

The Jing-Mai System in Vertebrate Development and Evolution

Rainer Machné

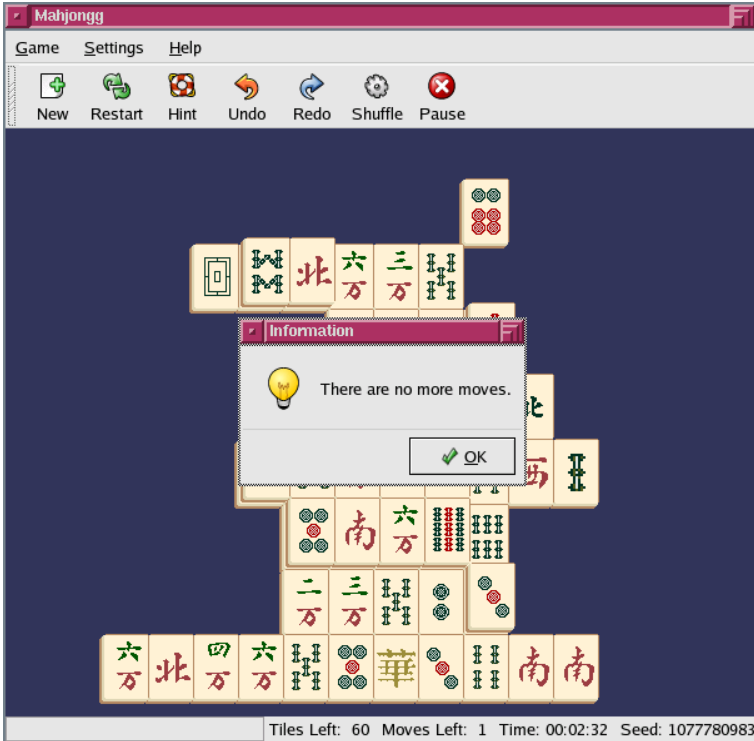
Bled, February 2004

Institute for Theoretical Chemistry and Structural Biology

Institute of Microbiology and Genetics

University of Vienna

not:



Outline

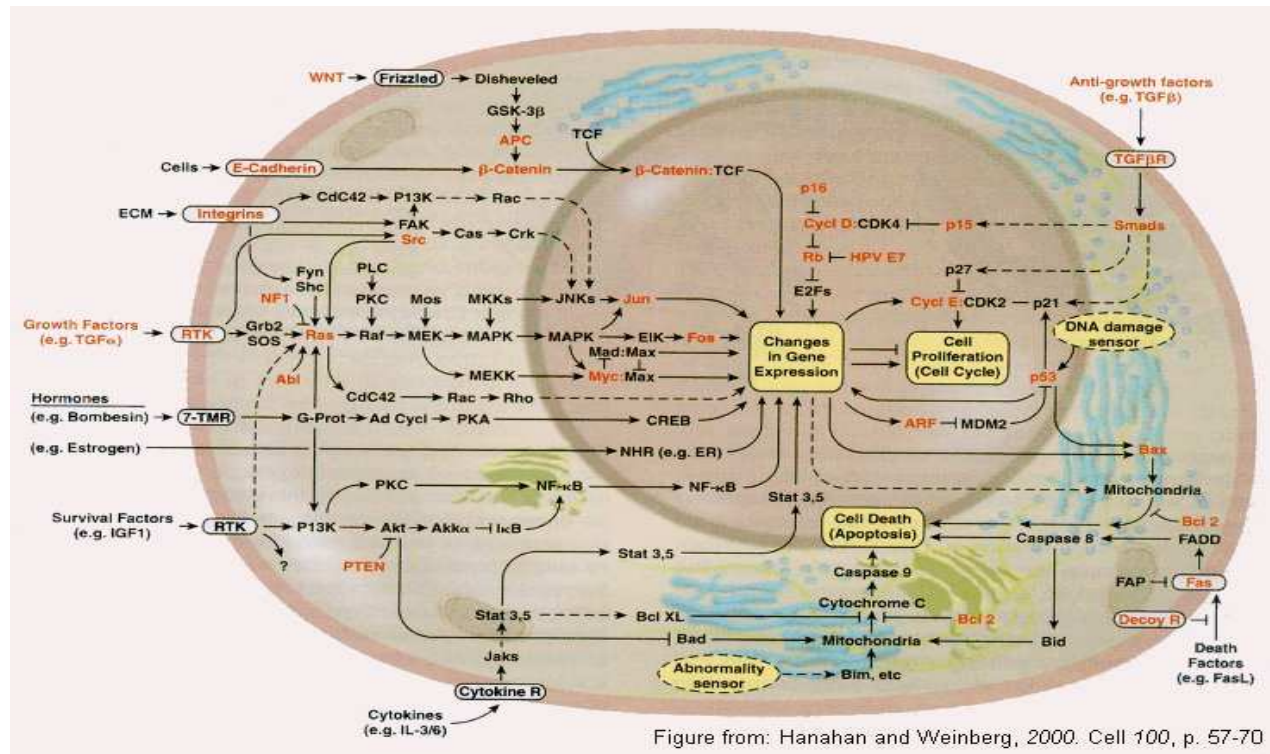
- The Multiscale Complexity of Biological Signaling Networks
- Developmental Models: Morphogenes and Gene Regulatory Networks
- The Jing-Mai System and Neurocristopathies
- Vertebrate Innovations: Neural Crest and Hyaluronan

Outline

- Jing-Mai Hypotheses
- The Biochemistry of Yin and Yang
- Fractal Rhythms
- TCM: a translation problem

Biological Signaling Networks

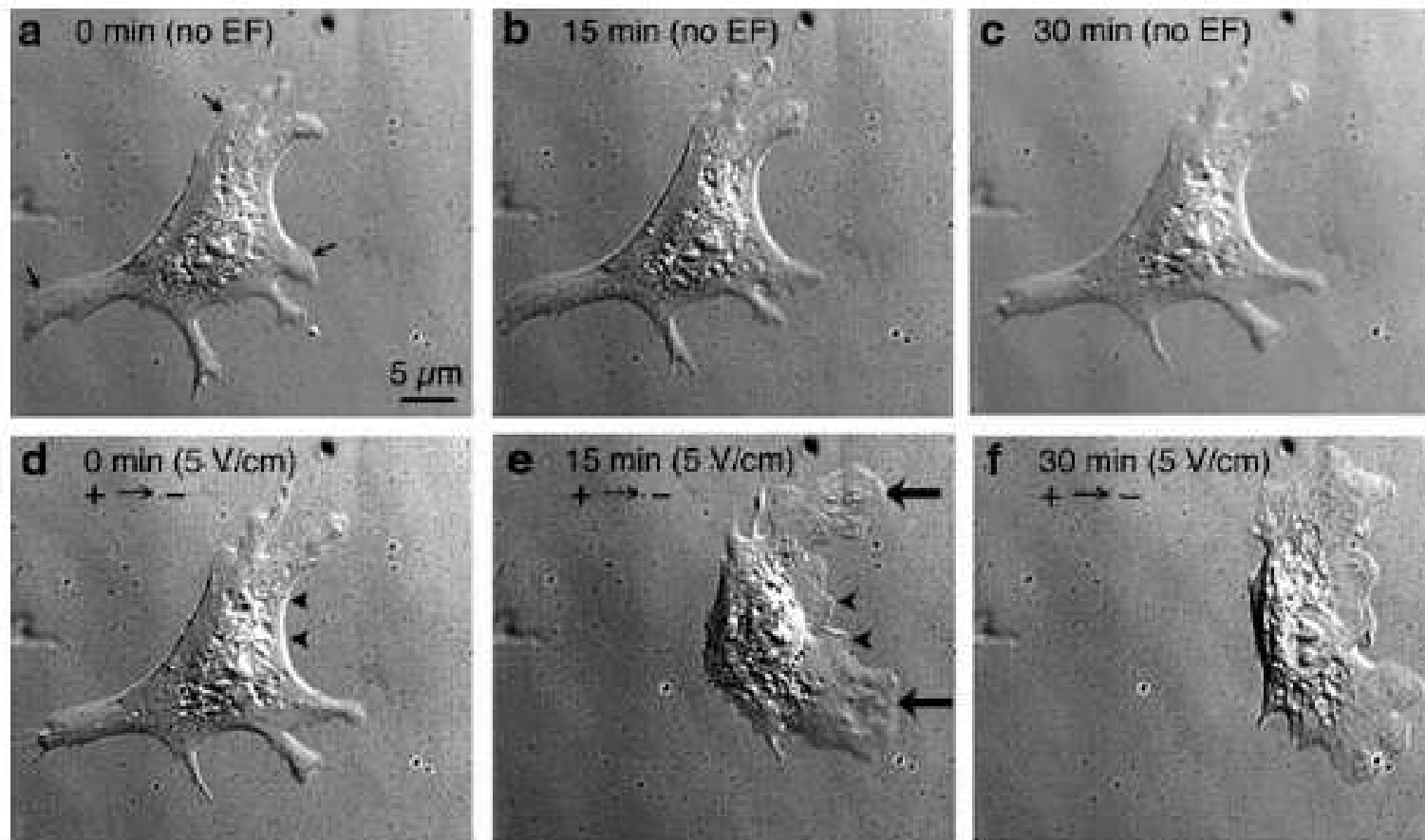
proliferation vs. differentiation, migration vs. adhesion



putting together the pieces, beginning to unravel the net

Hanahan and Weinberg 2000

A migrating cell

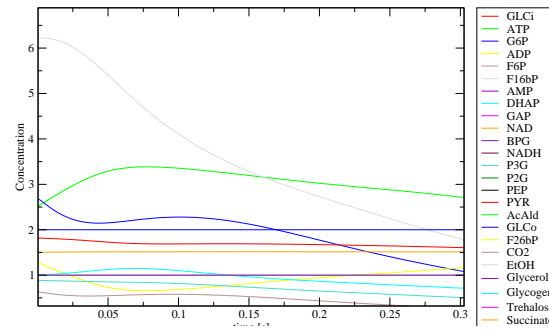


cells are gels, not aqueous bags

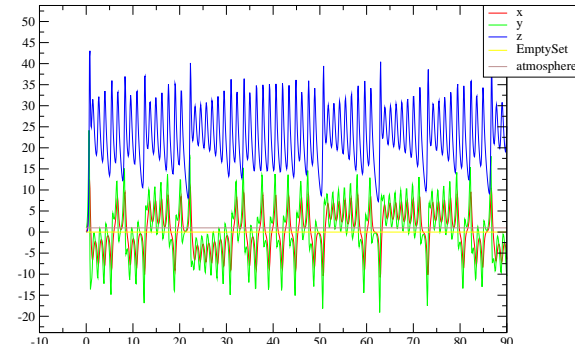
Li 2002, Pollack 2003

SBML - exchanging and merging models

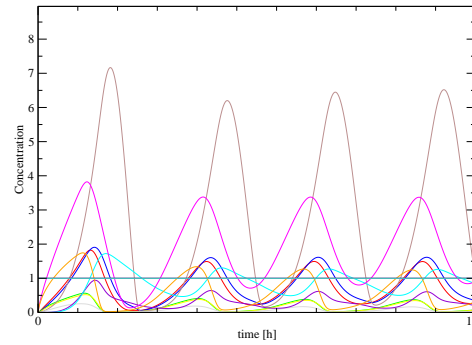
Yeast Glycolysis



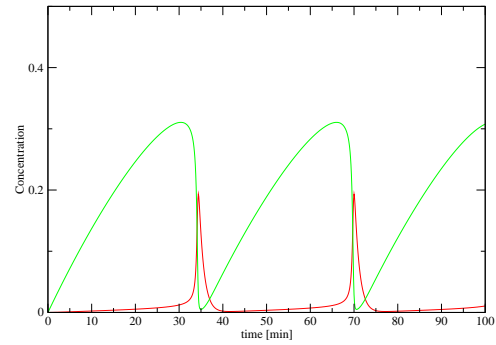
Lorenz EN (1963) Deterministic nonperiodic flow. Journal of the Atmospheric Sciences



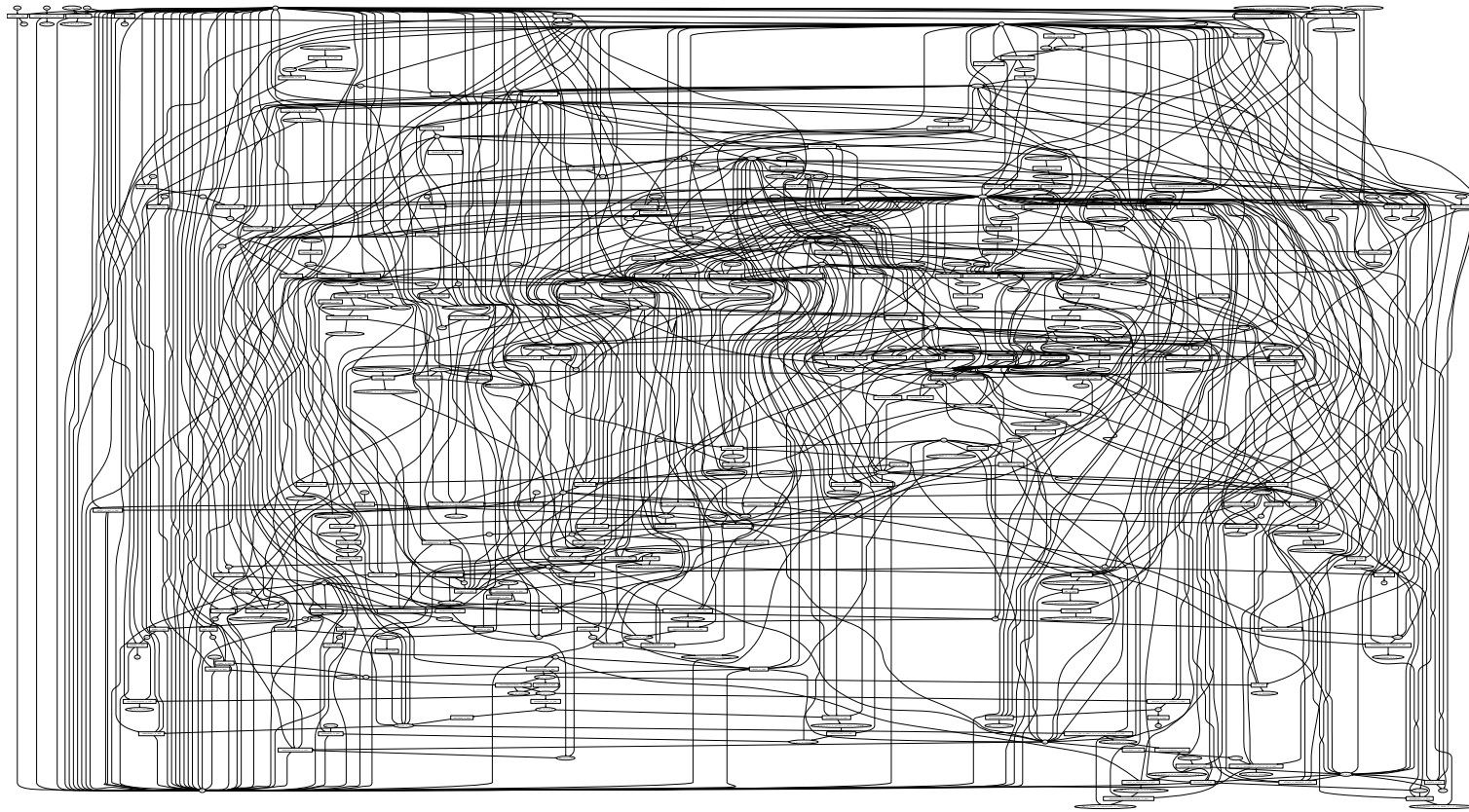
Circadian rhythms, bityrhmic



Cell Cycle



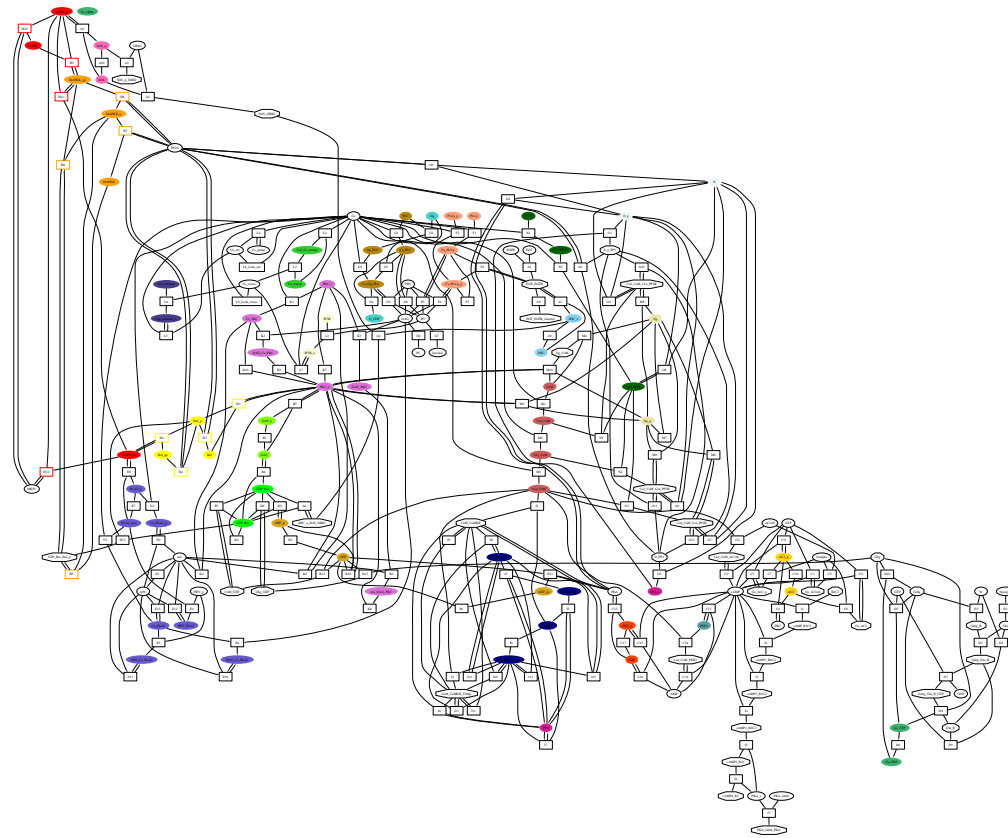
Metabolic Network of *Chlamydia trachomatis*



metabolic networks: long known and well understood

Krieger 2004

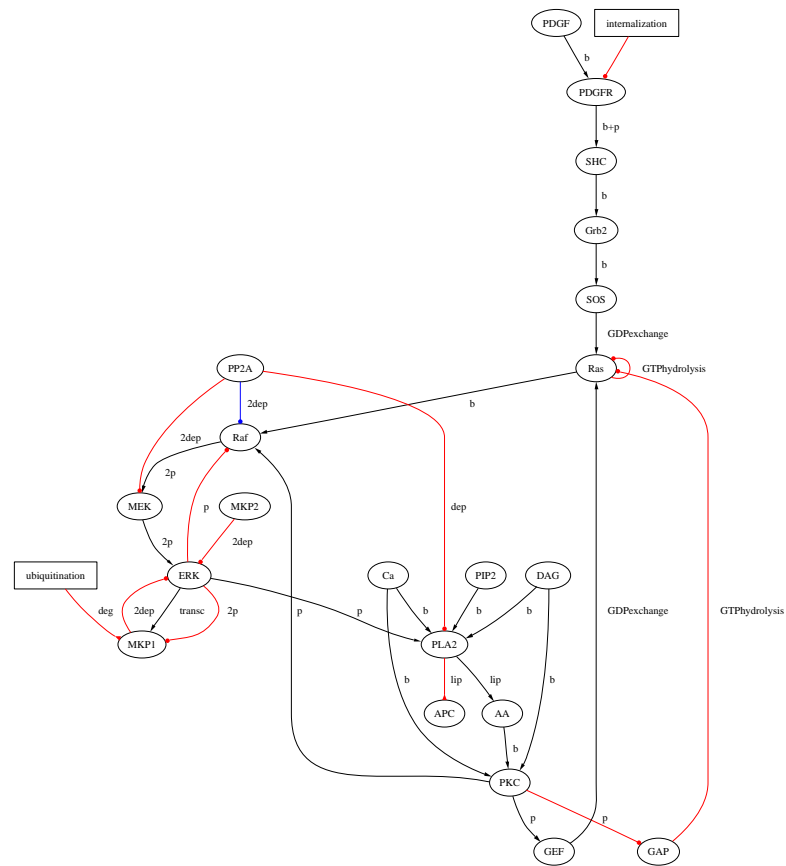
Emergent Properties of BSN



a tiny fraction of the whole signaling network

Bhalla, Iyengar 1999

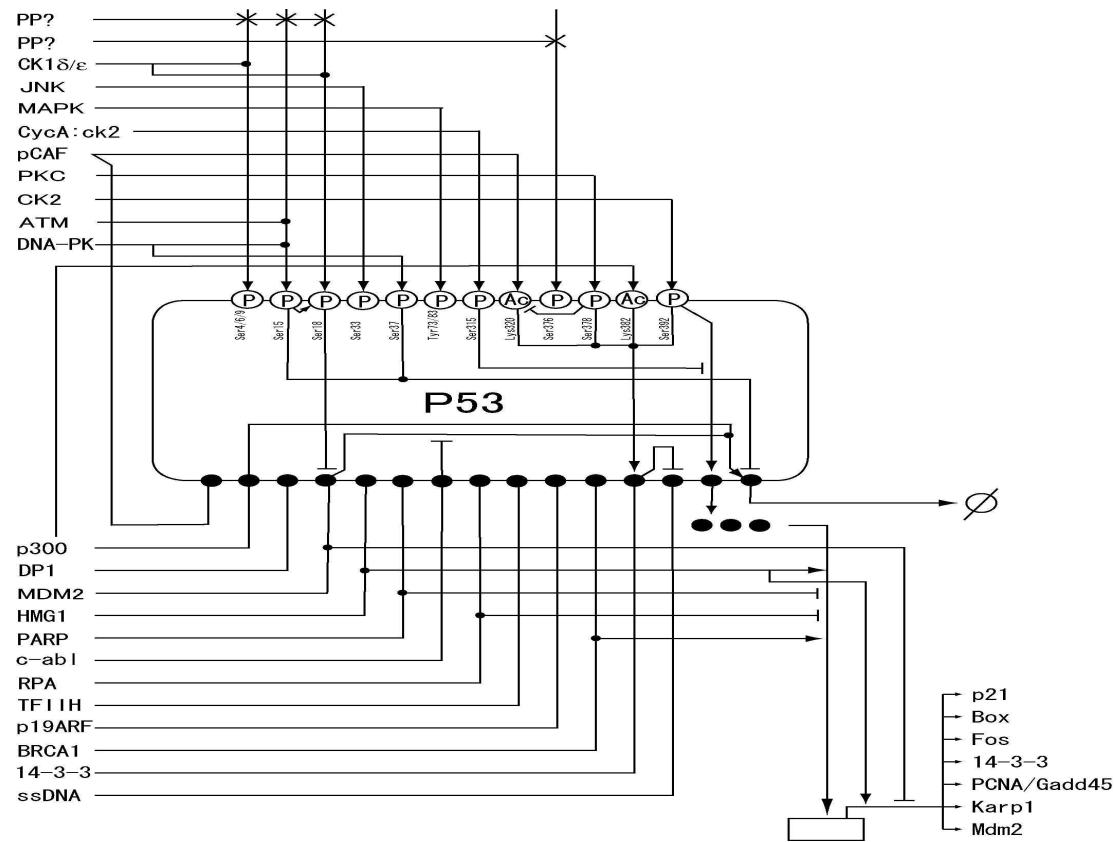
bioLogic: Inhibition-Activation scheme



abstraction of Bhalla, Ram, Iyengar 2001

⇒ intermingled feedback loops : switches and oscillators

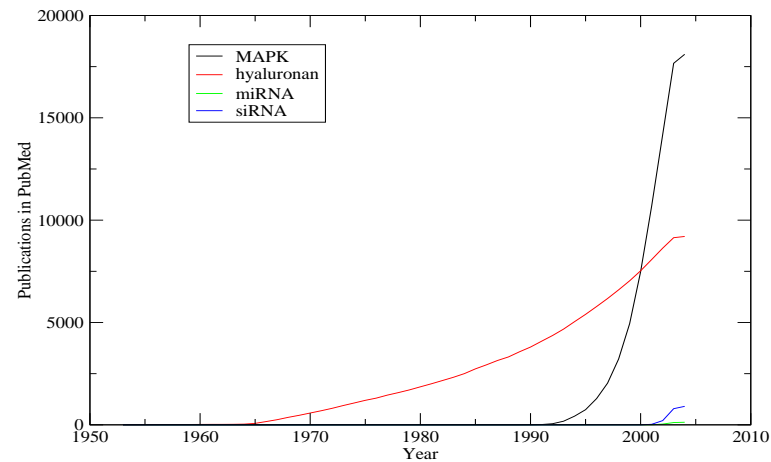
Block diagram of the 'Hub' protein p53 in Kohn notation



combinatorial complexity constrains conventional modelling approaches

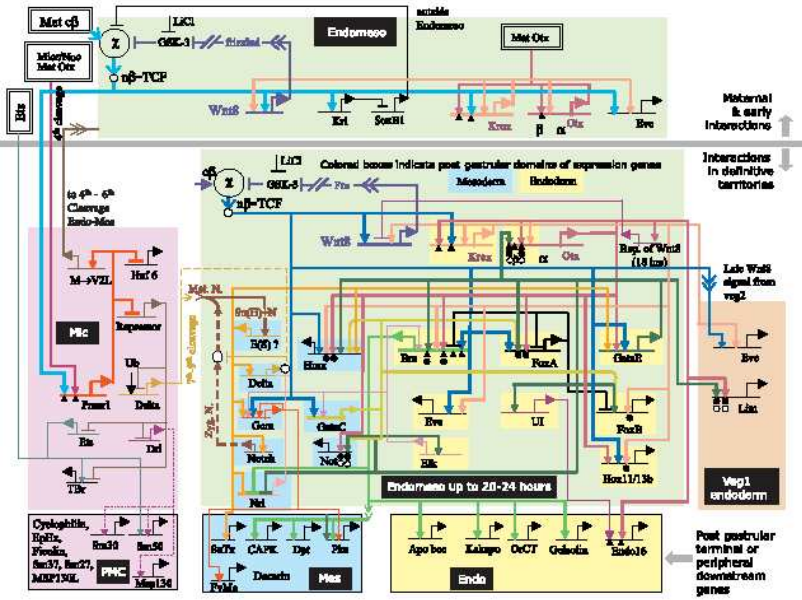
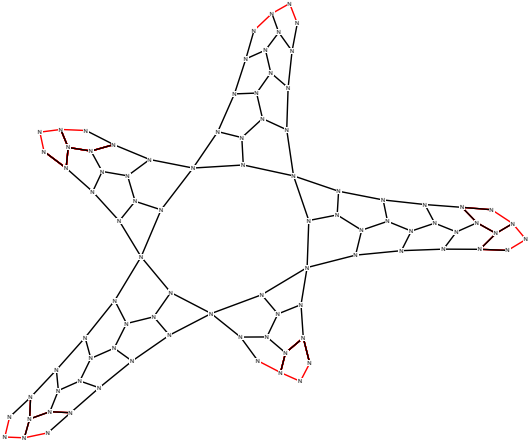
Kohn 1999, Maimon 2001, Kitano 2002

‘Conceptual Biology’ : Biology as Literature Science



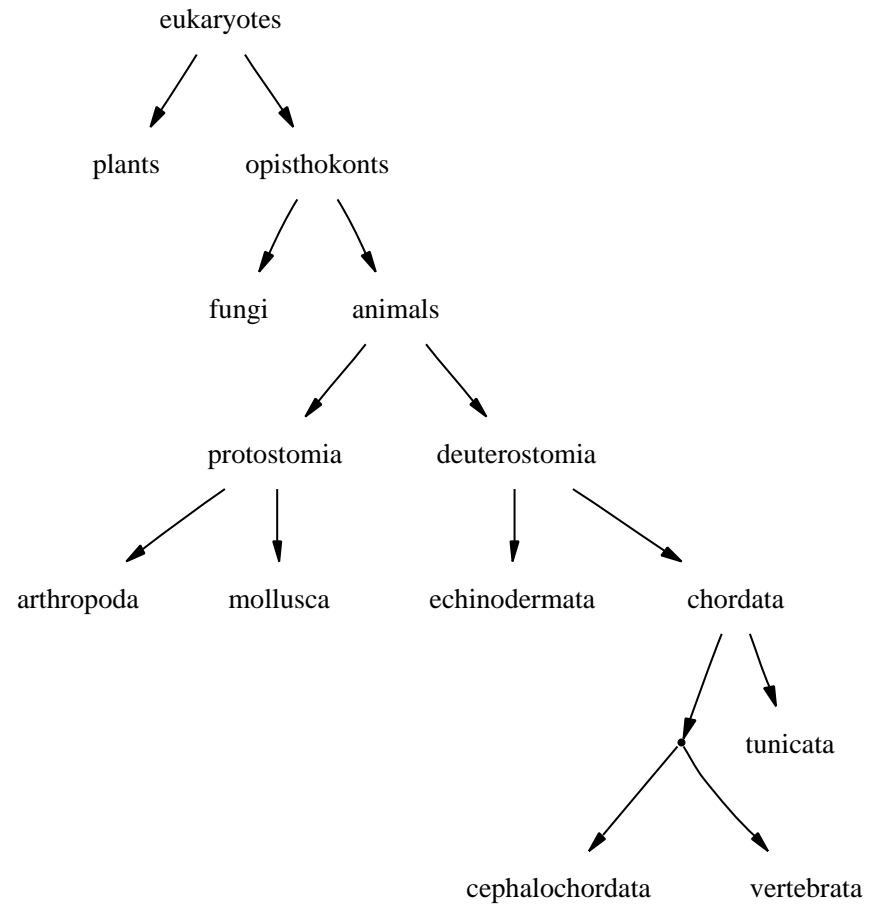
- * Conceptual Continuity \Rightarrow integrating diverse data and knowledge from atoms to medicine - from genes to society?
- * Multiscale Complexity \Rightarrow compound graph every edge/node is a complex network itself
- * Dangerous Small World property \Rightarrow find your own ‘conspiracy’ theory

Models of Sea Urchin Development



Beck 2004, Davidson 2002

Incomplete Phylogenetic Tree



The Jing-Mai System and Congenital Heart Diseases

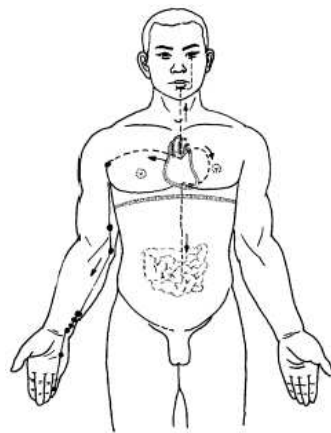


Fig. 3. The Heart *Jing-Mai*.

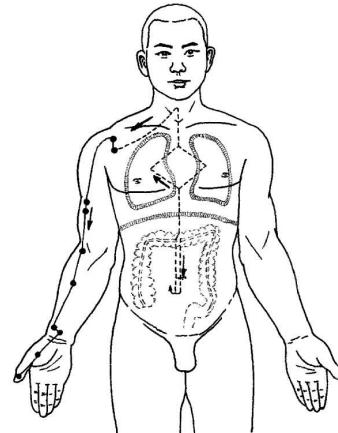


Fig. 6. The Lung *Jing-Mai*.

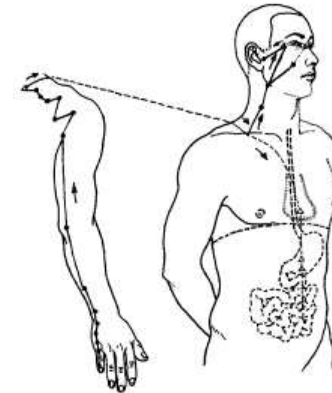


Fig. 4. The Small Intestine *Jing-Mai*.

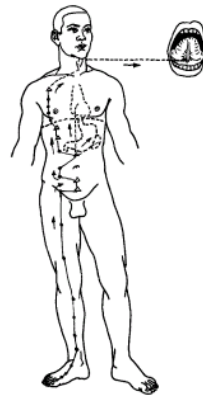


Fig. 5. The Spleen *Jing-Mai*.

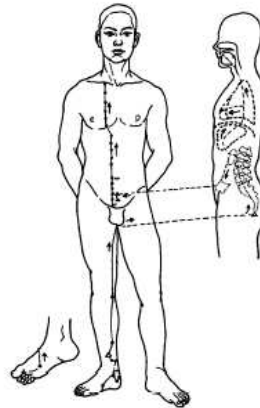
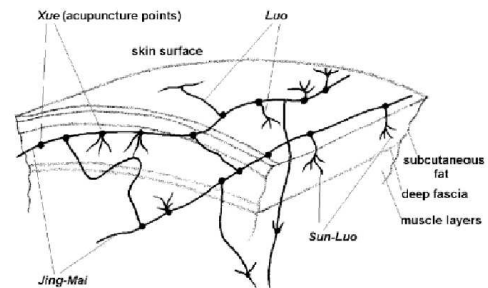
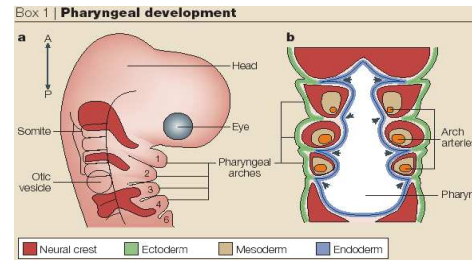
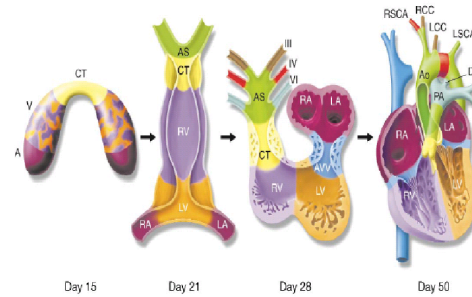
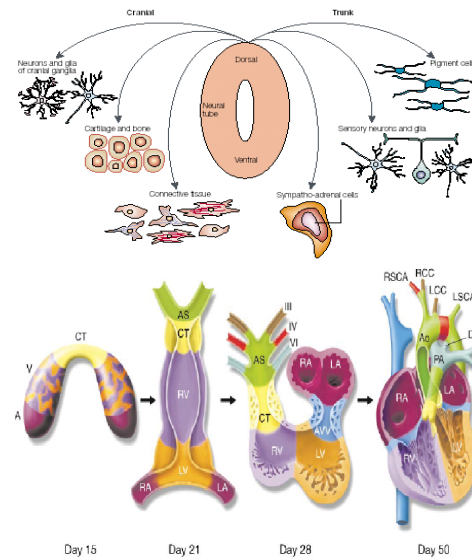
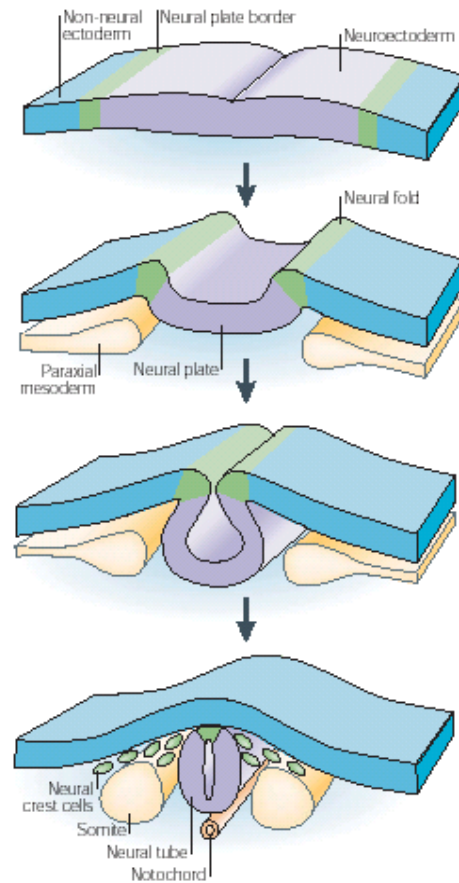


Fig. 2. The Kidney *Jing-Mai*.

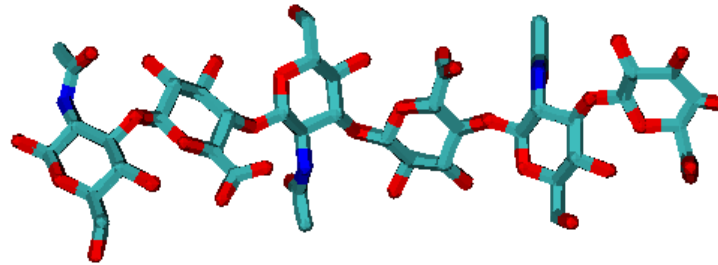


The Neural Crest Cells - 'the' Vertebrate Innovation



Knecht 2002, Gammill 2003, Srivastava 2000

Hyaluronan - another Vertebrate Innovation

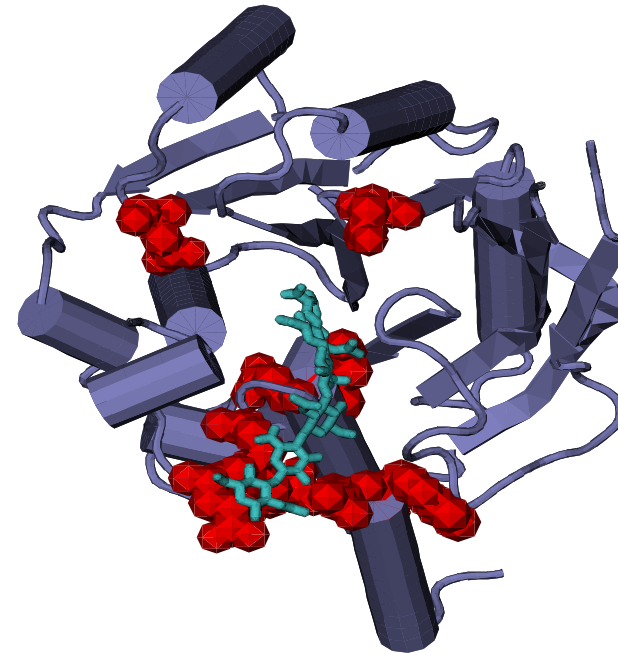
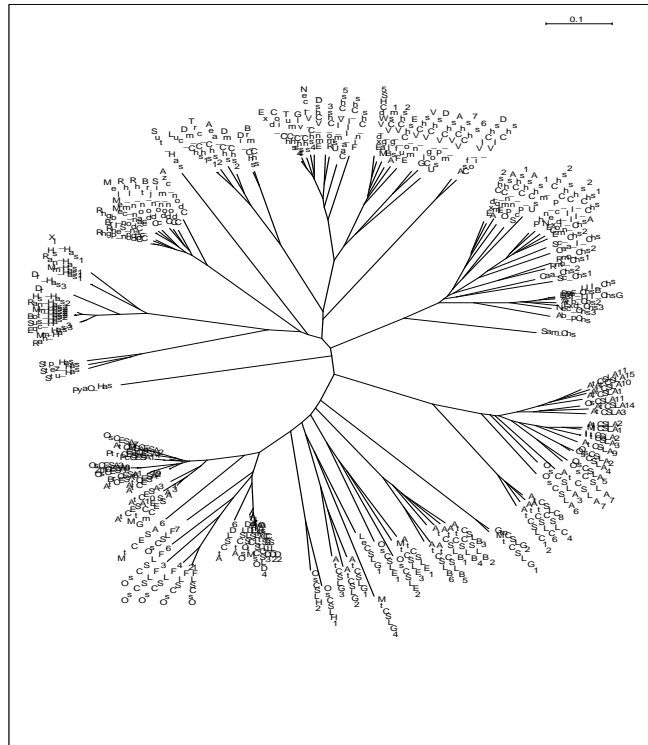


Bio(electro)chemical properties:

- ⇒ long chains connected via hydrophobic interactions
- ⇒ forms a highly hydrated matrix
- ⇒ establishes diffusion and streaming potentials
- ⇒ conversion of mechanical force to potential difference and ionic current

Glycoforum, Toole 2001, Barrett 1975 and 1976

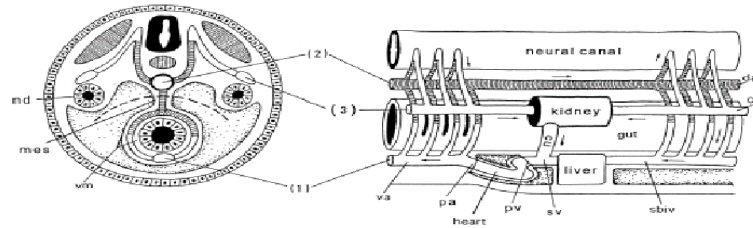
The third Polymer : Sugars



The 3 formgiving polysaccharides ?

Spicer 1998, Lee 2000

Some other Vertebrate Innovations and Hyaluronan



Heart: EMT into cavities, ECM expansion, electrical environment in excitation?

Endothel: stimulated by fragments, migration in angiogenesis

Dynamic Epidermis: thick HA layer, high turnover rate, wound repair

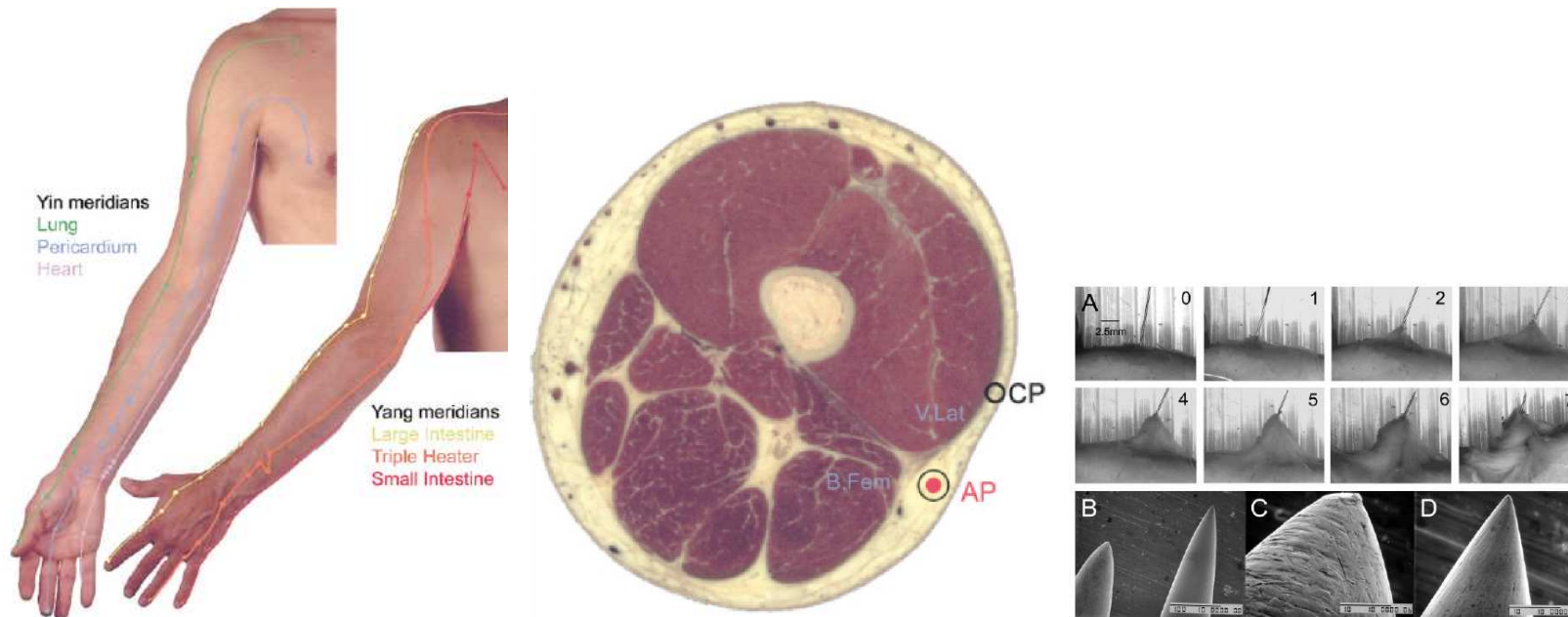
Adaptive Immunity: stimulated by fragments, transport to lymph nodes, carrier of antigens?

Endoskeleton: condensation, major compound of cartilage, synovial fluid and connective tissue

⇒ strongly hydrated ECM, embeds signaling molecules, single cell migration, electromechanical signaling?

Shigei 2001, Shimeld 2000,
Karvinen 2003, Camenisch 2002, Schroeder 2003,
Mummert 2003, Termeer 2003, Roessler 2003,
Toole 2001, Knudson 2003

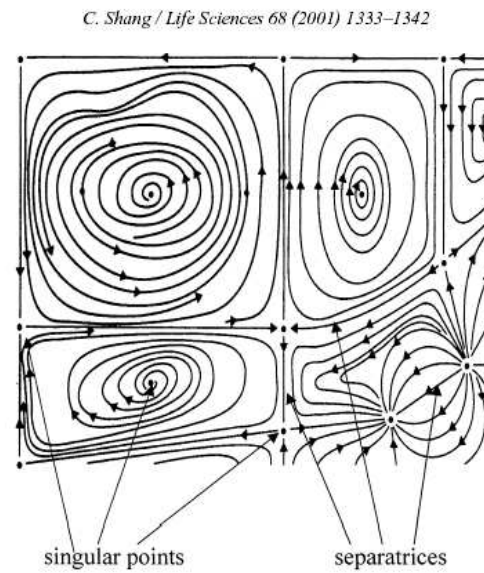
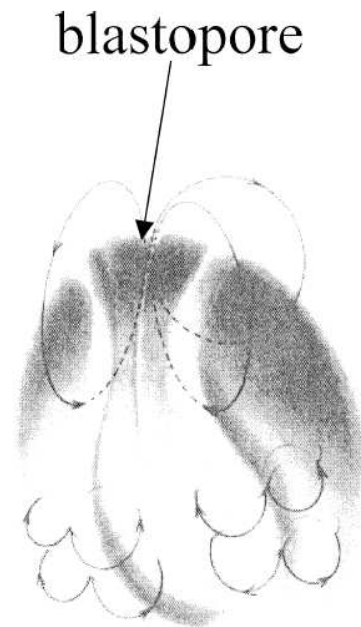
The 'Interstitial Connective Tissue' Hypothesis



Electromechanical signaling?

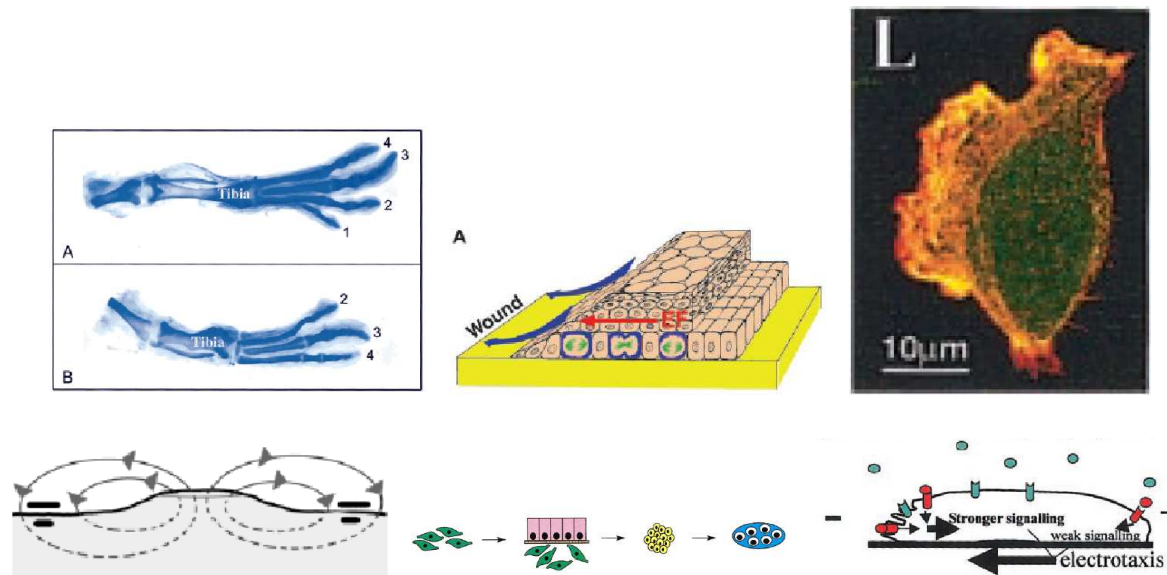
Langevin 2002

The 'Electrophysiology of growth control' Hypothesis



Shang 2001

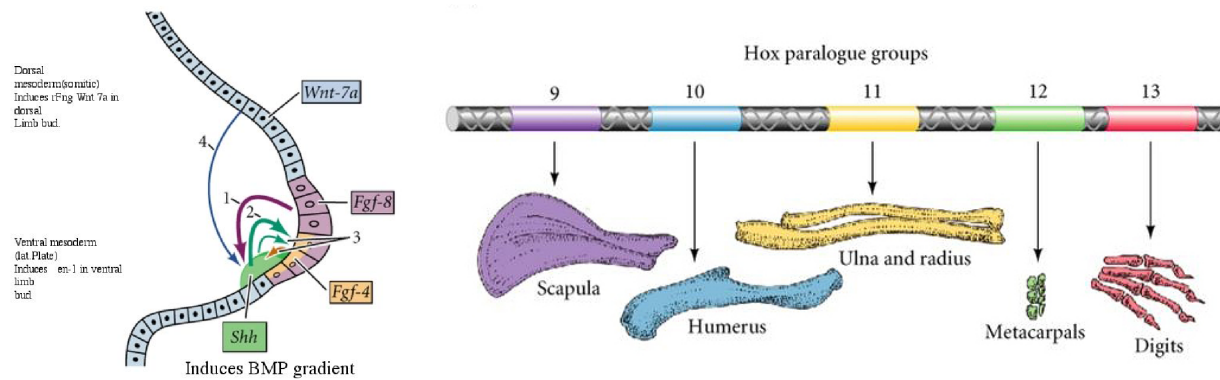
Transepithelial Potentials and Galvanotaxis



Endogenous electrical fields as directional signals in development and repair?

Robinson 2003, Altizer 2001, Zhao 2002, Song 2002, Hall 2000

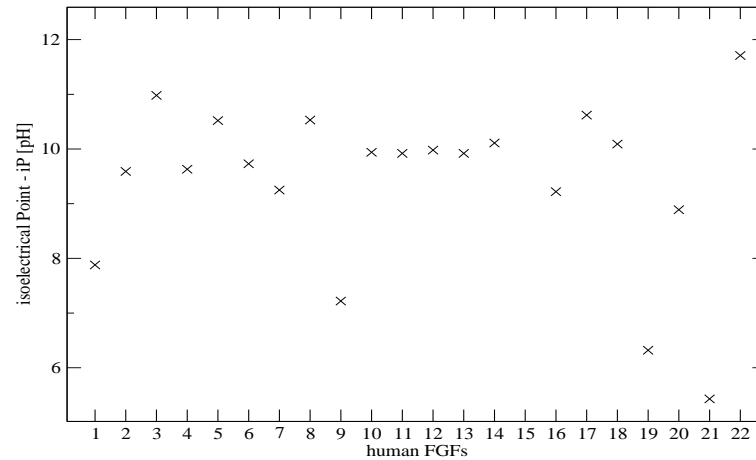
Mapping the GRN on the Jing-Mai System?



Are the Xue (acupuncture points) Organizing Centers,
ie. Morphogen Sources

Bastiani

Establishment/Stabilization of Morphogen Gradients?



Fibroblast Growth Factors are differently charged at physiological pH

The Biochemistry of Yin and Yang

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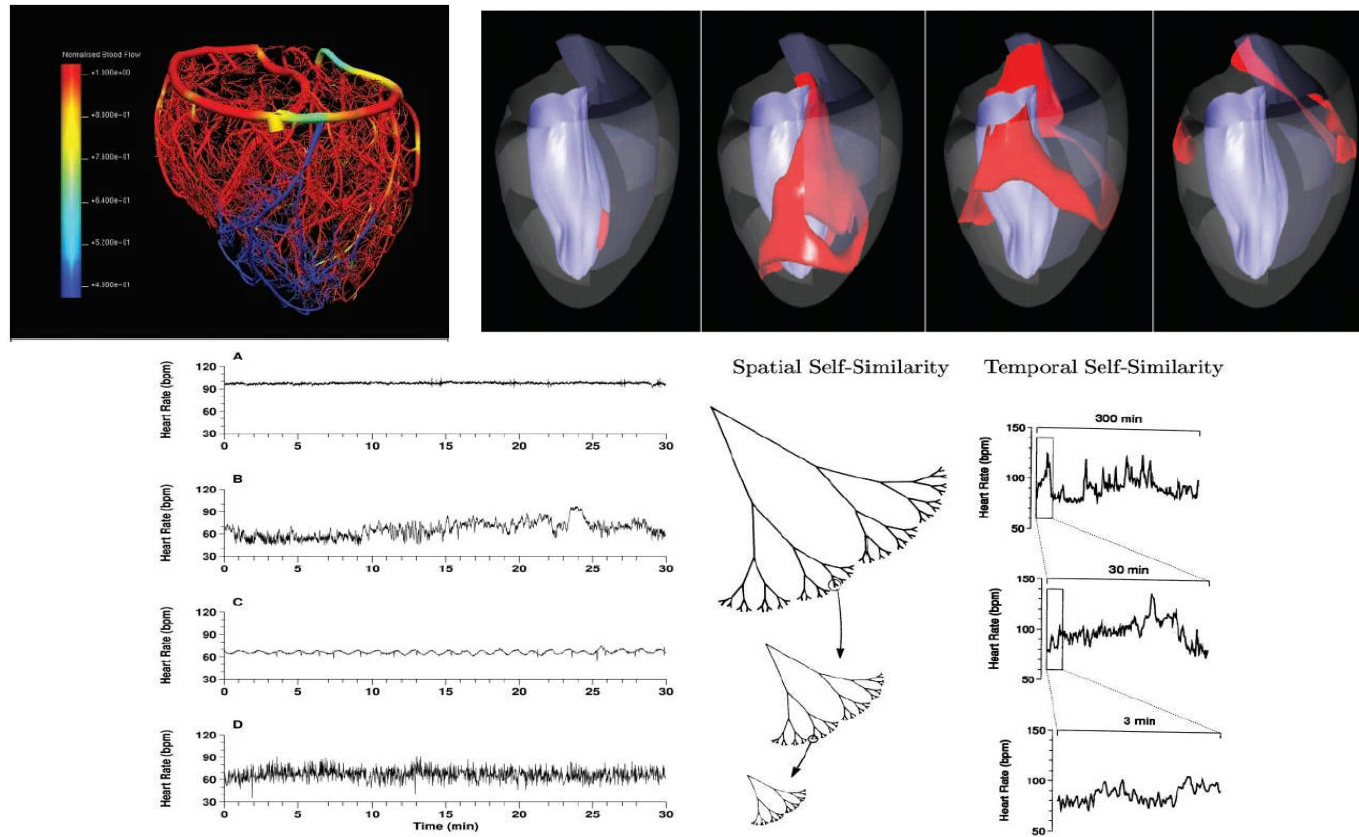
Yin-tonic herbs : antioxidant activity

Yang-tonic herbs : mitochondrial ATP production?

...

Ko 2004, Ou 2003

Fractal Rhythms in Physiology and the Pulse Diagnosis



the Qi circulates through the Jing-Mai in circadian rhythms

Noble 2002, Goldberger 2002

TCM : a translation problem

Jing-Mai: developmental paths and connections?

Yin/Yang: ATP production and REDOX management?

Qi: 'life energy' ? 'natural air'

⇒ metabolism, mitochondrial oxidation?

Jing: the genes and the gene regulatory network?

Kaptchuck 2000, Li-Ling 2001 and 2003, Langevin 2002, Ko 2004, Ou 2003

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