NuGo Week - September 6th 2011

Is health a state or an ability? Towards a dynamic concept of health

Nutrigenomics & Health

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“Health”… because of my recent article in the British Medical Journal:

BMJ’s cover saying: …Health is in the air!

The article:

BMJ

BMJ 2011;343:d4163 doi: 10.1136/bmj.d4163

ANALYSIS

How should we define health?

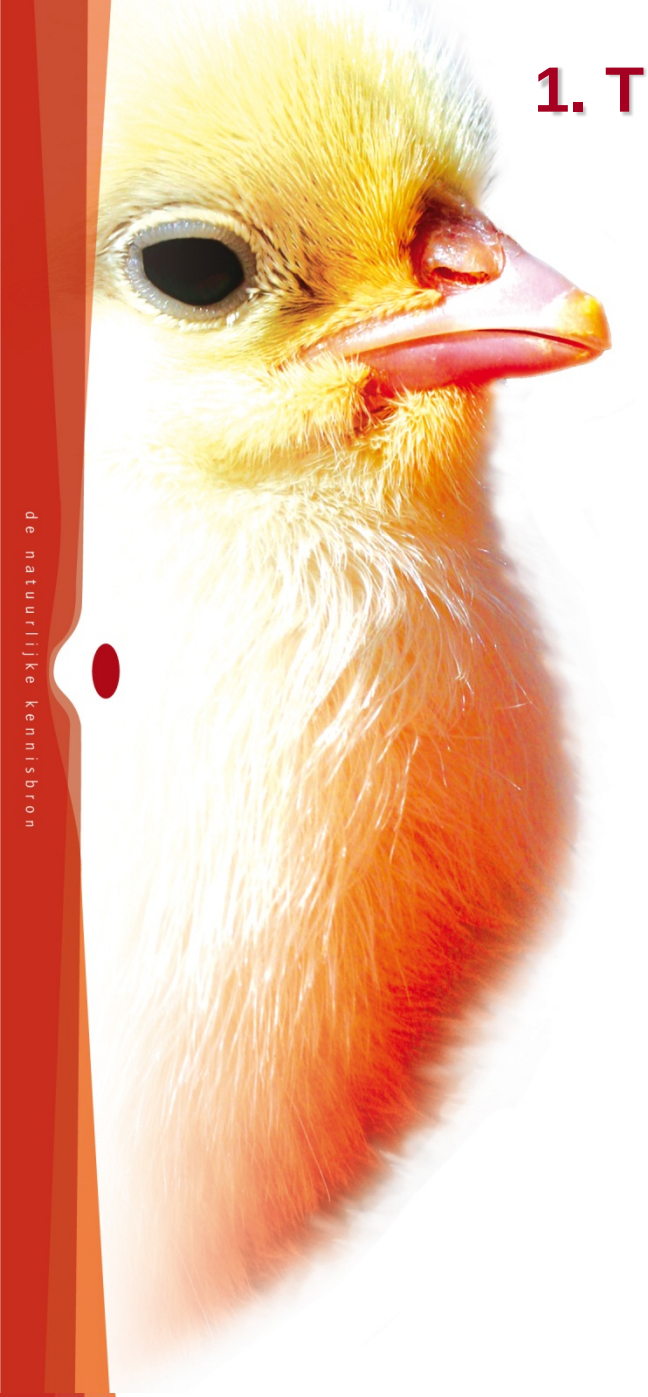
The WHO definition of health as complete wellbeing is no longer fit for purpose given the rise of chronic disease. **Machteld Huber and colleagues** propose changing the emphasis towards the ability to adapt and self manage in the face of social, physical, and emotional challenges

Machteld Huber *senior researcher*[1], J André Knottnerus *president, Scientific Council for Government Policy* [2], Lawrence Green *editor in chief, Oxford Bibliographies Online—public health*[3], Henriëtte van der Horst *head* [4], Alejandro R Jadad *professor*[5], Daan Kromhout *vice president, Health Council of the Netherlands*[6], Brian Leonard *professor*[7], Kate Lorig *professor*[8], Maria Isabel Loureiro *coordinator for health promotion and protection*[9], Jos W M van der Meer *professor*[10], Paul Schnabel *director* [11], Richard Smith *director*[12], Chris van Weel *head* [13], Henk Smid *director* [14]

The history behind it ……

The content of my talk:

1. The history behind the article
2. The content of the article
3. The meaning for nutrigenomics
4. The challenges ahead



1. The history behind the article

In 2006-2008 I conducted an explorative feeding study in chicken, model for humans, in search for possible **health effects** from two different food types:

A blinded intervention study in an **immunological chickenmodel (3 lines),** 150 chicken in 2 generations, receiving an immunological **challenge** in the 2nd generation.

Only the feed differed: **A** or **B**

Partners: WUR, TNO, RIKILT

de natuurlijke kennisbron

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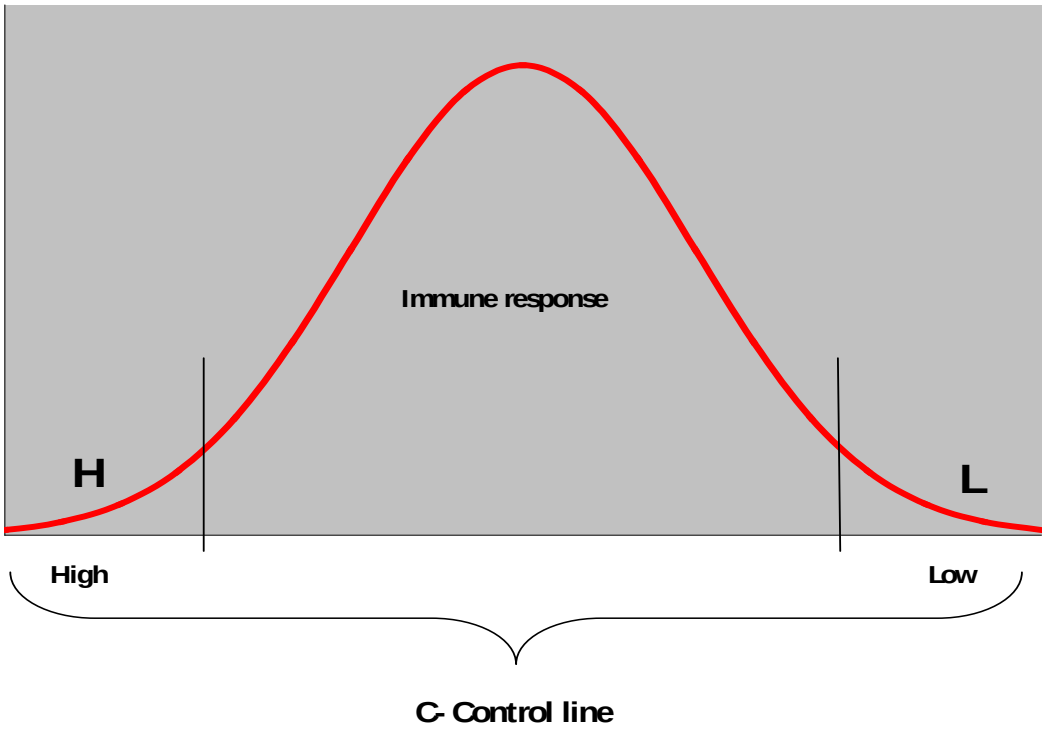
The Animals

3 special immunological chicken lines: H, C, L

3 x 2 groups of 25 chicken each

H = High responders, L = Low responders,
C represents 'normal'



The Animals

The parameters that we measured:

- General health parameters: weight, growth, feed intake,illnesses, egg production, fertility, etc.
- Immunological parameters: innate and specific, cellular and humoral
- Metabolomics of blood and liver
- Genomics of the gut
- Post mortem evaluation of organs

The Animals - Results

First outcome: all animals were healthy!

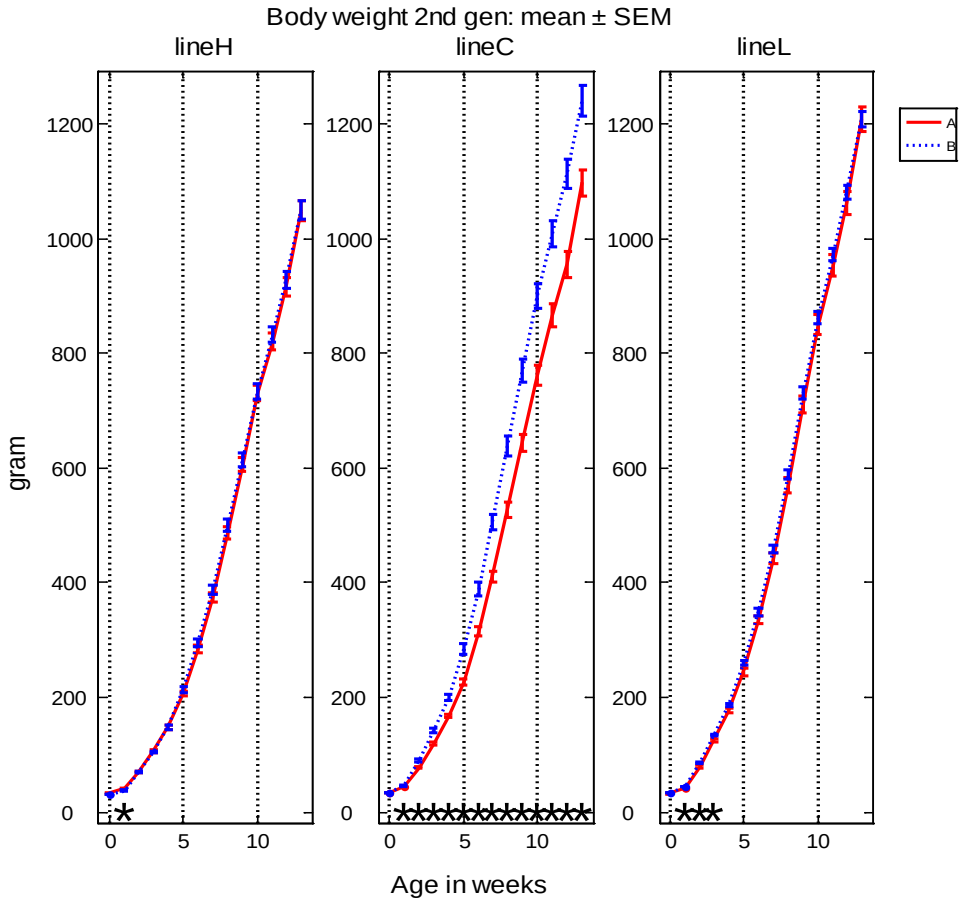
This could be expected as both feeds were adequate.

Yet there were many physiological differences, especially after we gave at 9 weeks an immunological challenge with KLH (from the keyhole limphet haemocyanin molusc).

The Animals - Results

- **Weight:** Animals on **Feed B** gained more weight than on **Feed A**

Feed A is Red **Feed B is Blue**



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The Animals - Results

- **Immune system:**

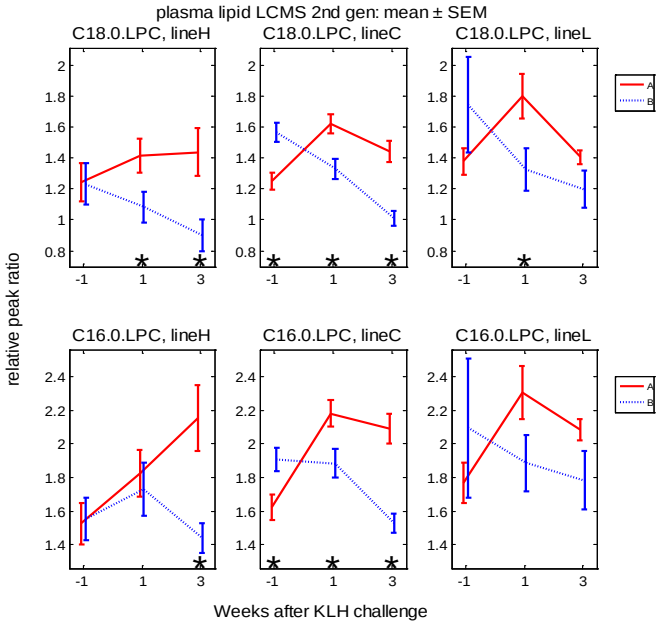
  Animals on the Feed A showed
  a **stronger ‘immune responsivity’,**
  in the innate as well as the adaptive immune system,
  called a **more ‘alert’ immune system.**

The Animals - Results

- **Metabolomics:** A broad spectrum of differences in all platforms. Animals on the **Feed A** showed a **stronger**

  'Acute phase response' after the challenge with KLH

  and a **stronger liver metabolism** afterwards.



Two most discriminating metabolites in the lipid platform

The Animals - Results

- **Genomics:** Animals on **Feed B** showed **less active genes** in the natural **cholesterol synthesis.**

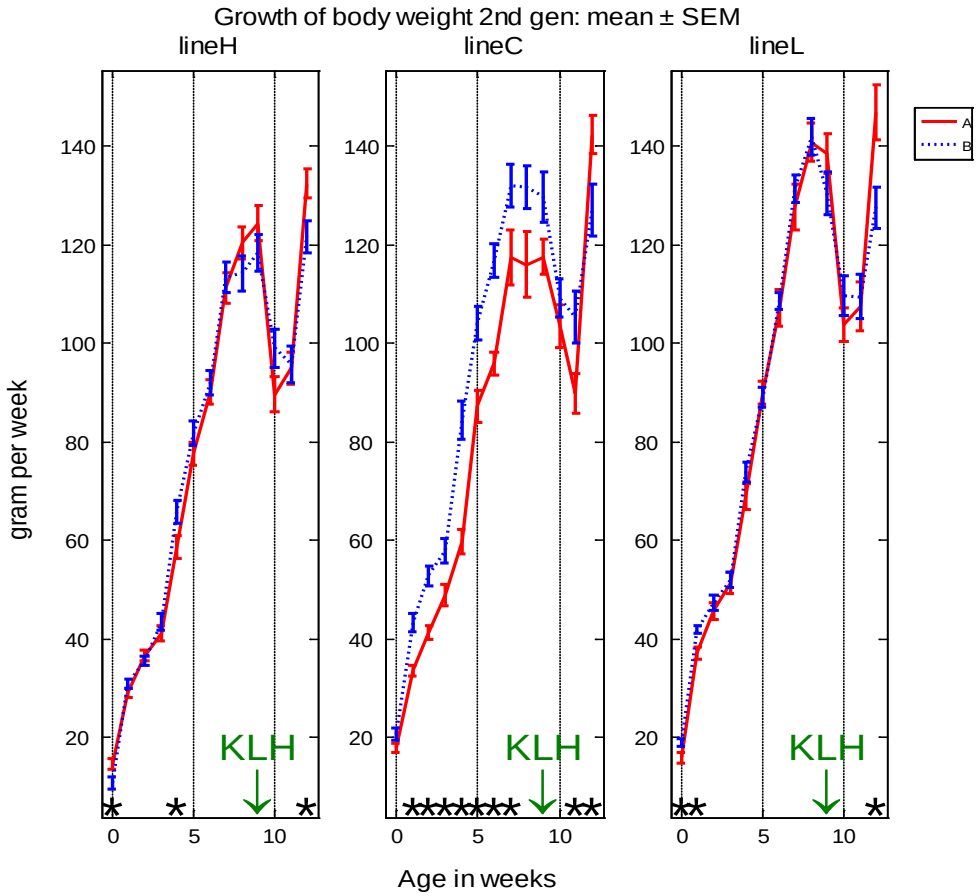
  However in the blood no differences in cholesterol levels.

- **Post mortem:** No abnormalities, but some differences in organ weights.

- **Overall:** A **long list of significant physiological differences** was found between the Feed groups **A** and **B**.

The Animals - Results

- **Growth:** Animals on the **Feed B** grew stronger till the KLH challenge. After that the **Feed A-group** took over (*catch-up growth*).



The Animals - Results

<u>Question:</u> Which group is healthier?

<u>Conclusion:</u> Scientifically we did not know!

In science the concept of ‘Health’ is not operationalized!

Yet the great majority of researchers had a preference to be themselves either **animal A** or **animal B**.

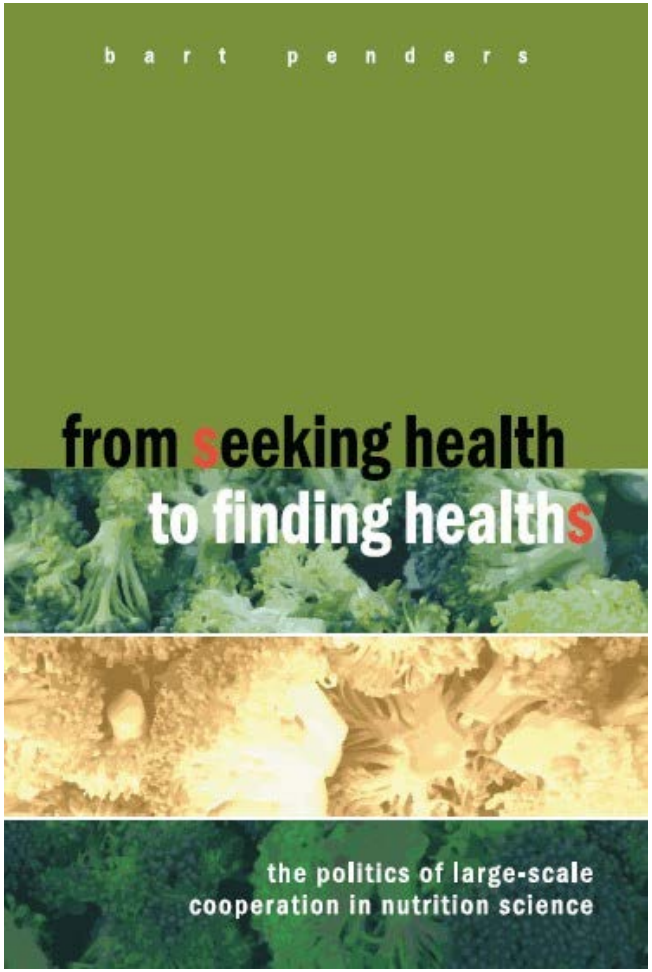
Do you? And why?

More problems with “Health” ….

In 2008 Bart Penders wrote a thesis after having studied two large scale nutrition research programs that intend to increase health: **Gut Health** and **NuGo**.

He named his thesis: “*From seeking health to finding health**S***”.

He concludes that integrating the multitude of results, from the many institutes involved, into a **context of ‘health’** is the biggest challenge for such research programs.



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So ‘health’ is a problem!

How is health defined?

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Health is still defined by the WHO definition of 1948:

"A state of complete physical, mental, and social well-being and not merely the absence of disease, or infirmity."

Since then often criticized, but never changed.

A new definition seems to be needed!

This need was recognized by the

Health Council of the Netherlands (Gezondheidsraad)
&
the Netherlands Organisation for Health Research and Development (ZonMw)

because
In prevention programs and healthcare the
definition of health determines the outcome measures.

Health gain in survival years may be less relevant than social participation;
an increase in coping may be more relevant than complete recovery.

I was asked to organize a two-day
Invitational Conference, with a broad range
of international experts (40) in December 2009:

**“Is Health a state or an ability?
Towards a dynamic concept of health”**

2. The content of the article

Limitations of the WHO definition:

1. The word *complete* in “states of complete well-being”

   “would leave most of us unhealthy most of the time”
   and it supports medicalisation, as always something can be found to be treated.

2. The demography of diseases changed since 1948.
   Ageing with chronic diseases becomes the norm.
   This formulation denies the human’s capacity to cope.

3. This definition is impracticable as ‘complete’ is neither operational nor measurable.

Arguments in the discussion about Health:

1. The definition should move from an endpoint to a function.

2. Health should be connected to concepts like: a ’resource’; a ‘capacity’ or ‘ability’ towards active ‘coping’, ‘adapting’ and ‘self management’ in relation to life’s events. When successful, this will result in increased ‘resilience’ or the capacity to maintain and restore one’s individual ‘integrity’ and ‘state of equilibrium’, as well as a sensation of ‘well-being’.

3. The three domains of health: the physical, mental and social, can well be maintained.

4. Better than a ‘definition’ is a ‘concept’ or ‘conceptual framework’ of health. Besides an overarching ‘general concept’ which is a characterization, ‘operational definitions’ should be elaborated.

5. The **general concept** that met consensus among the participants: “*Health as the ability to adapt and to self manage*”.

Which is now published in the British Medical Journal:

3. The meaning for nutrigenomics

As the **Health Council of the Netherlands** stated recently in an advice concerning nutritional research:

Scientifically there is no difference between:

1. Promotion and maintenance of health
2. Prevention of disease
3. Reduction of disease risk

My conclusion: This is based on a concept of ‘Negative health’.
The concept “Health as the ability to adapt and to self manage” can be called a concept of ‘Positive health’.
This needs to be operationalized.

3. The meaning for nutrigenomics

Nutrigenomics is concerned with an operational definition for health in the physical / biomedical domain:

Here keywords are:

1. Homeostasis – Stability through constancy, maintenance of constancy: pH, osmolarity, glucose levels, oxygen tension

2. Allostasis – Stability through change (by adapting setpoints). Mediators of change: inflammatory cytokines, HPA axis hormones (cortisol and catecholamines), autonomic nervous system

3. Capacities or abilities – Resilience – elasticity & Robustness - ability to function despite disturbances

The outcome: To stay well despite experiencing stress.

Then how to measure Health?

Measuring health by measuring adaptability → Mild Stress challenges!

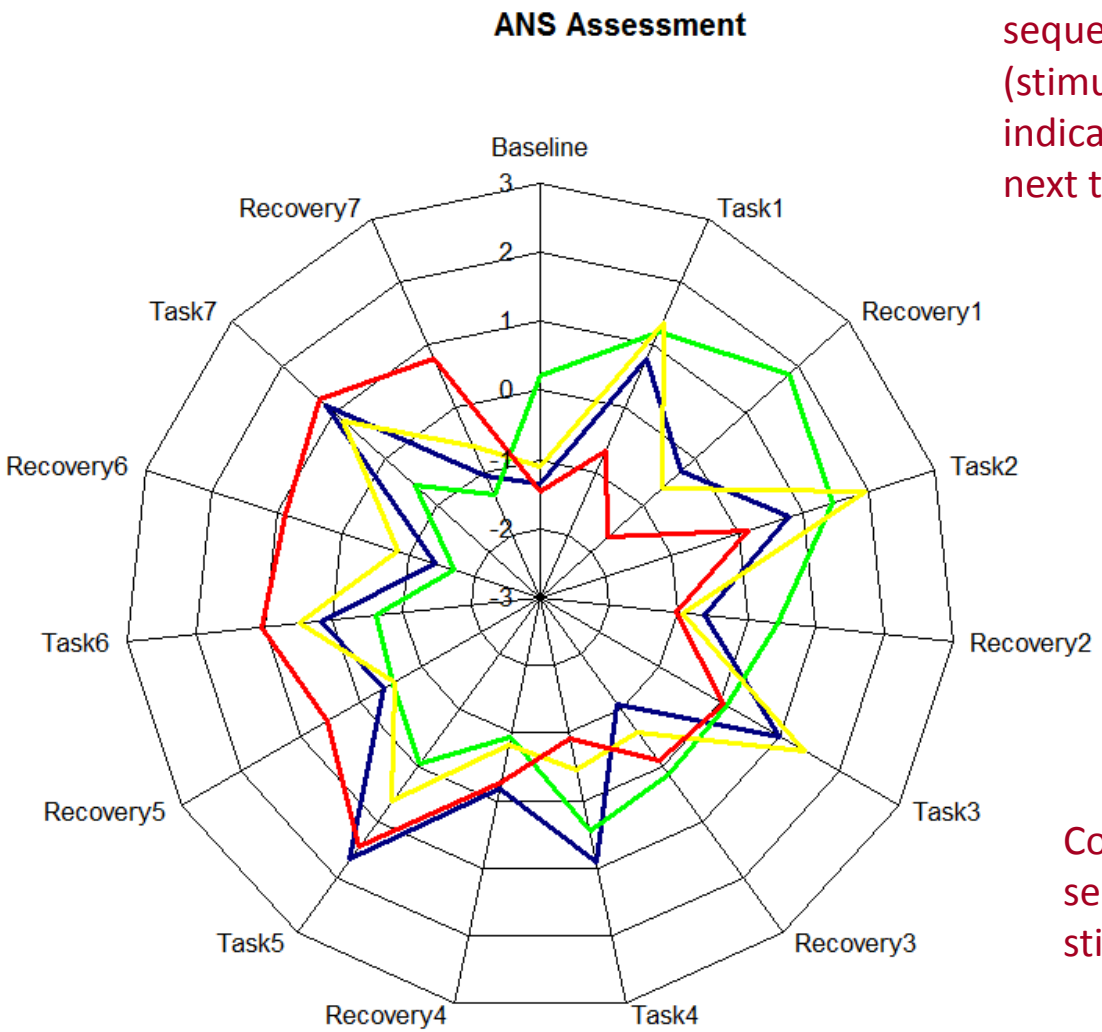
The challenge is to find parameters that are measurable and which reflect resilience and the ability to adapt.

It could be a multi-parametric ‘fingerprinting’, assessing different systems with parameters and physiological responses (e.g) at the:

- Autonomic nervous level (or system)
- Cardiovascular level
- Endocrine level
- Immunological level

System	Parameter	Physiological Response
Nervous	Electrodermal Parameters	Skin conductance, Skin potential, Sweat gland counts, etcetera..
Cardiovascular	Cardiovascular Measures	Heart rate, Cardiac arrhythmias, Cardiac output, Stroke volume, Myocardial contractility, Pulse transit time, Blood pressure, Total peripheral resistance, etc.
Endocrine	Neuroendocrine Parameters	Corticosteroids (Cortisol, Mineralcorticoids, Urinary metabolites) Catecholamines (Adrenaline, Noradrenaline) B-endorphin, Testosterone, Prolactin, Growth hormone, Insulin, etc.
Immuno	Immune-Related Parameters	Immunoglobins- IgA, IgE, IgG, IgM, Lymphocyte subsets Natural killer cell activity, Mitogen-induced lymphocyte proliferation, Antigen titers to latent Epstein-Barr virus, etc.

Example: Autonomous Nervous System



Preliminary example: clockwise sequence of response to tasks (stimuli) and recovery of the indicated parameters, followed by a next task, etc.

Coherence of responses to a sequence of exposures to mild stimuli, can be identified

An inspiration from another field could be:

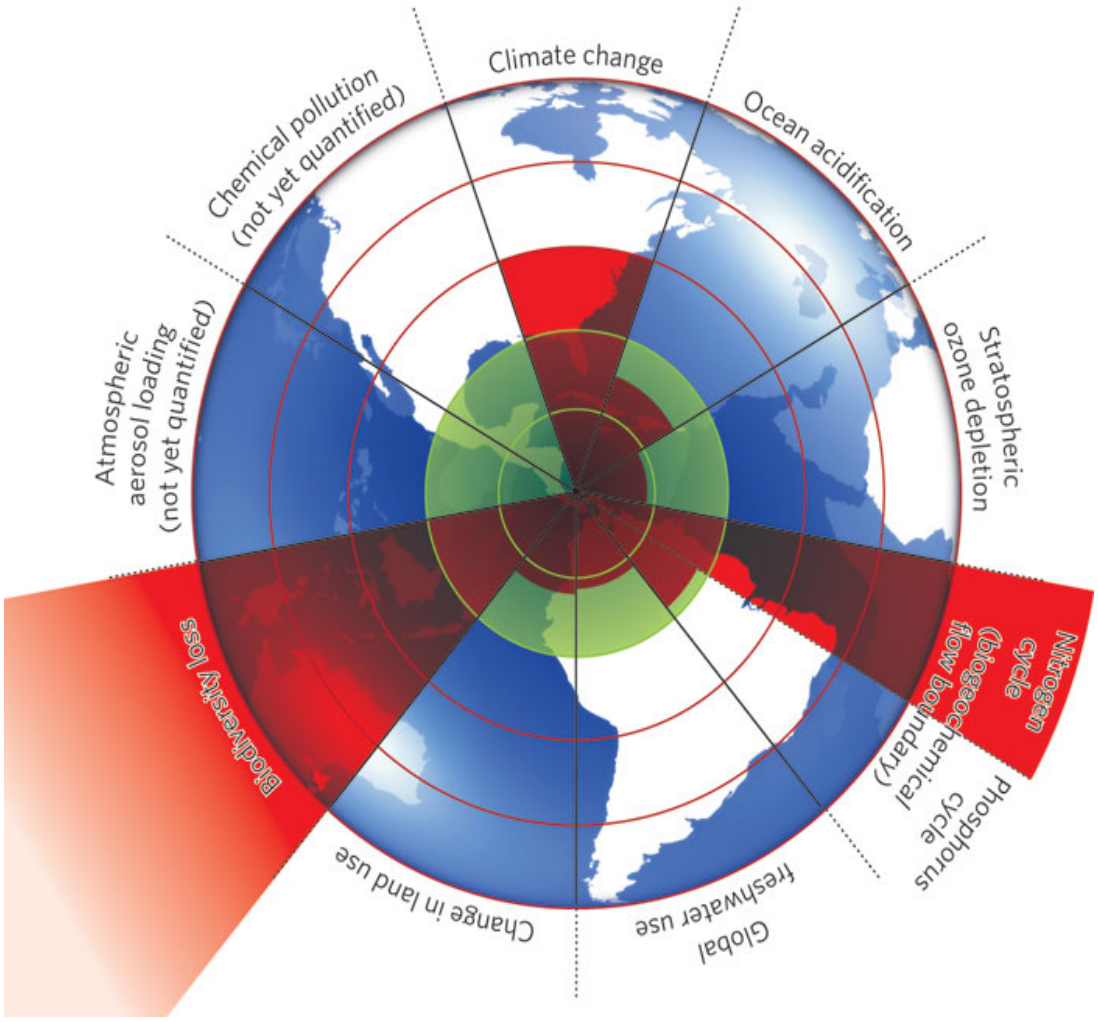
Rockström et al., described in Nature the *Health* of the earth (2009):

The Health of the Earth:

The earth is a complex system with a self-regulatory capacity that maintains a stable environment within a relatively narrow range and that can respond to changing pressures with restoring balances, within certain thresholds.

Rockström et al., Nature 461, 472-475 (24 September 2009) |doi:10.1038/461472a;

Rockström et al. describe the different factors that influence the resilience of the system. The red sections are already threatening the system‘s stability.



Instead of the earth we have to work with humans who are threatened…..

From:

To:

I thank my partners for this presentation:
Leon Coulier, TNO; Ron Hoogenboom, RIKILT; Fred Wiegant, Utrecht University.
André Knottnerus, Health Council; Henk Smid,the NL Organisation for Health Research and Development.

I wish you an inspiring week
and
thank you for your attention!

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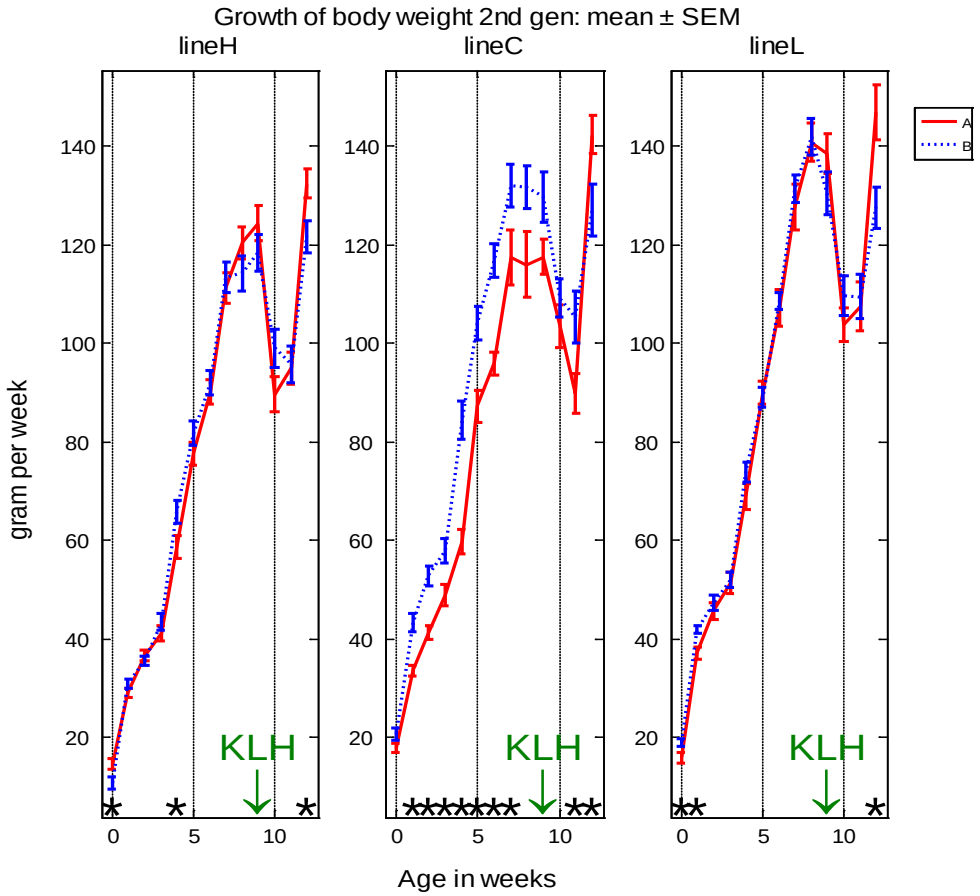
We described the ‘catch-up growth’ as a phenomenon of ‘resilience’….

- **Growth:** Animals on the **Feed B** grew stronger till the KLH challenge. After that the **Feed A-group** took over (*catch-up growth*).



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The study was named:

"Organic More Healthy?"

and
was published in the BJN:

Huber M et al. Effects of organically and conventionally produced feed on biomarkers of health in a chicken model.

BJN (2010), 103:663-676

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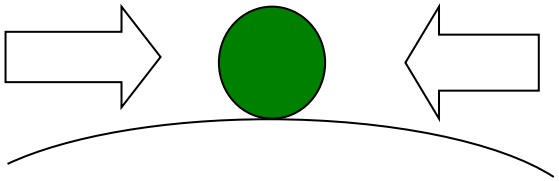
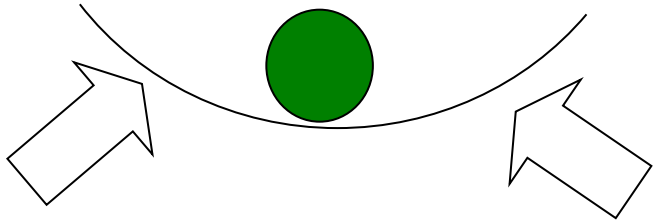
Different production approaches

Control model
Conventional approach



- focus on a problem
- controll variation
- continuous monitoring
- direct intervention
- static equilibrium

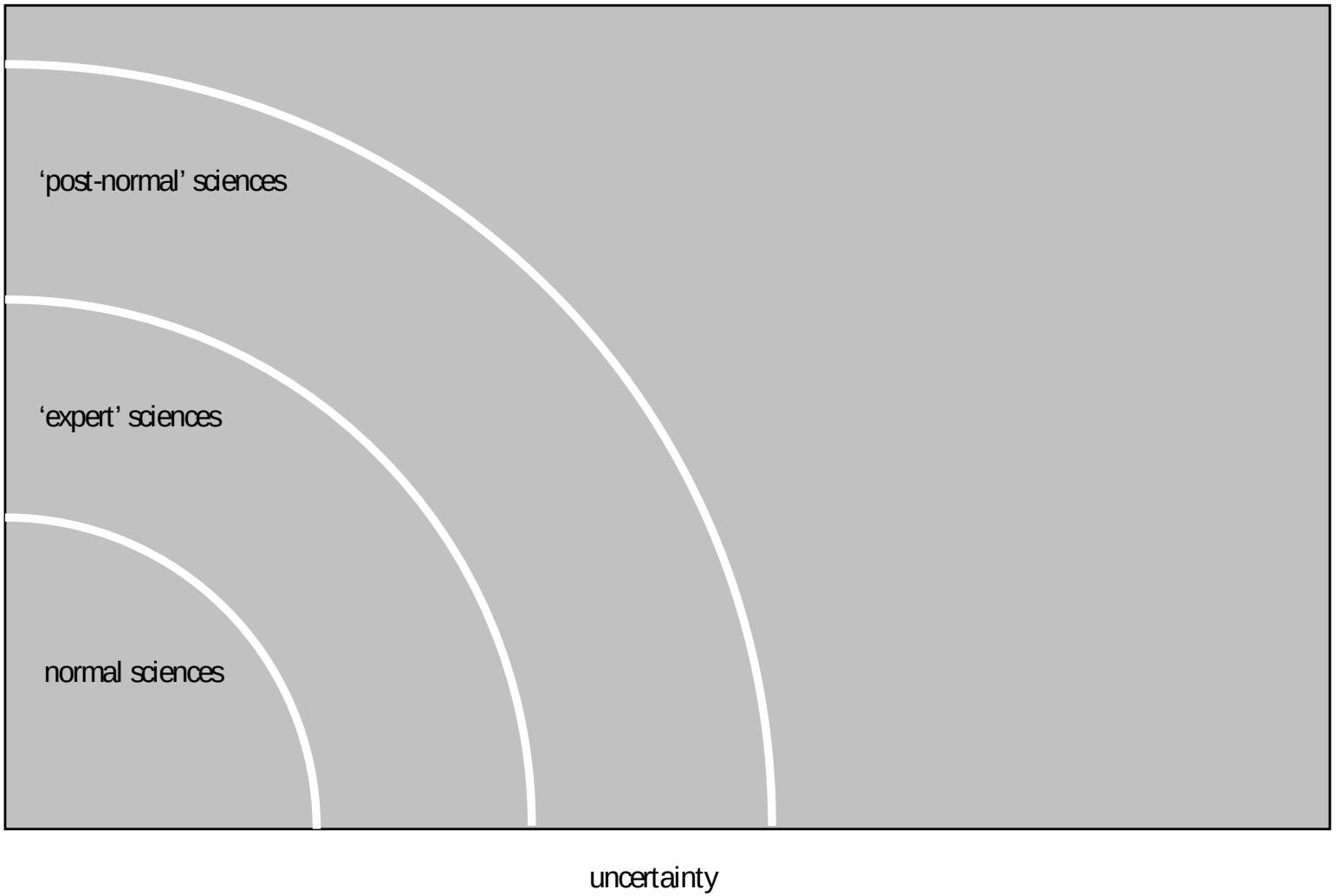
Adaptation model
Organic approach: robustness



- focus on the system
- use of variation
- stimulation of selfregulation
- indirect intervention
- dynamic equilibrium

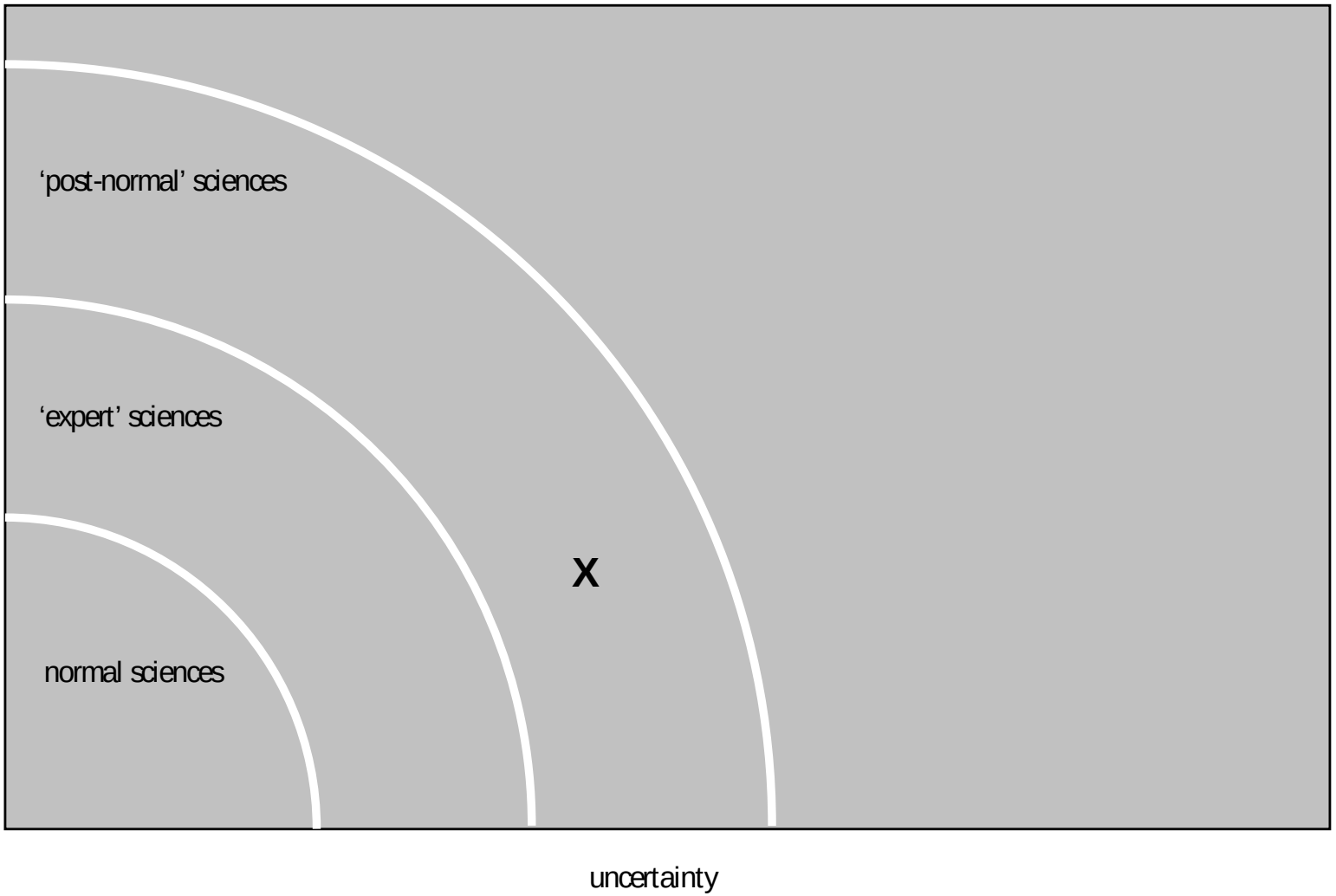
(Ten Napel *et al*., 2006; WUR/LBI)

Classification of scientific research



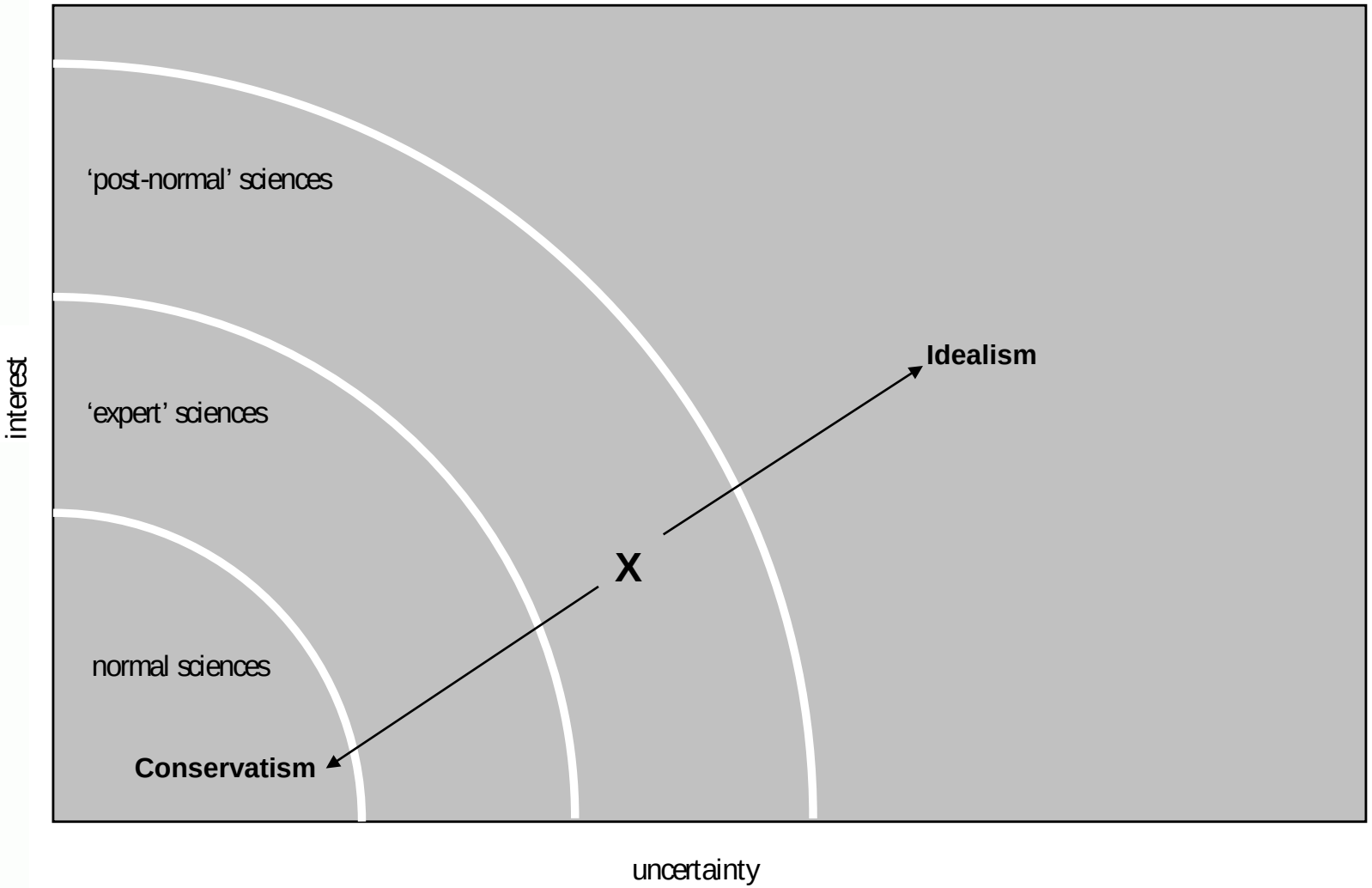
Funtowicz and Ravetz (1991)

Classification of scientific research
X = ‘Organic healthier?’



Funtowicz and Ravetz (1991)

Risk for extreme interpretations



Funtowicz and Ravetz (1991)