

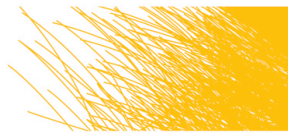
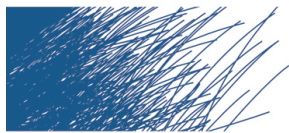
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No genetics without epigenetics? No biology without systems biology?

On the meaning of a relational viewpoint for epigenetics and current systems biology

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Research project on Systems Biology (GOA)

“Complexity thinking in a post-genomic era: a science-philosophical study of Systems Biology and its implications for (i) molecular biology, (ii) philosophy of biology, (iii) sustainable agriculture, and (iv) image building and perception with regard to (transgenic) organisms in various media”

- four disciplines involved: philosophy, molecular biology, agricultural biology, communication sciences
- four Phd students (resp. Philippe De Backer, Joris Van Poucke, Yann De Vos, Pieter Maesele) and one post-doc (Danny De Waele)
- philosophy is coordinating the research
- continuation of research on epigenesis and epigenetics

1. Systems Biology: What is it and what can it be?
2. Ambiguity of Current Systems Biology
3. Complexity: a problem of objectification
4. Kant's inspiration
5. Relational Epistemology

1. Systems Biology: what is it and what can it be?

- human genome project → relative failure of gene-reductionism and gene-centrism
 - growing awareness that the identification of unique, *material* parts is *not* sufficient to account for the *functionality* of a living being
- more encompassing organizational contexts
- new modelling & computational techniques
- overwhelming mass of structural data about the building blocks of the living organism

Its general ambition: “turn data into knowledge“ – “bring genomes to life”

- to overcome the relative failures of the genome projects
 - to recover or discover function in a world of material sequencing and production of data without function
 - to interpret the huge amount of data that became available in the new high-throughput technologies
- what is the biological meaning (function) of structural data?
- meaning within a context: a complex account of the organism
- more than the parts: cohesion, integration, interaction, ... systems perspective.
 - which context, which interpretation?

Different approaches

Bottom-up approach: priority of the local (Krohs & Callebaut)

Roots: omics data and traditional pathway modelling in molecular biology

- starts from physiological (functional) local data (pathways) and extends these using omic data
- local, embedded, implicit functionality
- results in a growing network (adding of components)

Top-down approach: priority of the global

Roots in biological cybernetics, systems theory and omics

- starts from global data (omics data), assuming that these describe the whole system
- external design-reasoning on global functionality (engineering perspective)
- tries to model the regularities on the global level

Challenges

- come to a clear concept of wholeness (ontological question of how to define wholeness) (Krohs & Callebaut, 2007, p. 209)
- to recover biologically embedded functional organization starting from the global level.
- hope = modules or units identified in the bottom-up approach will eventually *converge* with modules identified top-down, experimental research converges with computational analyses of structural data

2. Ambiguity of current Systems Biology

A problem related to structure and function, parts and wholes

General ambition = *Neither/nor*

Neither atomistic materialism, *nor* mystical holism

- starting from the parts (genes) alone is not sufficient to know the organism → no gene-reductionism, no gene-centrism
- starting from the whole alone is not sufficient to know the organism → no vitalism, no mystical holism

Factual situation: either/or

- *either* it looks, top-down, for a substantification of wholeness that will allow for an adequate understanding of the parts (“finding a clear concept of wholeness”, Krohs & Callebaut)
- *or* it sticks to the parts and attempts to generate and understand organized wholes on that basis.

A problem for Systems Biology?

- search for integration or unification in a dualistic space: *either* the parts (local, internal functionality, bottom-up) *or* the whole (global, external functionality, top-down)
- from *either/or* to *and/and*
- conflation between both is excluded , cf. modern gene concept

- **Classical, gene-reductionist, account: conflation of two types of reductionism (cf. modern gene concept)**

- Part-whole reductionism (Mendelian – phenotypic traits)
- Material reductionism (physicalism- basic material constituents)
- Conflation of both views
- Ideal: knowing the genes = knowing the organism

- **Unhappy marriage?** “(...) contemporary biology relies upon an unhappy marriage between atomism and a materialistic (and often mystical) holism in which a predominantly atomistic and functionalist conception of the organism *per se* is coupled with a holistic conception of a ‘central directing agency’ conceived as a material entity – the so-called ‘genetic programme’ – which is supposed to determine, order and unify the atomic units and events. The organism as a real entity, existing in its own right, has virtually no place in contemporary biological theory”(Webster & Goodwin, 1982: 6).

Systems Biology: the same (unhappy) marriage, a new marriage, or no marriage at all?

- At this moment SB *reveals* the untenability of the modern gene concept (as epigenetics has done at a certain moment) – symptomatic significance
- Complex account: which place does SB give to the organism?
- Complexity talk is just metaphorical, wishfull thinking, a veneer?

3. The message of complexity: transcending oppositions

Hypothesis one: a complex account needs to avoid the either/or opposition between two independently identified partners (parts and wholes) to be integrated afterwards

- Finding a clear concept of wholeness goes hand in hand with finding a clear concept of parts
- Challenge is to find a non-oppositional, non-dualistic way of dealing with parts and wholes

Hypothesis two: account of function and structure transcending the opposition between an internalist implicit view, as well as the externalist view on function

Hypothesis three: adequate theory of objectivity: avoiding the opposition between the objectively- real and the subjective-metaphorical

3.1. Complexity involves priority of context

- Context → formal organization
 - to address the living system as a complex system, is to attempt to understand it from the perspective of the *specific contexts* that make it possible and that as such *formally* transcend the isolated data but allow an understanding in an integrated and systematic way.
- Here: priority to formal principles specific to biological organization
 - formal = not material content, but conditioning/constraining the content
 - analysis of *possibility* of a (complex) relation between parts and wholes (cf. Maturana & Varela, theories of self-organization)
 - justification = experience, “there is life”

3.2. Complexity shifts its awareness to conditionality

- from oppositionality to conditionality:

→ complexity of the organism = dependency on context: what there is, depends on how it is carried through a context

→ take into account not just the “beyond” (*epi*), but also the perspective out of which something is considered as a “beyond”

- *entertaining the in-between*: co-constitution instead of dualism and symbiosis: no reduction, no holism

→ no objectivity without subjectivity, no parts without wholes, and vice versa (no genetics without epigenetics, no biology without systems biology, ...)

→ engaged participation

3. 3. Complexity involves tarrying with the negative

- life is a matter of conditionality, of *suspension*, of entertained tension in between a materiality of parts and an ideality of wholeness
- *formal* organization = idea of suspension: life is *not* in the parts, it is *not* in the whole, it is *beyond* or *in-between*, *it is neither/nor*
- conflating parts and wholes (classical gene-reductionism) implies an elimination of this suspensive organization, a reduction of life to dead matter (symbiotic marriages are killing?)

4. Kant's viewpoint on the living – its implications for objectivity and subjectivity

- a theory of conditionality
- how is universal and necessary knowledge possible?
 - subject-related construction of object
 - domestication of phenomena
 - logic of discharge
- exceptions: living systems are problematic in relation to objectification
 - impossible objectification *reveals* subjective conditionality
 - potential value of complexity theories (incl. epigenetics and Systems Biology)

The living as intrinsically resisting objectification

- living systems are organized and self-organizing beings (natural purposes)
 - organised essentially in view of certain purposes
 - absence of external, objectively certified rule
 - nothing for nothing: each part in function of the whole and the whole in function of each part
 - not chaotic, not anything goes
- epistemology
 - necessity of considering living beings *as if* they are purposive wholes
 - life = matter of principle (formal conditionality): *if* there would be an external a priori rule that could capture a living system, it would not be a living system.
 - “supplement of meaning” as knowledge principle: external addition, subjective engagement
 - → Relational epistemology

5. Conclusion: relational epistemology

- context is of the essence: formally prior to the parts, and qualitatively different (experience of “there is life”).
 - absence of an objective foundation in either the parts or the whole (neither/nor)
 - supplement, perspective, context.
- context *for* the parts (meaning of the parts = place in the context):
constraint = possibility
- supplement = supposition of intrinsic purpose = supposition of dynamic structure (circular causality)
 - structure *is* not, it is to be supposed, carried
 - supposition = contextual determination
 - stratification of this idea (biosemiotics)

-no rule that dictates the passage from sufficiency (experience) to necessity (reflection)

→ objectification is a matter of choice, negotiation: which most adequate external supplement?

→ relational epistemology needs to articulate the conditionality of the necessities and choices: what do you want science for?

-Systems Biology points to that possibility, but will it contribute to a further critical analysis of objectivity in relation to subjectivity?

Cf .status of the supplement of meaning

- universal subject
 - human interactively engaged agent – symbolic structure
 - epigenetic structures?
 - systemic stratification?
- ethical perspectives: from a logic of discharge to a logic of engagement?



Acknowledgements

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