Grundlagen der Systembiologie und der Modellierung epigenetischer Prozesse

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Stem Cell Systems I

stem cells

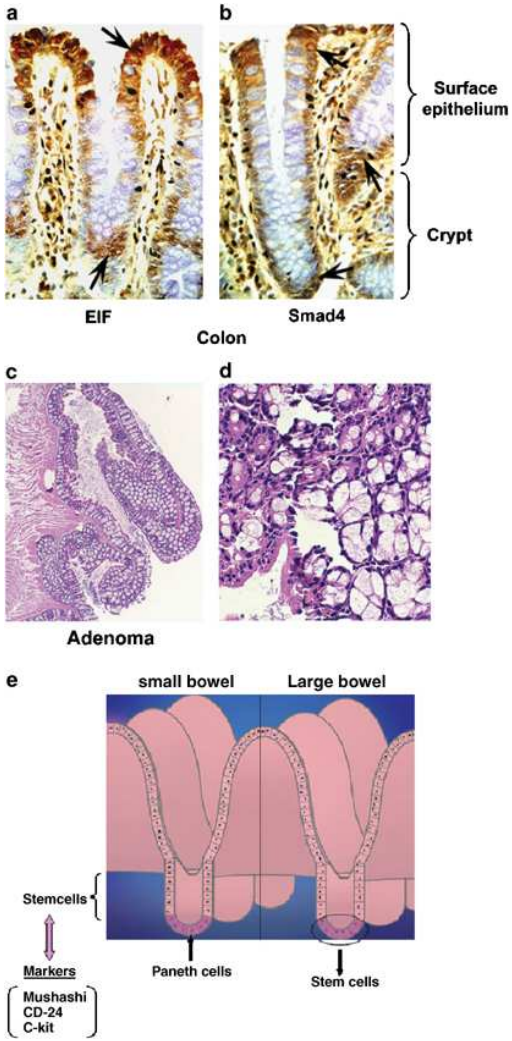
- ability to renew themselves through mitotic cell division
- differentiate into a diverse range of specialized cell types
- in embryos: give rise to the required celltypes to build up the organism
- in adults: maintain the normal turnover of regenerative tissues (skin, blood,...) and replenishes specialized cells (repair system)

Stem Cell Systems II

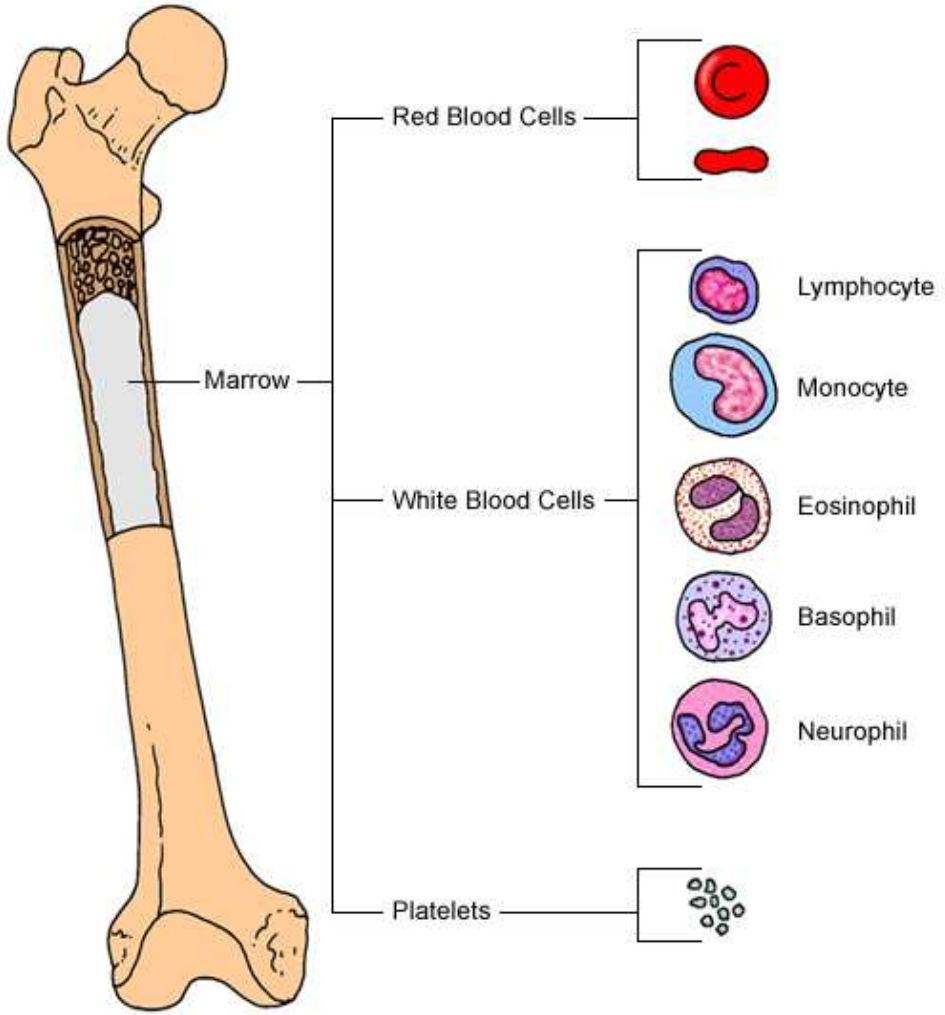
potency

- a stem cell is **totipotent** if it can differentiate into embryonic and extraembryonic cell types necessary to construct a complete, viable organism (e.g. from morula stage)
- a stem cell is **pluripotent** if it can differentiate into nearly all cells (e.g. from germ layers)
- a stem cell is **multipotent** if it can differentiate in a number of cells all part of a family of closely related cell types (e.g. hematopoietic stem cells)
- a stem cell is **oligopotent** if it can differentiate into only a few cells (e.g. lymphoid or myeloid stem cells)
- a stem cell is **unipotent** if it can produce only one cell type, its own, but has the property of self-renewal

Localization of Stem Cells



crypts



bown marrow

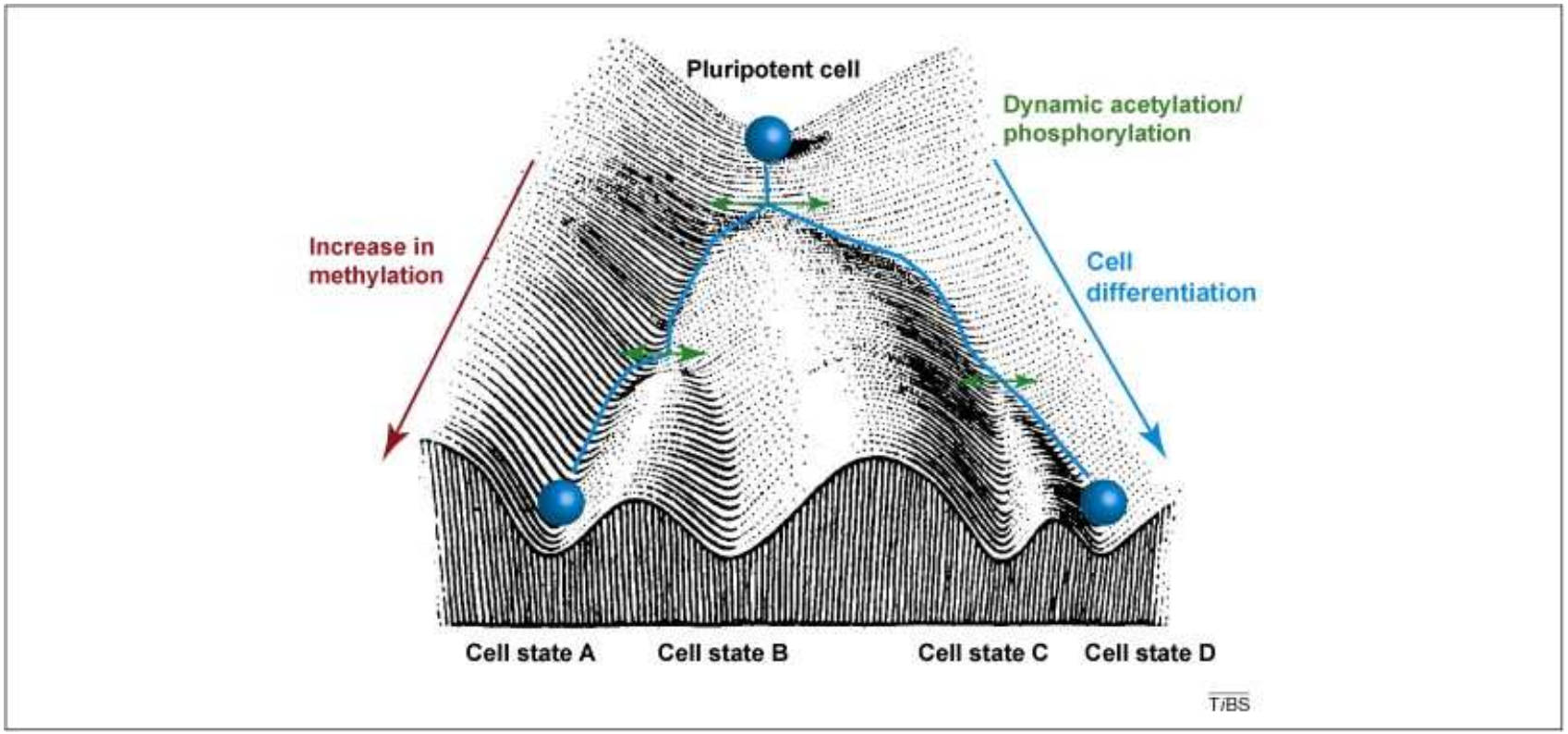
Renewal or Differentiation?

- renewal by symmetric cell division and maintance of the "stemcellness"
- differentiation by asymmetric cell division yields
  - on stem cell
  - one progenitor cell with limited self-renewal potential that terminally differentates into a mature cell (evnetually after several rounds of cell division)

How is the decision made?

- caused by intracellular or intercellular factors?
- stochastic or regulated asymmetric distribution of proteins?
- asymmetric distribution of proteins or epigenetic marks?

Waddington's Epigenetic Landscape



The "Chaos Hypothesis" by Kunihiko Kaneko

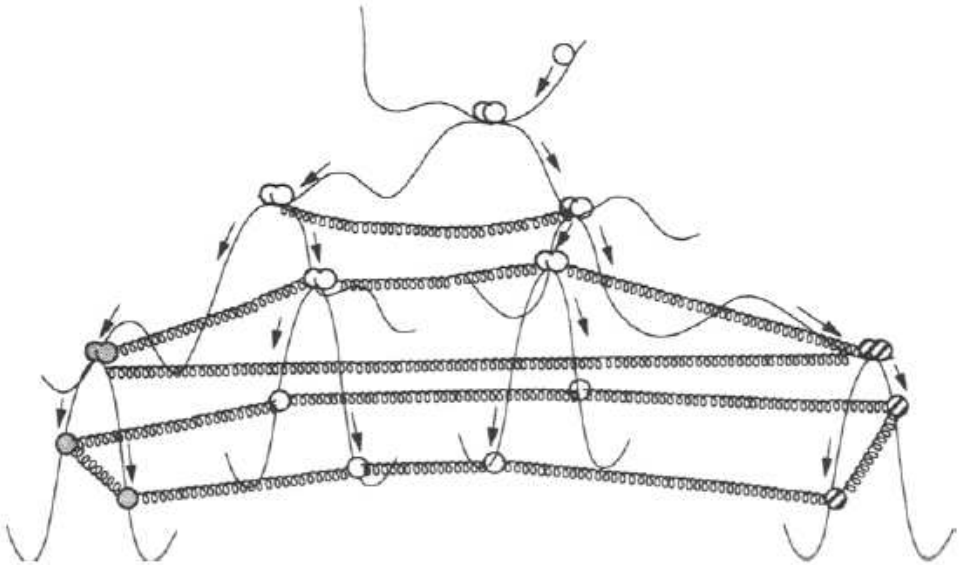
- chaotic (defined by Chaos Theory)
  - **sensitive to initial conditions** – "butterfly effect", measured by the Lyapunov exponent *lambda*, if *lambda* > 0 then the system is chaotic
  - **topologically mixing** – a continuous map $f : X \to Y$ is said to be topologically mixing if for non-empty open sets of the phase space $A, B \subseteq X$ exists an integer $n > N$ such that

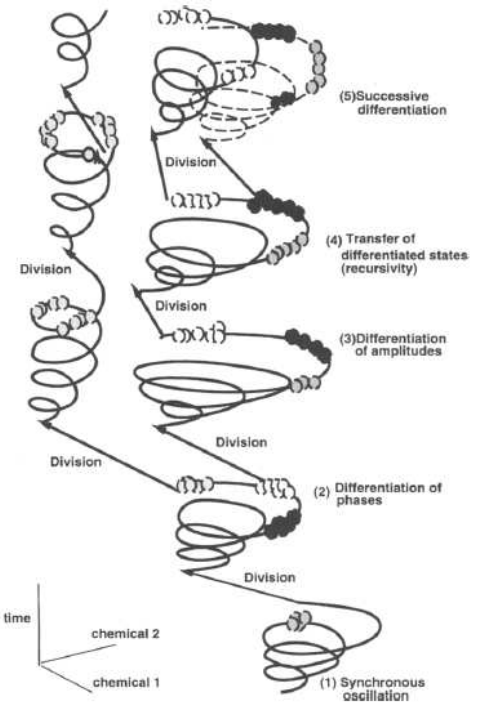
$$f^n(A) \bigcap B \neq \emptyset \tag{1}$$

  - **periodic orbits must be dense** – every point in the phase space is approached arbitrarily closely by periodic orbits
- a deterministic process yields a stochastic behavior

How about stability?

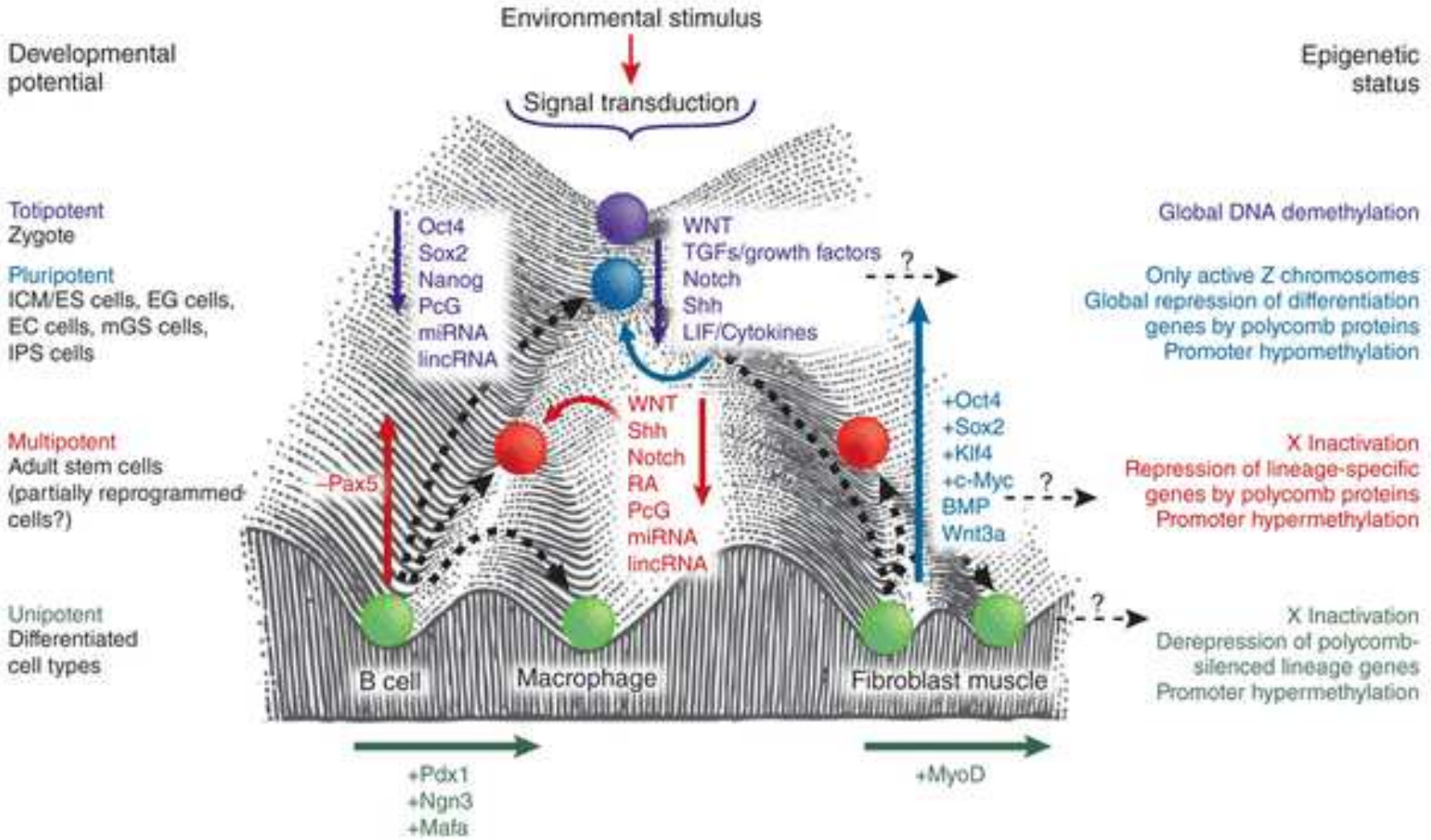
The "Isologous Diversification Theory" by Kunihiko Kaneko





Interplay between intra- and intercellular dynamics introduces coupled dynamical systems causing oscillatory chemical reactions. Fluctuations are orbital instabilities providing some stability towards external perturbations.

De-Differentiation or Irreversibility?



Regression of a specialized cell or tissue to a simpler, more embryonic, unspecialized form. Nevertheless, these cells retain ("memorize") their former histological specificity.

Hematopoietic Stem Cell System