

VU Research Portal

Emergence of design

Kolodkin, A.N.

2011

document version

Publisher's PDF, also known as Version of record

[Link to publication in VU Research Portal](#)

citation for published version (APA)

Kolodkin, A. N. (2011). *Emergence of design*.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal ?

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

E-mail address:

vuresearchportal.ub@vu.nl

Contents

Abbreviations	7
Chapter 1. Philosophical foundations: Systems Biology, emergence and design	9
1.1. Systems Biology through the prism of Emergence. How holism and reductionism meet each other in a computer model	11
1.1.1. What is Systems Biology? Raising the question	11
1.1.2. Concept of Emergence	13
1.1.3. Deeming the emergence to be less strong	20
1.1.4. Empowered by mathematics and computers...the right moment for systems biology to take strong emergence as strong as it is	22
1.2. Reconstruction of Emergence in systems biological models	23
1.3. Three strategies to build a model: top-down, middle-out and bottom-up	26
1.4. Use of systems biological models	30
1.5. Deeper understanding based on Systems Biological Model. Design issue	34
1.6. Aim and outline of this thesis	35
Chapter 2. Methodology: a protocol for design studies	39
Chapter 3. An example of a Design Study: “Hot” and “cool” glycolysis	43
3.1. Sulfolobus sulfataricus. Introduction	45
3.2. Blueprint model of the relevant part of glycolysis	47
3.3. ‘Paradoxical features’ of Sulfolobus glycolysis	47
3.4. Design study: Does Sulfolobus waste ATP?	49
Chapter 4. Example of a Design Study: Nuclear Receptor Signaling; a triple conveyor belt conveying a message	55
4.1. Nuclear Receptors. Introduction	57
4.2. Blueprint scheme of nuclear receptor signaling	60
4.2.1. Integrating the knowledge into a single scheme	60
4.2.2. Different NR networks as instantiations of the same master scheme	65
4.3. ‘Paradoxical features’ of Nuclear Receptor signaling	69
4.4. Design study of ‘paradoxical’ features	71
4.4.1. Why does Nuclear Receptor shuttle between the nucleus and cytoplasm? (NR-RE complex is neglected)	71
4.4.2. Why does Nuclear Receptor shuttle between the nucleus and cytoplasm? (NR-RE complex is taken into account)	83
4.4.3. Why should there be active export rather than active import of	

importins? (NRL-RE degradation being neglected)	87
4.4.4. Why should there be export rather than active import of importins? (taking NRL-RE degradation into account)	91
4.4.5. Why should there be both active export of unliganded and active import of liganded receptors?	94
4.4.6. Why should both n/c transport and binding to DNA be regulated?	100
4.4.7. Why should all pathways run through the same NPC?	103
Chapter 5. The GR-PXR dialogue	109
5.1. GR-PXR dialogue. Introduction	11
5.2. Blueprint model of the GR-PXR dialogue	112
5.3. 'Paradoxical features' of the GR-PXR dialogue	114
5.4. Design study of 'paradoxical' features	115
5.4.1. Why should activated GR inhibit its own transcription?	115
5.4.2. Why should the affinity of ligand for GR be about 1000 times smaller than that for PXR?	117
Chapter 6. General discussion	121
6.1. General discussion of results from our examples of design studies	123
6.2. Emergence and design	131
6.3. Emergence of design in the Silicon Human	133
6.4. Physics and stamp collecting	140
Summary	145
Bibliography	149
Acknowledgements	161
Samenvatting	165
Summary in Russian	169
About the author	171
List of publications	173
Appendix 1	177