Systems Biology

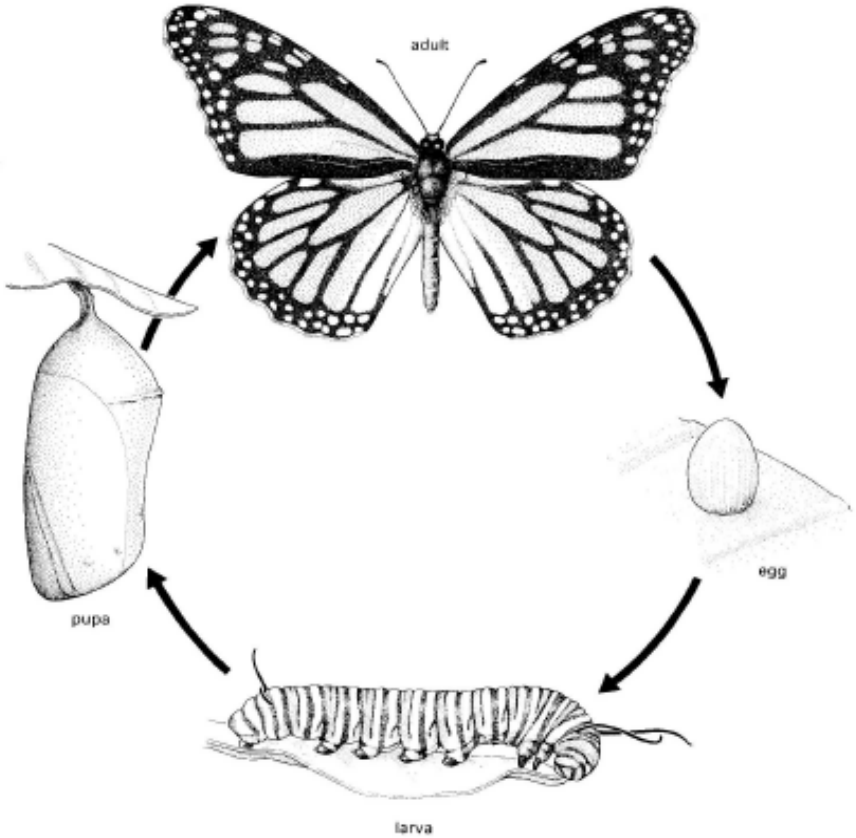
Towards Life

The whole in the parts

Total metamorphosis: one genome two proteomes…

…the genome only the notes: the music is played elsewhere!

O. Wolkenhauer *www.sbi.uni-rostock.de*



Picture from P.J.Gullan and P.S.Cranston: *The Insects*, Blackwells Science, 2000

Bringing the genome towards life….

20th Century Biology:
Reductionistic Approach:
(Genome sequencing, DNA arrays, proteomics)

21th Century Biology:
Integrative Approach:
Systems Biology

What is Systems Biology towards life ?

•Systems biology integrates experiment and modelling to explain the functional organisation of cells.
• It aims at quantitative experimental results and building predictive models.

… not Genomics: Identification and molecular characterisation of components
… not Bioinformatics: Management and mining of data and information

The Functional Organisation of the Cell

Bio-Medicine:

Diseases can be understood/treated
through an understanding of how cells function.

Systems Biology:

Cell functions are dynamic nonlinear processes
that can be understood through modelling and
simulation.

Towards Life…..

SYSTEMS BIOLOGY 40 years ago…….

Mike Mesarovic in *System Theory and Biology*, 1968:

"In spite of the considerable interest and efforts, the application of systems theory in biology has not quite lived up to expectations…"

"The real advance in the application of systems theory to biology will come about only when the biologists start asking questions which are based on the system-theoretic concepts rather than using these concepts to represent in still another way the phenomena which are already explained in terms of biophysical or biochemical principles."

Where are we? What's Next?

WE NEED TO LEARN FROM THE EMERGING CRITICS...

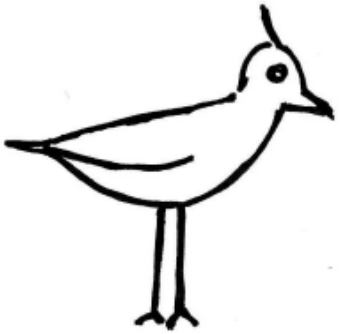
Ronald Plasterk, *Current Biology*, Vol.15, No.21, 2005:

“The fundamental misconception of systems biology advocates is that one could create a `virtual cell', and use big computers to model life and make discoveries……..

None of these modellers ever predicted that small microRNAs would play a role. One makes discoveries by watching, working, checking. They want to be Darwin, but do not want to waste years on the Beagle.”

Mathematical Models as Mediators

This is not a bird!



... idealizations force us into reduced models.
... assumptions force us into phenomenological models.
... all models are wrong, some are useful!

Why Modelling?

- ✘ *Managing uncertainty and complexity.*
- ✘ *It provides a language to generate and validate hypotheses.*
- ✘ *Modelling implies abstraction and hence a reduction of complexity.*

... systems biology is the art of making appropriate assumptions!

... *molecular characterisation* of components is not the purpose of kinetic modelling!!

... you need modelling to understand the *functional activity* (role) of microRNA.

We wont models to exactly reproduce biological complexity or we wont models to UNDERSTAND ... a little bit more cell behaviour?

WHICH ARE THE APPROPIATE QUESTIONS TO ADVANCE ….. TOWARDS LIFE?

How does the cell realise its functions?
Regulation, control and coordination of cell function.
The cell is alive . why is that?
How do we deal best with biological complexity?

Could we think all together in more questions?
….with150 brains thinking together here no doubt! !