Physiological Robustness

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History of project

- Discussions started in Tours in 2015
- What can robustness clarify about health, disease?

- Currently rethinking focus in steps
  - Physiological robustness (phil bio)
  - Objective preferences in health (phil med)
  - Health and physiological robustness
  - Disease and robustness (fragility, rigidity, periodicity…?)

- Also with Suresh Rattan (biologist AU) – health, healthy ageing, robustness biomarkers

Methodology: naturalization

- Not bringing philosophy to bear on sciences (conceptual analysis)
  - What we mean by a concept, common usage
- Method of extracting general concepts from sciences → *naturalization*
  - Scientific descriptions, systematic/unifying theories
- First step in naturalization of health (and disease) via robustness

A field of questions…

- Centrality, ubiquity of "robustness"
  - Vitality? Solidity? Sturdiness? Stability? Fortitude? …
- Unclarity, differing definitions, lack of/difficult operationalization
  - System, network 'stability'
    - State/structural vs. capacity/ability?
    - Outcome of system behavior or behavioral capacity itself?
    - How is this stability defined, measured?
- Broad view: robustness as property that *increases chances of survival*
  - Specific *physiological* property of living systems (vs. populations, ecosystems, gene pools…)?
  - = Fitness?? Biological concept also explaining survival, but different implications for organism-environment relations and populations vs. individuals?

Outline

- Disentangling ‘survival’ and ‘lifespan’ as key physiological concepts
- Is robustness redundant with fitness?
  - 4 ways to distinguish**
- Definition/naturalization, operationalization of physiological robustness
- Open issues: trade-offs in complex systems, forms of robustness

Survival and lifespan: conceptual families

- Fitness typically until adulthood (viability) or reproduction (fertility) (Sober)
  - Physiology of survival concerns all life history stages
- "Lifespan"
  - Essential lifespan (humans 40-50 yrs)
  - Average lifespan (life expectancy) (75-85 yrs)
  - Maximum lifespan (contingent on observation) (122 yrs)
  - Perturbations → lower chances of surviving as long as would have without
- Fitness for ELS/ALS, robustness for MLS (why some survive longer than others)
- "Survival"
  - Under severe conditions (hibernation, dauer…)
  - Yet 'fragile' (worsened by variations)
  - With 'vitality', 'normativity', 'antifragility', 'robustness'… → or *because* robust?

Biological and physiological robustness

- *Physiological robustness* = the *ability* to resist perturbations, that is, to increase the probability that individuals, or a population, survive as compared to other individuals, or other populations that do not have the same ability or do not have it to the same degree, in the face of the same challenges in the same environment

- Biological robustness as broader ability to resist = PR + environmental "protective factors"
  - Plant + pesticide, prey + parasites, metabolism + food access …
  - Not internal/external, but continuous/discontinuous distinction (biodemography)
  - Changing environment, protective factors changes PR
  - Not all robustness is physiological (e.g. against mutations)

- Reproduction → evolution, Fitness → reproduction, BR → fitness, PR → BR

Fitness vs. PR (1): Parts vs. wholes

Focus on survival probability → fitness?

Water flea and developmental plasticity costs for "likely future" (Matthewson & Griffiths) – if environs change, better off had it not developed to survive predation

Fitness

- Relative to environment of selected population, not to rest of organism
  - Fit traits regardless of vehicle
- "Competitive fitness"
- Antagonistic pleiotropy

Robustness

- Parts or wholes can be robust, but reference to whole seems necessary
- Self-regulatory processes
- Downward 'constraints' (Noble)
  - Whole resists perturbations, perhaps with trade-offs
  - Trade-offs affect maximum lifespan

Fitness vs. PR (2): Actual vs. possible

Fitness

- Classical – immediate, local environment (Gould)
- Long-term survival/fitness strategies (ecological fitness (Peacock))
  - Aspens cloning
- Traits explaining persistence relative to *actual* conditions (local or global)
- Fit relative to specified, likely conditions (e.g. developmental feedback)
  - Measured by *actual* number of offspring (averaged*), or average lifespan

Robustness

- Also explains persistence, but relative to possible, unknown, random conditions
- Ability to survive a *range* of conditions
  - Dispositional – to be able to survive as conditions vary (possibility)
- Conditional probability – based on "hypothetically varied circumstances" (Sommerhoff)
  - Had conditions been different, it *would have* survived (been robust)

Fitness vs. PR (3): Long vs. short-term scales

Fitness

- Different long-term survival strategies via eco-fitness (Peacock)
  - Cooperative fitness – mutually beneficial relations (symbiosis)
  - Constructive fitness – enlarging ecological space (plants)
  - Both improve (population) fitness over the course of generations

Robustness

- Individuals surviving at a given time
  - (Micro)seconds to decades
  - Based on regulatory processes occurring at multiple time scales during life history
  - Development, adulthood, ageing…
  - W/r/t perturbations relevant for (threatening, benefiting) systemic/organismic survival

Fitness vs. PR (4): Populations vs. individuals

Fitness

- Property of class of individuals
  - "homozygous for allele A at a particular locus" (Maynard-Smith)
  - Not offspring of given individual, but on average for a class
  - Individuals/traits are deemed fit relative to reference class

Robustness

- Can work for populations, subpopulations, or individuals (epistemic)
- Average lifespan → populations (epidemiology)
  - Heuristic – What allows most people to survive longer, on average?
- Maximum lifespan → individuals (clinical)
  - What will allow *this individual* to survival longer than she might have otherwise?
- No necessary link to reference class
  - A system's, organism's own norms of robustness
  - Its physiology, environ, trade-offs, etc.

Broadly…

- Fitness explains the *why* of survival, physiological robustness explains the *how* (?)
  - Ultimate vs. proximate explanations
    - *Physiological robustness* as the *ability* to resist perturbations, to increase the probability that individuals, or a population, survive
  - Robustness has to capture:
    - (Partly) holistic, conditional ability, during life history, of individuals

Defining/naturalizing: from homeostasis to robustness

- Coming from history of physiology
  - Homeostasis – regulated constancy as previous/strongest attempt to explain survival
  - Empirical and philosophical difficulties
    - "Dynamism" → "reactive homeostasis", "predictive homeostasis", "rheostasis", "homeorhesis", "allostasis" (Schulkin) and "homeodynamics" (Yates, Rattan)
    - Healthy aging, pregnancy, reproduction, hunger and sexual drive (Boorse 1977)
    - Parts vs. wholes (Ananth)
    - Pathological homeostasis (Bernard-Weil)
  - Prematurely rejected (for health), perhaps placing biological over physiological considerations
    - Reproduction, fitness given more weight over regulation and life-historical survival goals

Defining PR

- Recent physiology (systems-network biology) rethinking concepts
  - Allostasis, plasticity, resilience, homeodynamics, robustness
  - Robustness – central, but no agreed definition or level of application
    - Organic and inorganic, states and processes, individuals and populations, parts and wholes, mechanisms and structures
    - "resistance to perturbations in the parameter values" (Gross)
    - "a (property) of a (system) is robust if it is (invariant) with respect to a (set of perturbations)" (Alderson & Doyle)
  - Possible unifying framework – Dynamic Systems Theory
    - Any particular system's state in a given period of time can be precisely described in terms of sets of variables that vary together to maintain some goal state
    - Running → rates of heartbeats, respiration, perspiration, muscle contraction, glucose consumption, etc., increase and decrease together in patterns adjusted to one another as well as to environmental parameters, with the consequence of keeping the 'overall relation' of this covariation constant

Defining PR

- Co-varying variables allowing for system maintenance, "invariance"
  - "Directive correlation" (Sommerhoff) → directive covariation
  - Dynamic *relationship* between parts of system – robustness is the maintenance of this

- *Robustness = maintenance of the directive covariation of a system's variables within set boundaries, i.e. a system's relative resistance to deformation*
  - Tracks system's *capacity to resist perturbations* – what it can (would be able to) tolerate
  - At specified level of organization and specified perturbations (*always wrt X*) (Lesne)
    - Potentially holistic, conditional, life-history relevance
  - Quantitative, degrees → more or less robust
    - Can be determined for a given system (individual): compared to itself at different times, in hypothetical circumstances
    - What allows (would allow) *this individual system* to survive longer

Operationalizing PR

- Direct, reliable measurement of such capacity for 'resistance'?
- Possibility: measuring robustness ratio
  - "the ratio of a perturbing force or demand to the degree of disturbance of the system" (Bassingthwaigthe, Hunter, Noble 2009)
  - Ratio between internal/external demands placed on a system and the degree of change required by that system to meet these demands
    - More robustness → less disturbance relative to larger perturbations
    - Less robustness → more disturbance relative to smaller perturbations
    - "example of strong robustness would be the large change in cardiac output demanded by the body in going from rest to exercise divided by the small change in cytosolic ATP levels in a normal heart"
  - Still have to define magnitude and duration of 'disturbance' and 'perturbation'
    - "Normal heart" → Is reference class necessary? From heuristic to known conditions?

Open issues: trade-offs

- Hierarchical complex ("nested") systems have inherent trade-offs
- Robustness at one level needn't entail robustness at another
  - Evolutionary resource allocation (Piersma and van Gils)
  - Highly Optimized Tolerance (HOT) Theory (Carlson and Doyle)
    - More robust wrt X (common, general), less robust wrt Y (rare, unexpected)
  - Structural properties – strong, weak 'nodes' in network (robust via modularity, degeneracy…)

- How to specify 'optimal' trade-off that ensures maximum survival ability for individuals?
- Do nested-ness, trade-offs necessitate an organismic, holistic perspective?

Open issues: dimensions and forms

Robustness: maintenance of the directive covariation of variables describing the system	**State Robustness**	**Homeostasis**: process whereby a system repeatedly comes back to a set of values for a set of variables, up to a certain distance from these values, despite variations in parameters
		Allostasis: process whereby a system reversibly or irreversibly moves into another basin of attraction without breaking down
	Functional Robustness	**Resilience**: process through which a system maintains a given level of functional performance despite changing parameters
		Plasticity: process through which a system reversibly or irreversibly moves from a given level of performance to a different level without breaking down
	Age Robustness	**Endurance**: systemic process of maintaining state or functional stability in the face of a given quantity of damages before eventually collapsing
		Homeodynamics: systemic process of shifting from a given state or function to another in the face of a given quantity of damages before eventually collapsing

Thanks!

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