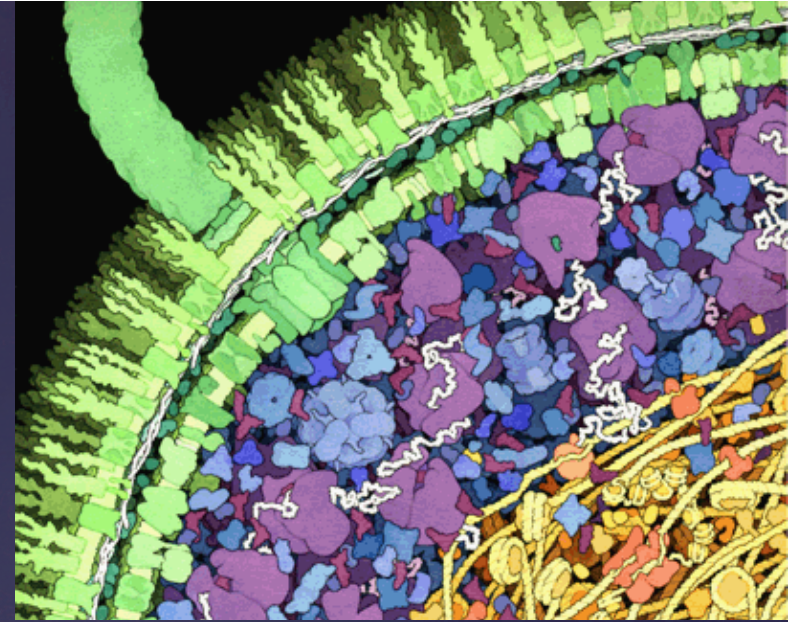


aspects of complexity



© Goodsell 1999.

an eclectic biological perspective

ESRC seminar series on 'Complexity and Method in the Social Sciences: An interdisciplinary approach' Warwick 21 February 2104

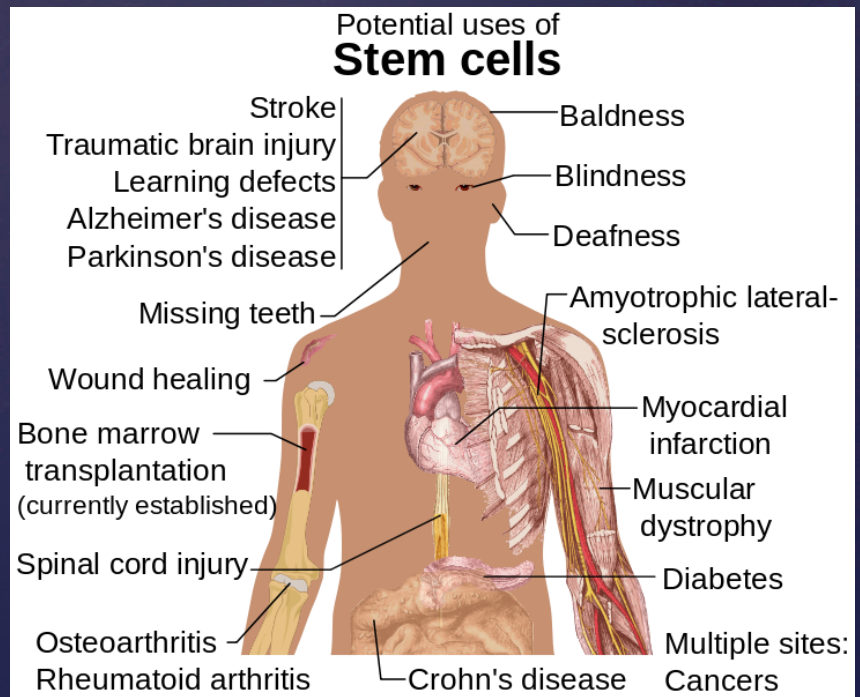
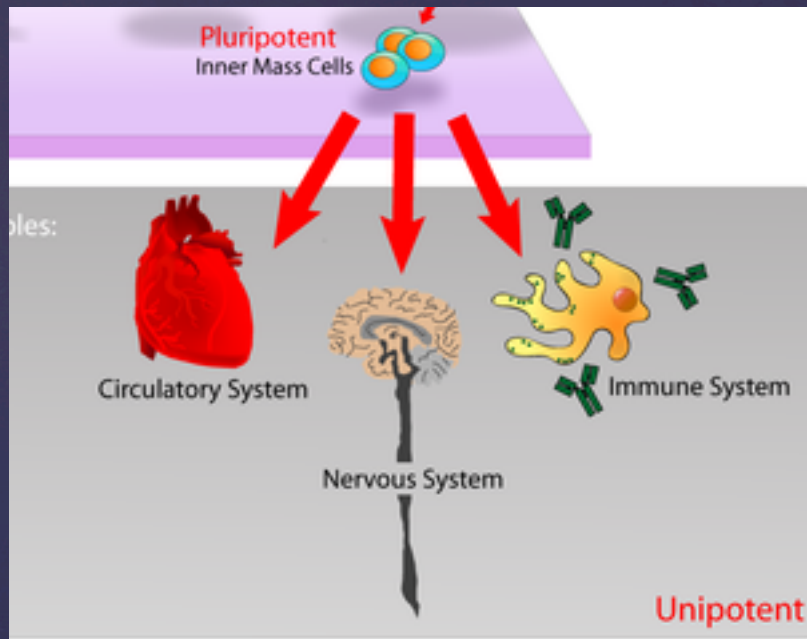
Leo Caves

York Centre for Complex Systems Analysis /
Department of Biology

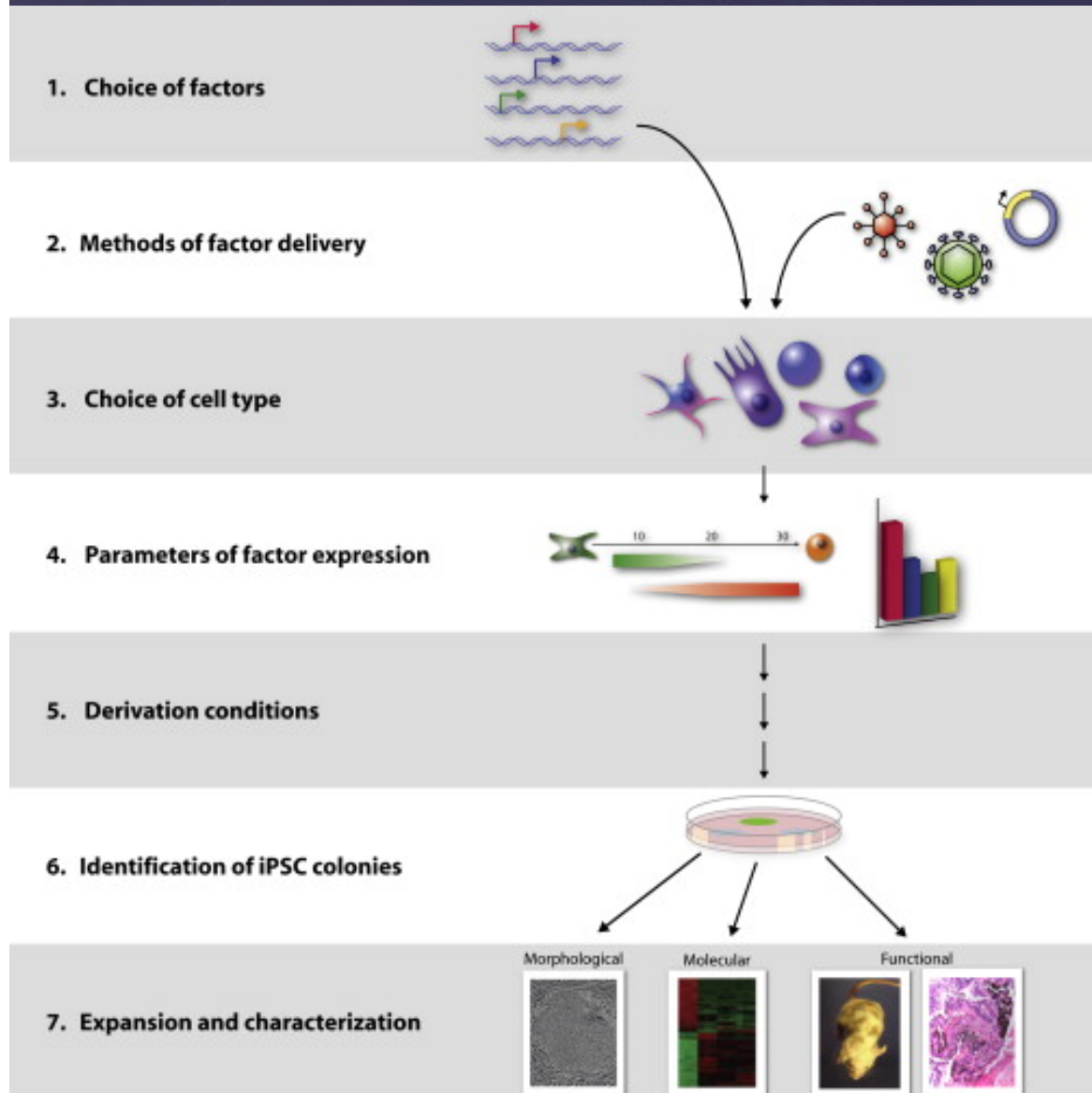
leo.caves@york.ac.uk

UNIVERSITY *of York*

case study: pluripotent stem cells



production: *inducible* pluripotent stem cells (iPS)



Factors:

DNA, protein, small molecules

Delivery: Viruses, transfection, ...

Timescale: weeks-months

Cost: high

Efficiency: few %

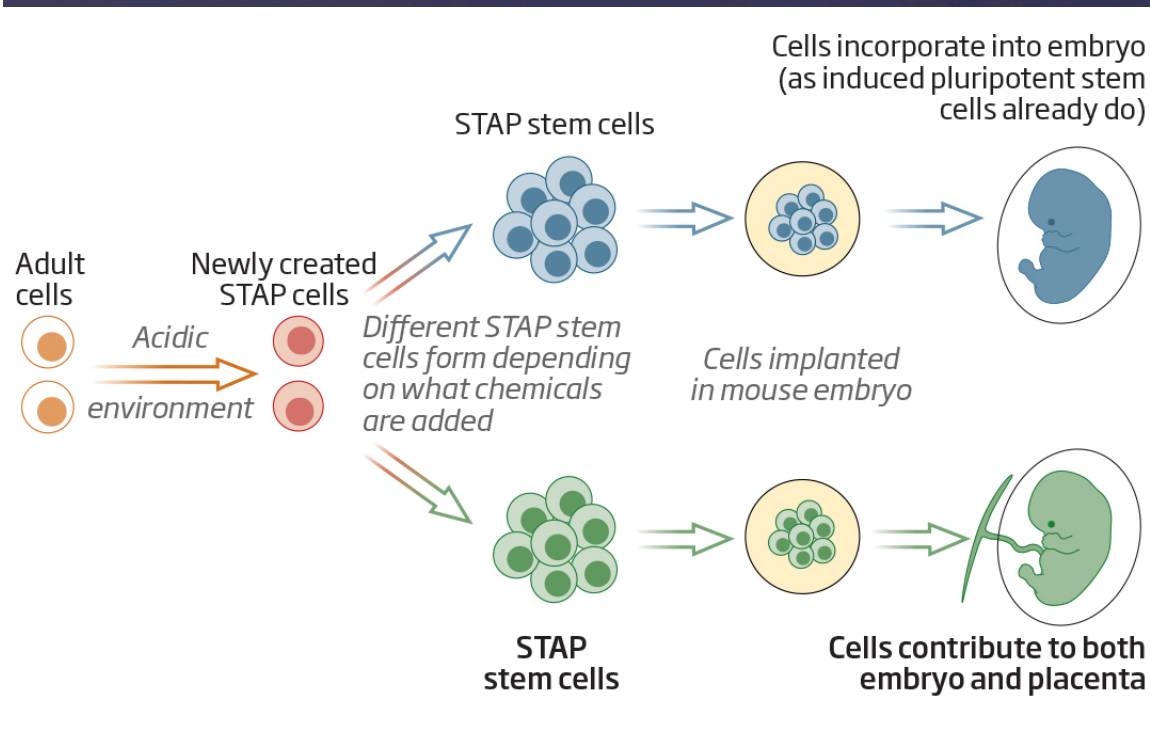
Risk: mutations, toxicity

Paradigm: *reprogram*

Maherali & Hochedlinger,
Stem Cell 2008

breakthrough: stimulus-triggered acquisition of pluripotency (STAP)

Obokata, Nature 2014



New Scientist

“Acid bath offers easy path to stem cells” Nature

Timescale: days

Cost: low

Efficiency (high)

Risk: low

Paradigm: *stimulate*
recontextualise

systems (and synthetic) biology (Kitano, 2002)

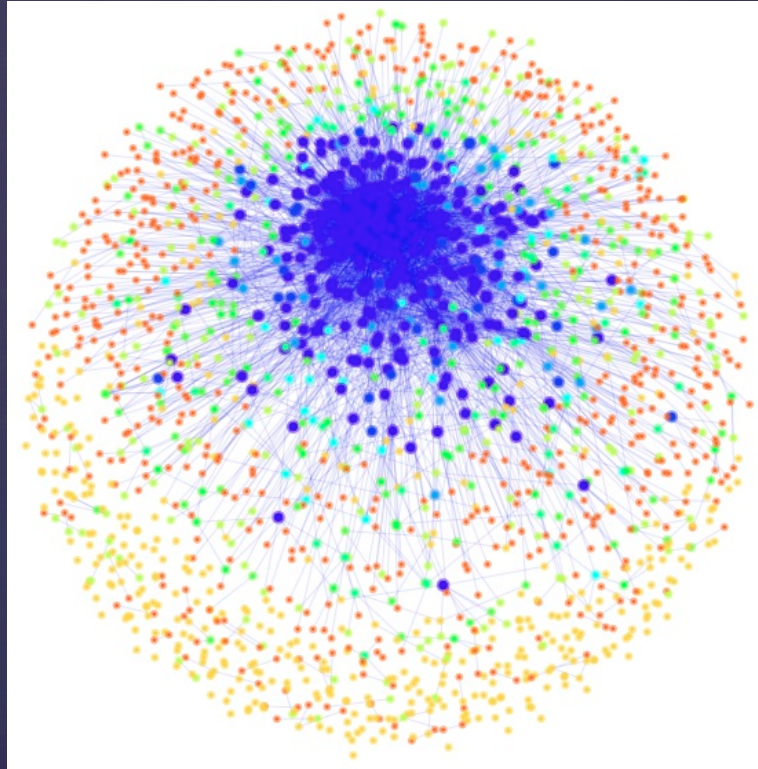
Structure: *components* (e.g. genes, proteins, metabolites etc)
interactions (networks)
mechanisms (modulating interactions)

Dynamics: *system behaviour over time*, under various conditions

Control: mechanisms that *systematically control the state* of the cell (system) can be modulated to minimise malfunctions and provide potential therapeutic targets

Design: Strategies to *modify & construct* biological systems having desired properties - devised based on definite design principles rather than by (blind) trial & error.

structure: biological networks



thesysbio.bio.ic.ac.uk

Mapping via experimental and computational methods

Data integration and network inference: Bayesian, Graphical models

Network analysis (c.f. SNA)

Architecture

Modules, motifs

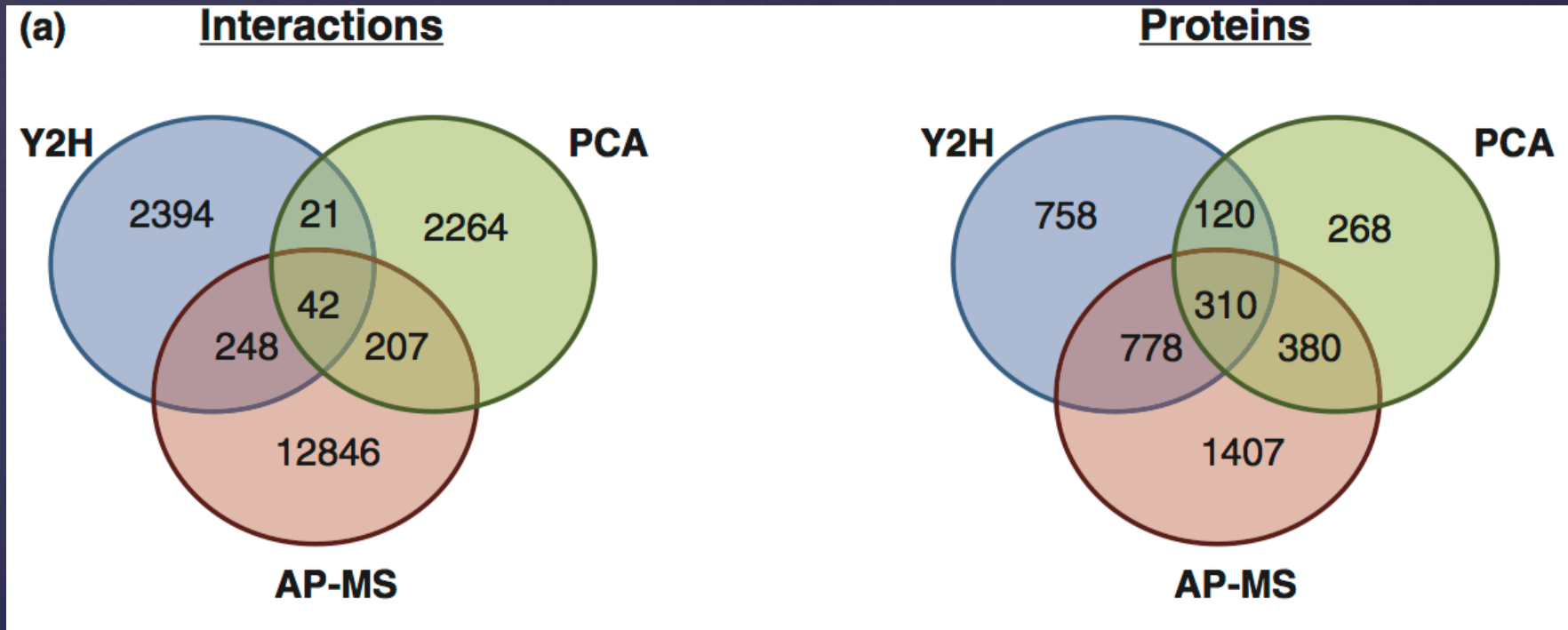
Targeting

Issues:

Incomplete data

Temporality

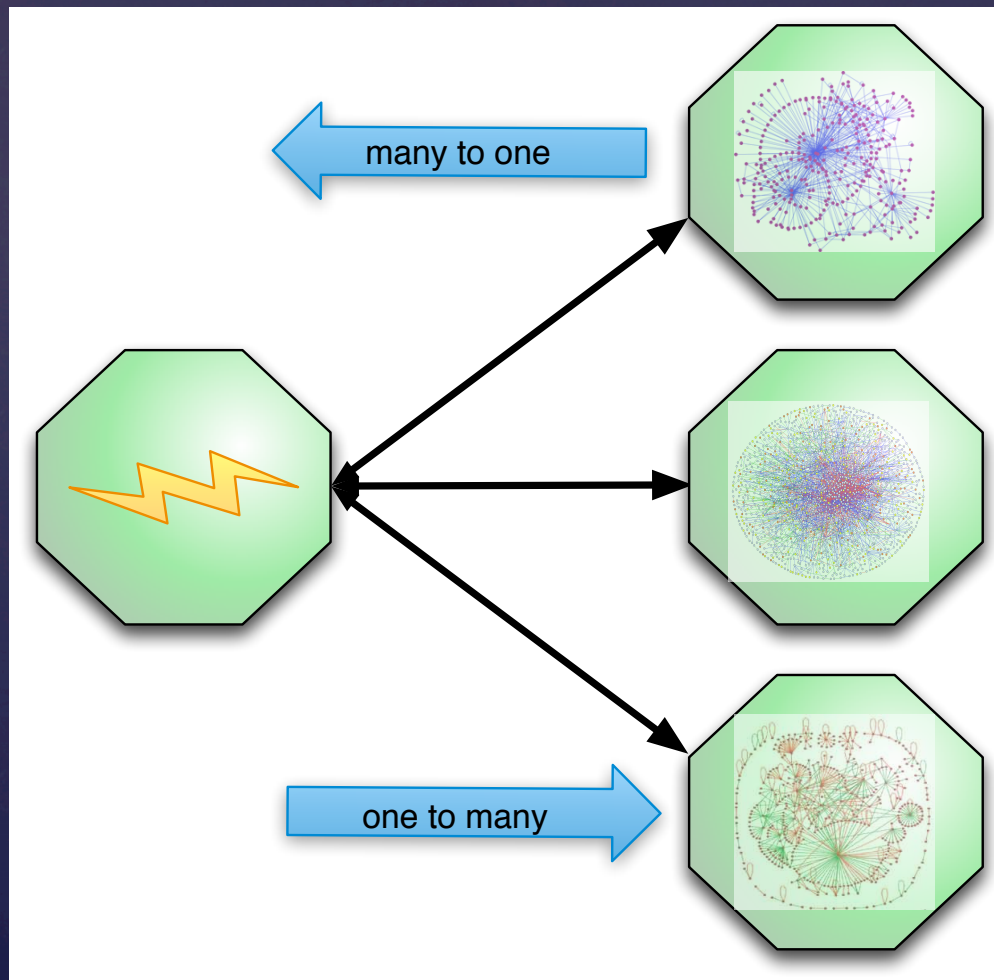
networks: experimental mappings are inconsistent



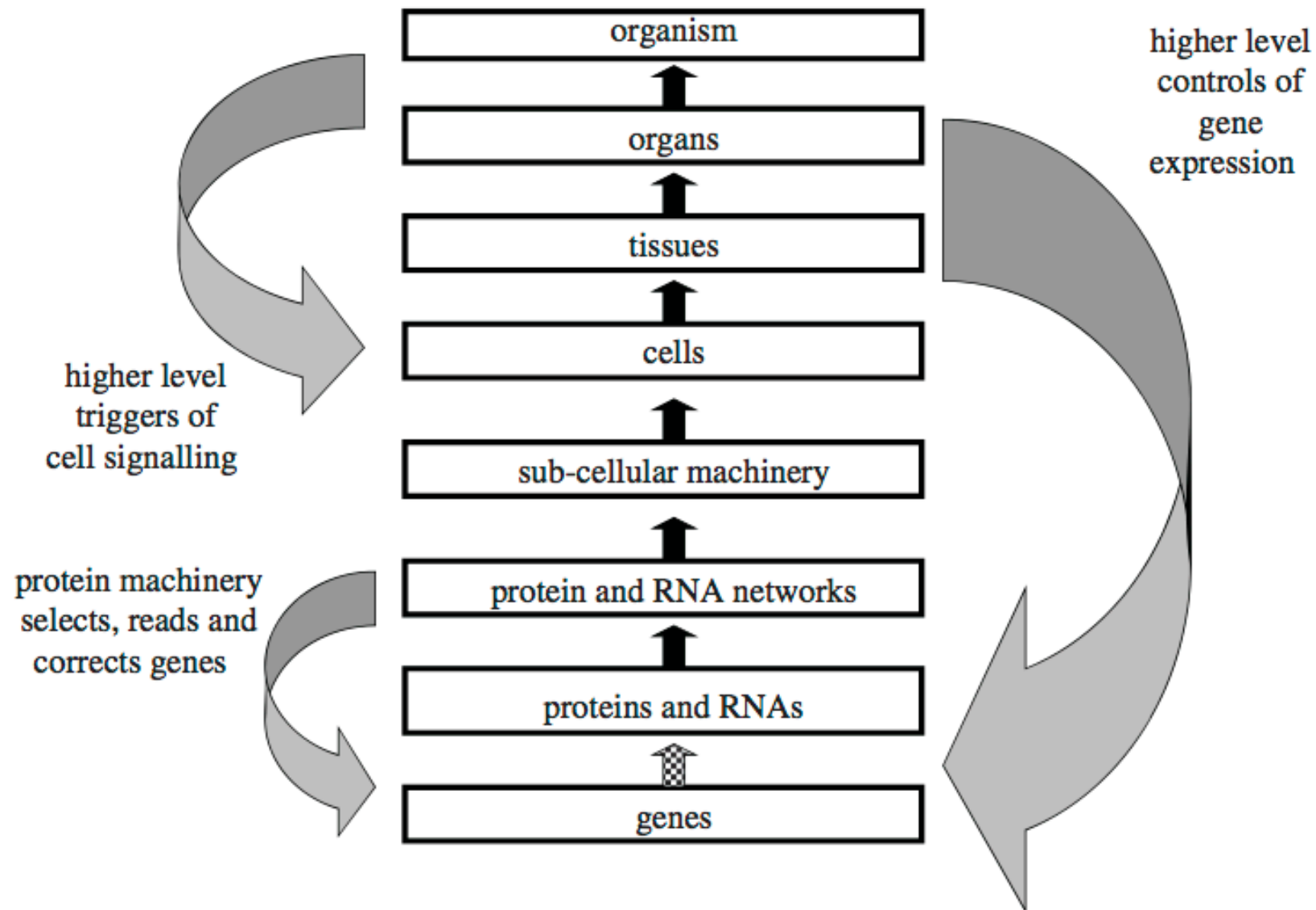
structure?

	“Classical view”	“New view”
proteins	fold to well-defined 3D structure	may be “intrinsically disordered”
interactions	highly specific	induce structure modulate specificity

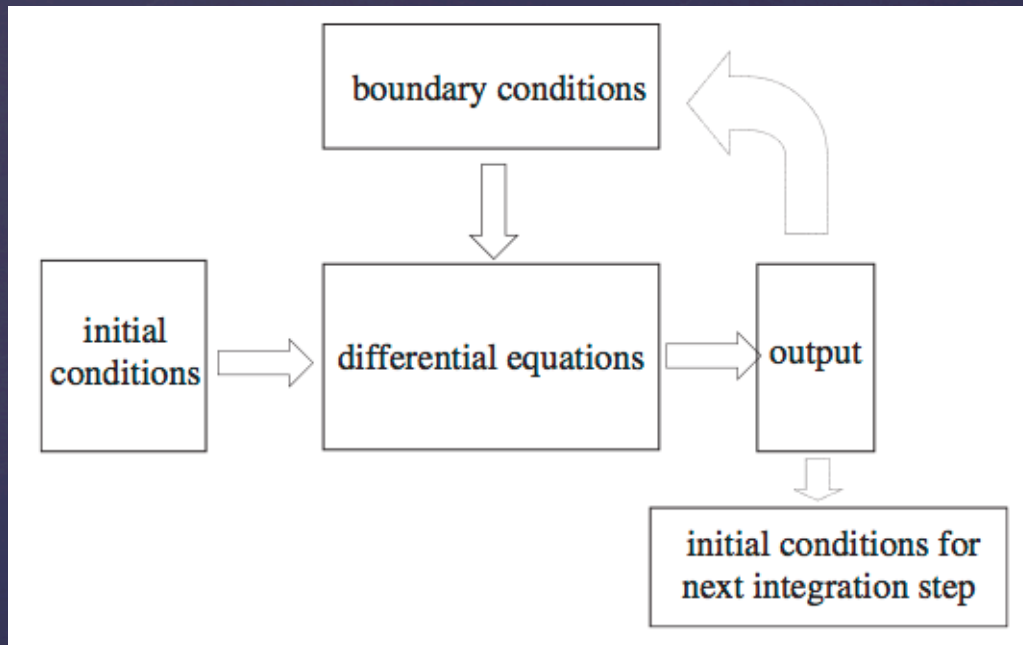
*structure? multiple realisability of “higher” level functions based on *equivalence classes* of “lower” level variables (Ellis, 2012)*



causation: bottom-up, top-down,...?



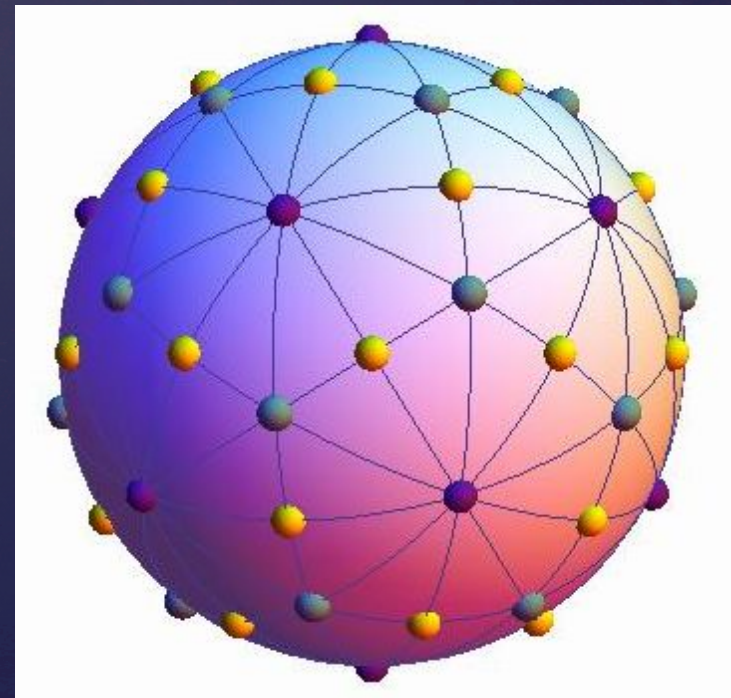
“biological relativity” : no privileged level of causation: (Noble, 2012)



Noble, 2012

webs of causation?

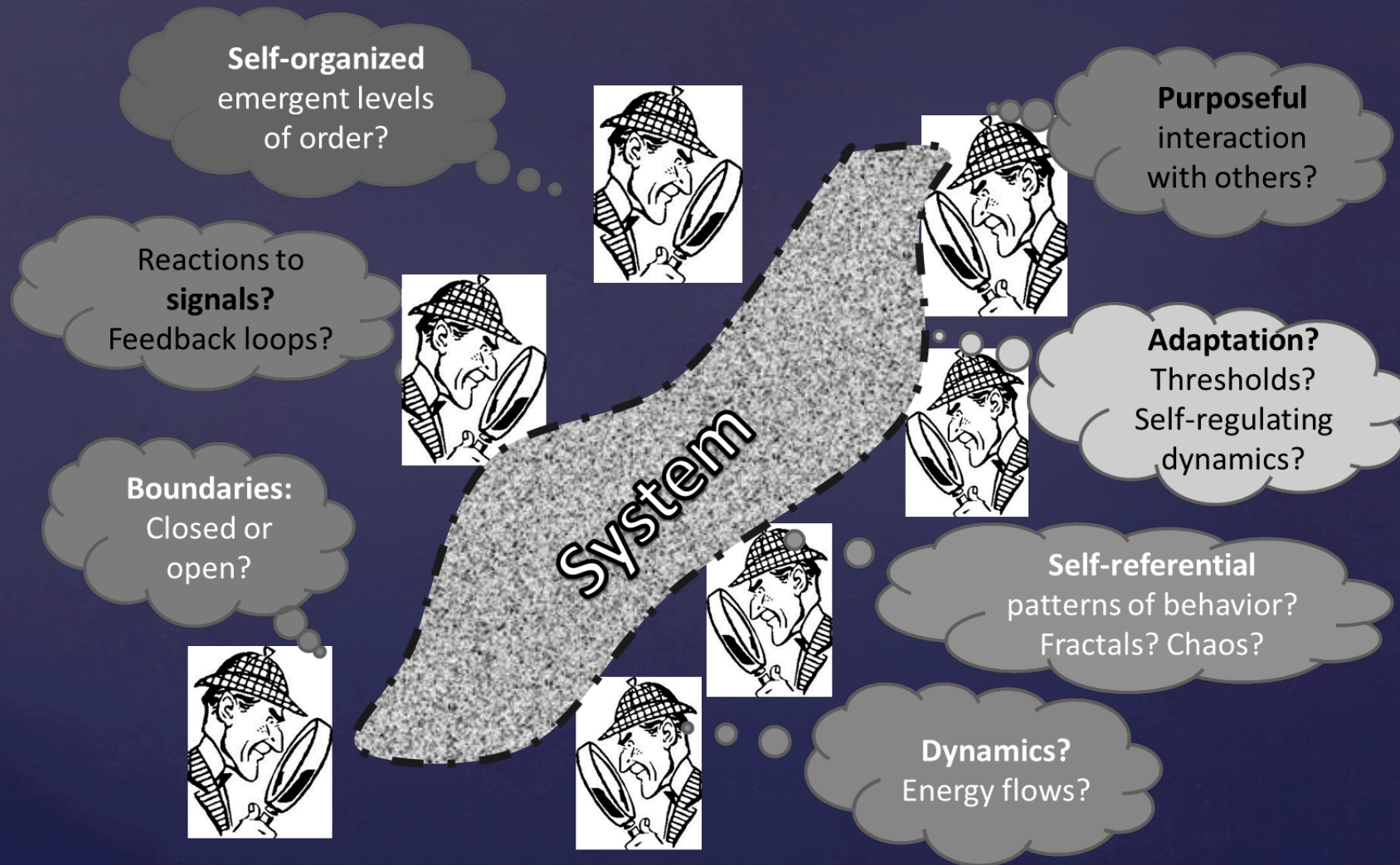
Hypernetworks?



systems: engineering, biological, social

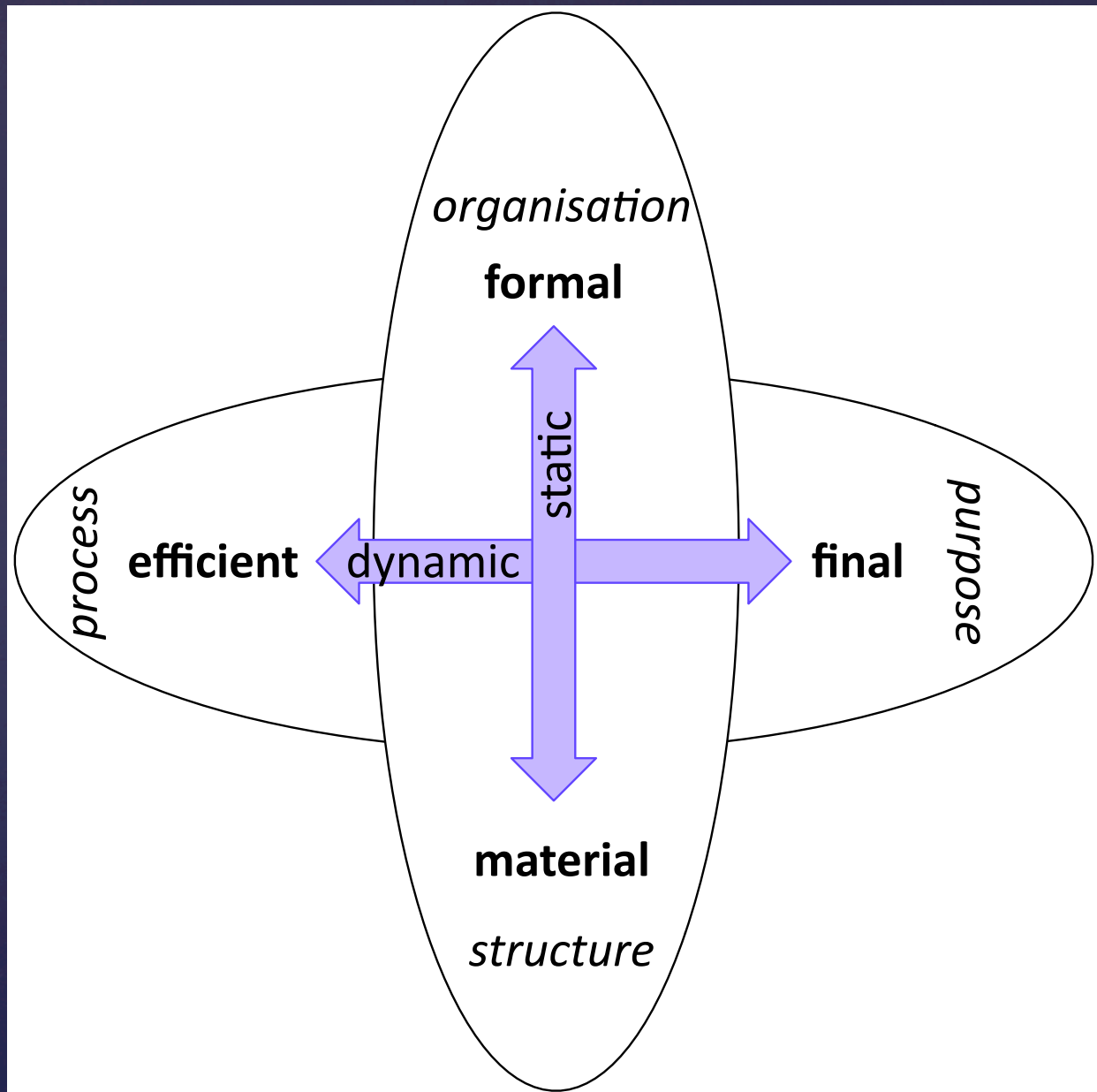
	Engineering Cybernetics	Biological Cybernetics	Social Cybernetics
The view of epistemology	A realist view of epistemology: knowledge is a “picture” of reality	A biological view of epistemology: how the brain functions	A pragmatic view of epistemology: knowledge is constructed to achieve positive results on humanity
A key distinction	Reality vs. Scientific Theories	Realism vs. Constructivism	The biology of cognition vs. the observer as a social participant
The puzzle to be solved	Construct theories which explain observed phenomena	Include the observer within the domain of science	Explain the relationship between the natural and the social sciences
What must be explained	How the world works	How an individual constructs a “reality”	How people create, maintain, and change social systems through language and ideas
A key assumption	Natural processes can be explained by scientific theories	Ideas about knowledge should be rooted in neurophysiology.	Ideas are accepted if they serve the observer’s purposes as a social participant
An important consequence	Scientific knowledge can be used to modify natural processes to benefit people	If people accept constructivism, they will be more tolerant	By transforming conceptual systems (through persuasion, not coercion), we can change society

multiple approaches



multiple explanations

Aristotle's four causes



stop press: STAP results under scrutiny

Errors in manuscript (figures)

Incomplete methodological description

Difficulties in reproducibility

Contextual approach

Prior investment

Paradigm shift?

As of 26/2/14

Blog following the developments:

<http://www.ipscell.com/>

Briefing: <http://www.biosciencetechnology.com/blogs/2014/02/new-stem-cell-sagas-0>

references

- Ellis G (2012) *Top-down causation and emergence: some comments on mechanisms* Interface Focus 2:126
- Hieronymi A (2012) *The Integration Challenge for the Systems Sciences: Highlighting Internal and External Interconnections*. Proc. of the 56th Annual Meeting of the ISSS. <http://journals.iss.org/index.php/proceedings56th/article/view/1823>
- Kitano H (2002) *Systems Biology: A brief overview* Science 195:2662
- Noble D (2012) *A theory of biological relativity: no privileged level of causation* Interface Focus 2:55
- Umpleby SA (2005) *What I learned from Heinz von Foerster about the construction of science*, Kybernetes 34:278
- Wodak S et al.(2013) *Protein–protein interaction networks: the puzzling riches* Curr. Op. Struct. Biol. 23:941

Stem Cells:

- Maherali N & Hochedlinger K (2008) *Guidelines and techniques for the generation of induced pluripotent stem cells*. Cell stem cell, 3:595
- Obokata H et al. (2014) *Stimulus-triggered fate conversion of somatic cells into pluripotency* Nature 505:641