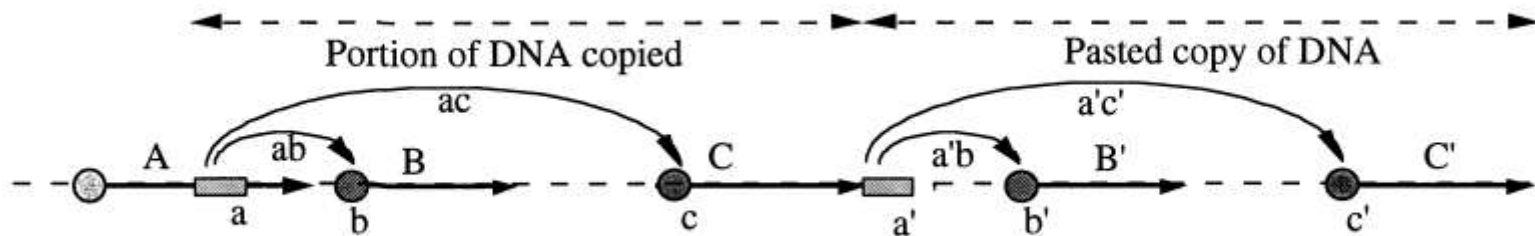


Its possible representation in DNA

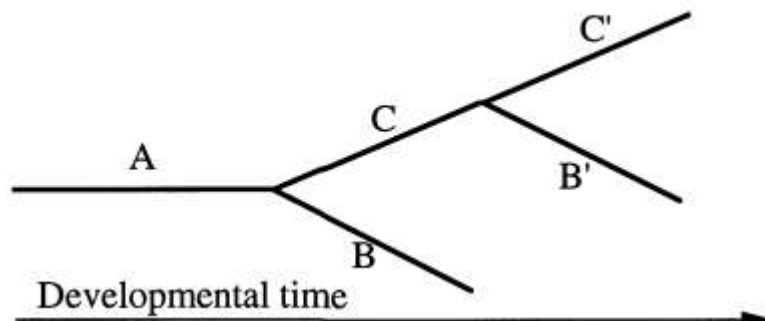




The evolved DNA

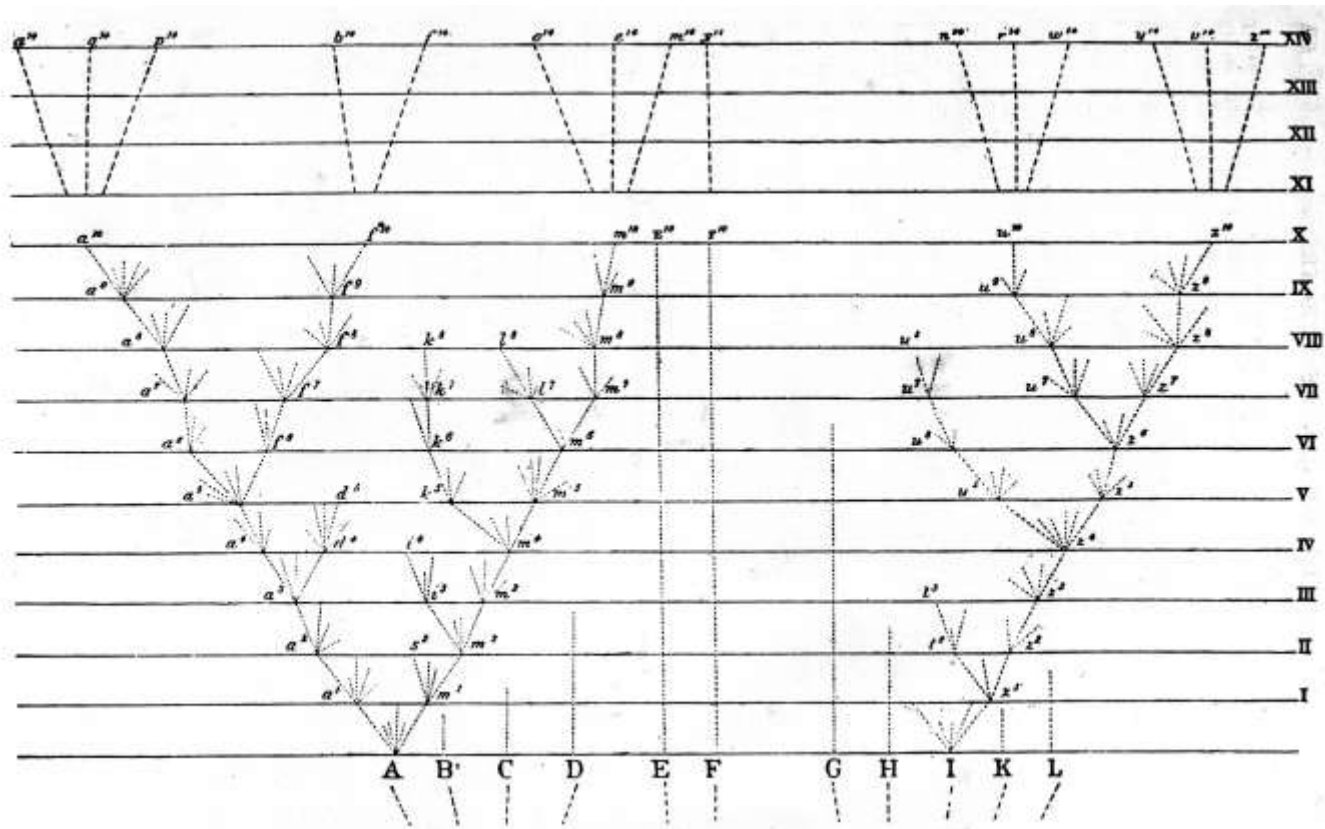


Its differentiation tree



Darwin's Fractal Phylogenetic Tree

- He said this diagram is applicable to both genera and families, i.e., he said it was self-similar, and thus what we now call a fractal
- *It is a tree of differentiation trees*



Progressive Evolution



- The mystery vanishes if the probability of growth of the differentiation tree exceeds that of pruning:
- Ratcheting!

Like frost
on a
window
pane, and as
inevitable

