Faculty of Design

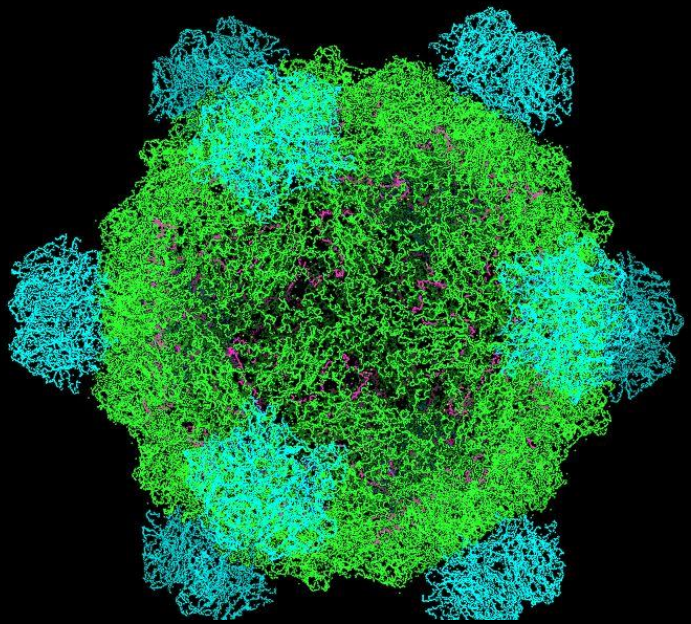
2015

Systems design combining rational design and evolution

Chen, Chih-Chun and Crilly, Nathan

Synthetic Biology and complex design problems

Chih-Chun Chen & Nathan Crilly



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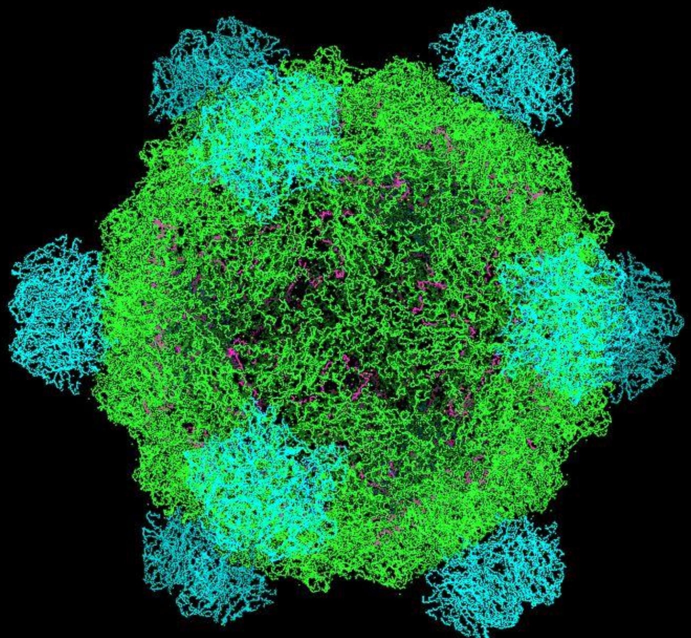

What is a complex design problem?

What is a complex design problem?

Two broad perspectives:

- “Wicked problems”: Problems which are “indeterminate”, i.e. formulating them is itself the problem.
- “Complexity engineering”: Designing a system with many interdependencies between the elements to achieve some desired outcome.

Crime as a “wicked problem”

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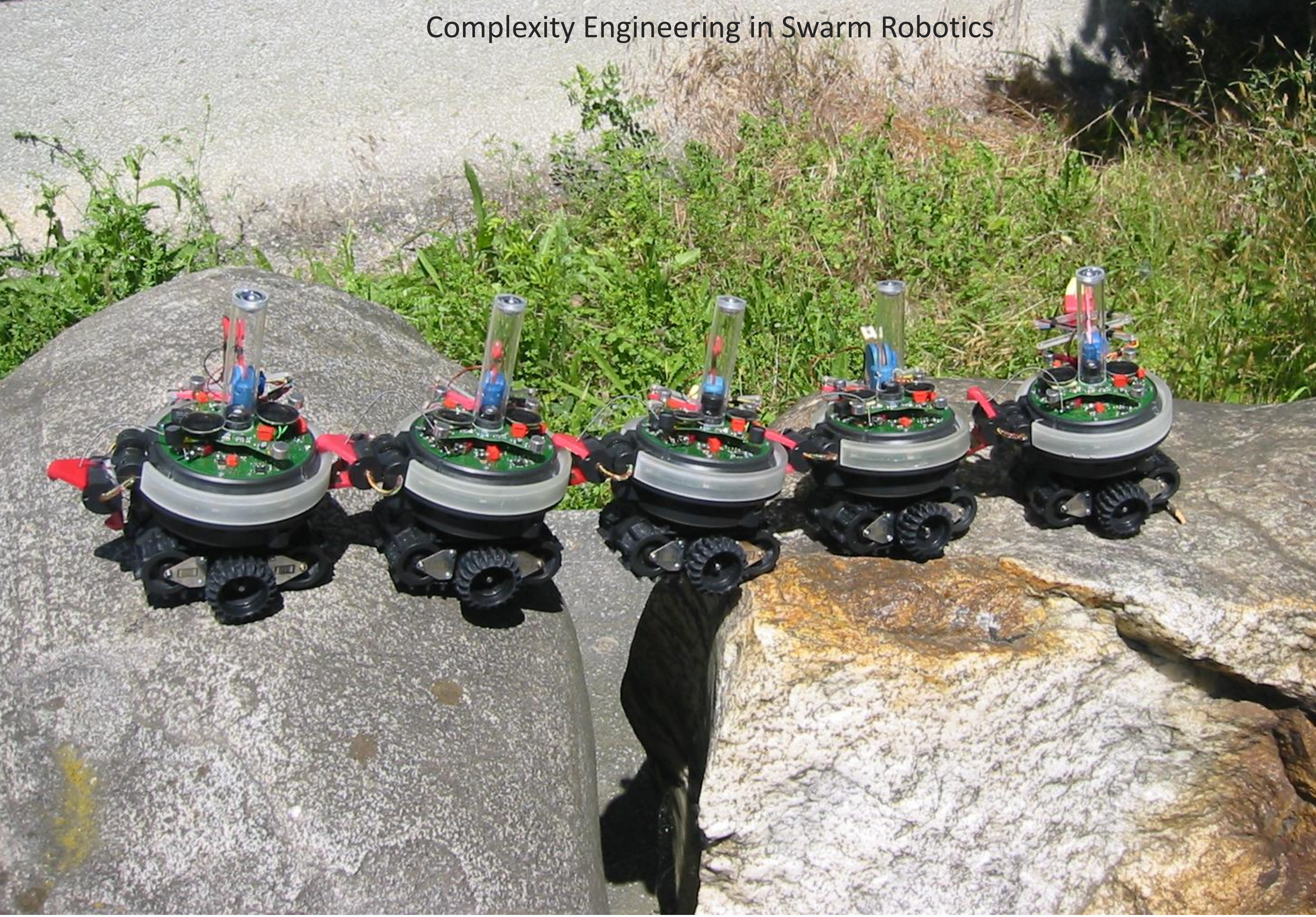
Complexity Engineering in Swarm Robotics



“Several s-bots in swarm-bot configuration passing over a gap" by Francesco Mondada and Michael Bonani at en.wikipedia.

Synthetic Biology as a design field

Synthetic Biology as a design field

"*Synthetic biology is a) the **design and construction** of new biological parts, devices and systems and b) the **re-design** of existing natural biological systems for useful purposes.*"

(SyntheticBiology.org)

"*Synthetic biology is the engineering of biology: the synthesis of complex, biologically based (or inspired) systems which display functions that do not exist in nature. This **engineering perspective** may be applied at all levels of the hierarchy of biological structures… In essence, synthetic biology will enable the design of 'biological systems' in a **rational and systematic way**.*"

(High Level Expert Group, European Commision)

Method and participants

Participants

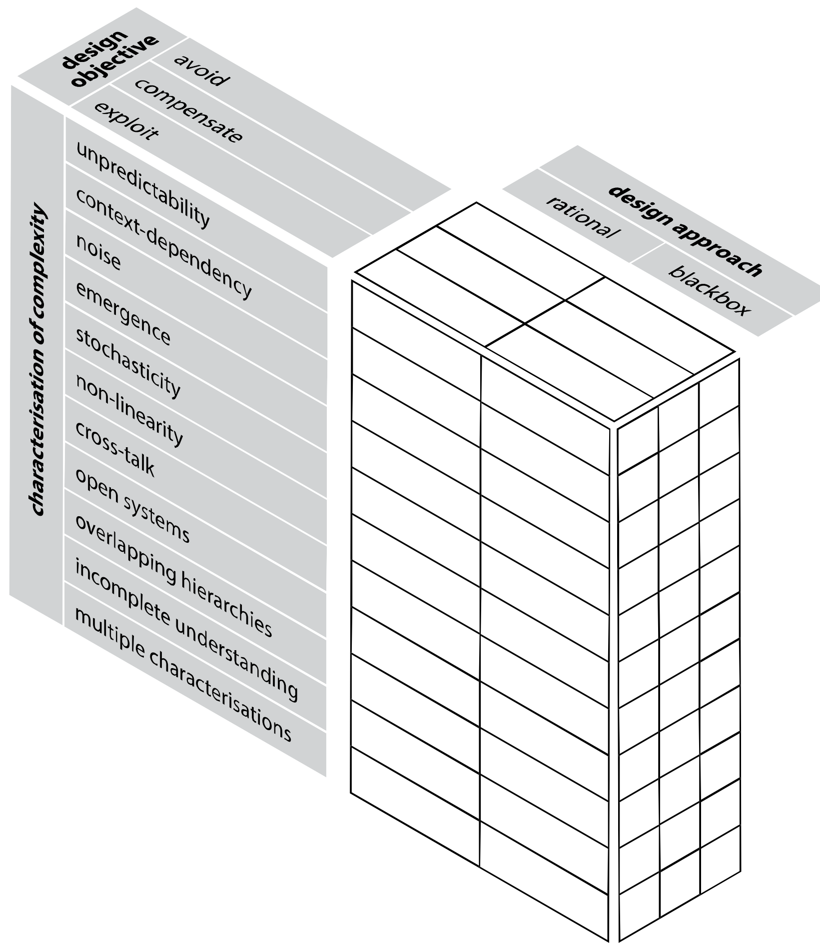
P	Subject of highest qualification	# years in Synthetic Biology	# years at current organisation	Organisation type
1	Nonlinear dynamical systems and control	5.5	5.5	Research
2	Synthetic Biology	4	2	Research
3	Pharmacology and Molecular Biology	9	5	Research
4	Computer Science	5	9	Research
5	Molecular Biology	10	14	Research
6	Science Policy	8	8	Research
7	Theoretical Physics	10	5	Research
8	Biology	8	0.5	Commercial
9	Biology	8	2	Commercial
10	Bioengineering	8	3.5	Research

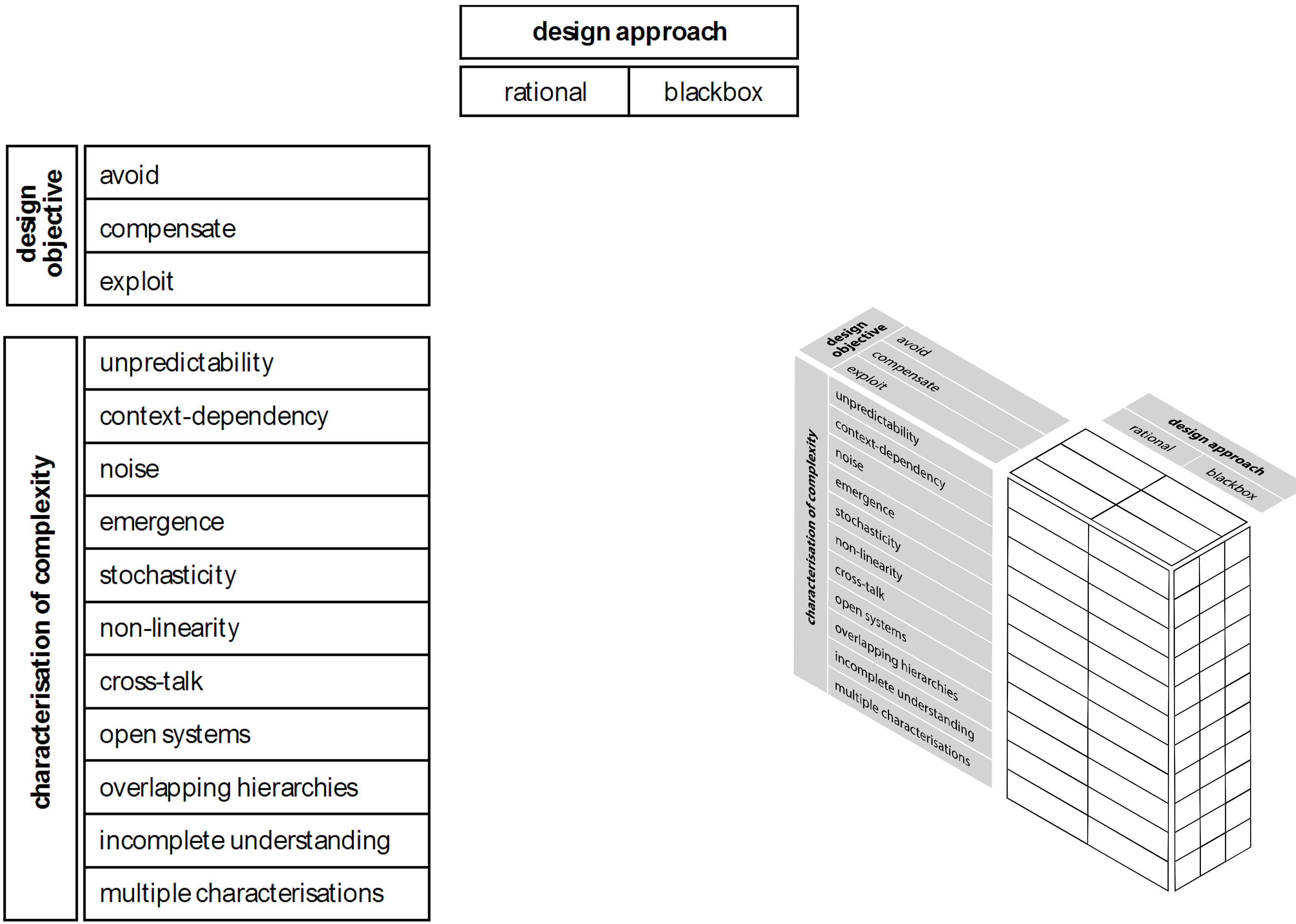
Interview topics

- How work fits into the field of Synthetic Biology as a whole.
- Challenges faced in work.
- The application of engineering and design principles in Synthetic Biology.
- The (potential) contribution of Synthetic Biology back to the engineering disciplines that first inspired it.

Findings

Building the framework from interviews





design approach
rational
blackbox
design objective
avoid
compensate
exploit
characterisation of complexity
unpredictability
context-dependency
noise
emergence
stochasticity
non-linearity
cross-talk
open systems
overlapping hierarchies
incomplete understanding
multiple characterisations

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Simplification

E.g. Mathematical modelling ignoring heterogeneity of components.

Experimentation

E.g. Systematic experiments based on understanding of components.

Exhaustive search

E.g. Trying out all the parameter configurations for parameters thought to make a difference.

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With well-defined objective

E.g. Reinforcement learning with a target range of outputs.

With multiple objectives

E.g. Multi-objective evolutionary search with several optimisation targets for different features.

With ill-defined objective(s)

Evolutionary search with a human-defined objective that shifts with changes in the environment.

design approach

rational | blackbox

design objective

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- compensate
- exploit

characterisation of complexity

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“As you go higher and higher in terms of levels, the number of parts and the number of interacting parts explodes. I guess uncertainty and complexity arise from *increasing numbers of interacting parts*.” (P3)

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"… there may actually be things for engineers to learn about *how biological systems are filthy and messy but nevertheless make optimal decisions*." (P5)

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"... <u>*we can try to start doing directed evolution, where we make random mutants*</u> in the system and hope that the performance of the system improves. And if that's the case, then we just go with that."

(P10)

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rational	blackbox

design objective

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- compensate
- **exploit**

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- **cross-talk**
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"*We could start designing things in a very different way. One example is computer cores, which are limited physically in size due to the way we build computers today, which is to ensure there is no crosstalk between two wires*, i.e. when current flows into one wire there is no impact on the other wire. This constraint means we do not explore every possible configuration of circuit network. *If we didn't have this constraint, we could miniaturise a lot more. Biology is doing that*." (P1)

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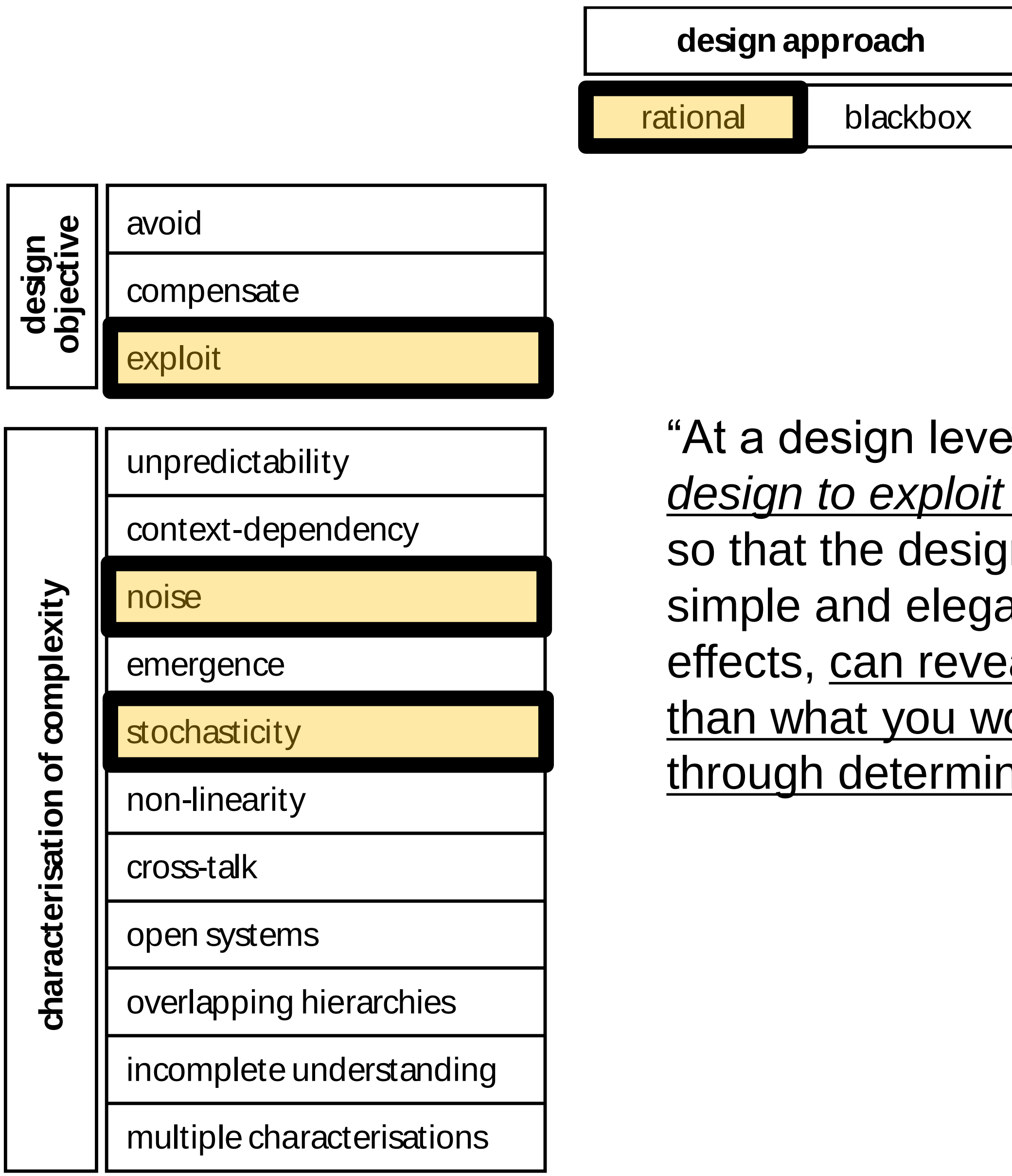
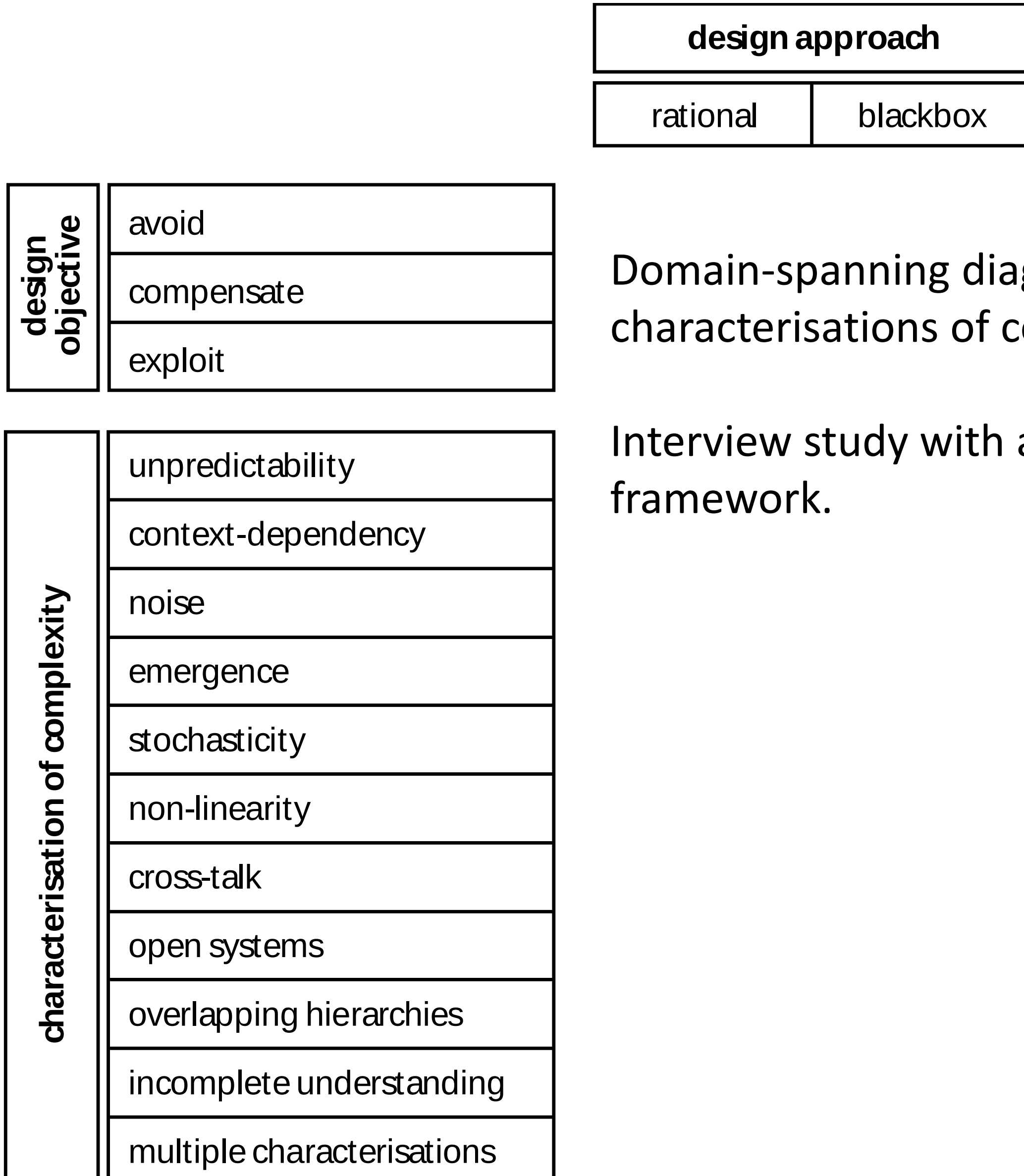
"So for example what I was describing to you before about the end of the promoter becoming the beginning of the RNA. This arose as a major problem in predictability, and three or four research papers came up with ways around it, three of which were based on, 'if you now add this extra bit of DNA in between, it now cuts this bit and this bit out so that you get a clean break between the two', *so that's effectively like building a fence between one property and another so that you engineer a solution that is modular*." (P3)



"At a design level it is not clear *how we can design to exploit noise and stochastic effects* so that the design, while still being very simple and elegant, through the stochastic effects, can reveal a much richer dynamics than what you would expect in the dynamics through deterministic design." (P1)

Further work and related work in progress



Domain-spanning diagrammatic representations of characterisations of complexity.

Interview study with a different discipline to extend framework.

Further reading

On domain-spanning design principles:

Chen C-C and Crilly N (2014) Modularity, redundancy and degeneracy: Cross-domain perspectives on key design principles. Paper presented at the *8th Annual IEEE Systems Conference*, 546-553, Ottawa, March 31-April 3.

On design issues in Synthetic Biology:

Kwok R (2010) Five hard truths for synthetic biology. *Nature* 463:288-289.

Agapakis C M (2014) Designing synthetic biology. *ACS Synthetic Biology* 3(3): 121-128.