An evolutionary perspective of nutritional and human health; from reductionism to systems approaches

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Reductionism to system approaches

First International Conference on EastWest Perspectives on Functional Foods held in Singapore in 1995
Historical Perspectives

- **300KYA**
  Oven/Fire

- **150KYA**
  Speech Words

- **170KYA**
  Clothing

- **100KYA**
  Beads

- **40KYA**
  Hunter Tools

- **40KYA**
  Weaving

- **20KYA**
  Shoes
  Ceramics

- **10KYA**
  Agriculture
  Rice
  Domestication/ Sheep
  Villages
  Husbandry
  Wine

- **5-4 KYA**
  Wheeled Vehicle
  Bronze Age Starts
  Civilisation

- **220 YA**
  Industrial Revolution

- Survival (Health)
- Energy
- Food
- Water
- Mobility
- Communication
- Shelter
Two key lessons from the history of successful innovation

Creativity + Application → Scale (Complexity)
Complexity + Sophistication → Personalisation
Scale/complexity/personalisation

- Everyday common illustrative examples
- Specifics examples that relate to food and nutrition
- The future challenge and opportunities in food and nutrition
**Scale/complexity/personalisation**

**Measurement of time**

Unmet need/convenience
diversity of application

- Sundial/Celestial
- Water clock (Clepsydra)
- Candle Clock, time stick
- Oil lamp clock
- Hourglass
- Pendulum clock
- Portable mechanical clock
- Watch

Accuracy/reliability/portability
Scale/complexity/personalisation

Flight

Speed/distance/reliability

Scale/Complexity-Sophistication/Personalisation

Carrying capacity
Scale/complexity/personalisation

Food/nutrition

Population density, growth of civilisations

Growth and evolution of nutrition and Food Sciences
Reductionism to system approaches: Nutrition

The roles of **Scale, complexity sophistication and personalisation** in the transition from reductionism to System approaches.

Specifics examples in food and nutrition with four small molecules:
- Ascorbic acid
- Niacin
- Butyrate
- Long chain fatty acids
Reductionism to system approaches: Ascorbic acid

- Deficiency described in ancient civilisations.
- Foods discovered, and rediscovered.
- 16th and 17th century Scurvy a major problem with sea voyages.
- James Lind’s/supplementation experiments with citrus fruits.

Essential for the post translational hydroxylation of proline and the stability of the collagen helix.
Reductionism to system approaches: Ascorbic acid

Additional areas of focus include:
- Cofactor for neurotransmitters and carnitine
- Neuronal function
- Role as water soluble antioxidant, free radical scavenger. Pro-oxidant
- Prostaglandin production
- Catabolism of bile Cholesterol to bile acids
- Wound healing/pro-inflammatory/collagen formation
- Adrenal steroid metabolism
- Inhibition of LDL oxidation. Interaction with Folate
- Transcriptional regulation of the SLC23 genes controls the tissue distribution of SVCTs
- Iron absorption
Reductionism to system approaches: Ascorbic acid the CNS


- High concentration in the CNS
- Steep concentration between blood and neuronal cells. Sophisticated entry into neurons
- Monovalent reduction of metal ions in hydroxylation reactions
- Prevention of lipid peroxidation
- Differentiation of embryonic stem cells into neurons
- Cofactor for the formation of dopamine
- Proposed as possible neuromodulator
- Regulation of acetyl choline and catecholamine release from vesicles
Reductionism to system approaches: Ascorbic acid

Historical/Societal observations

Unmet need: Scurvy
Human trials/identified foods and intake

Underpinning nutritional science/Bioactive Identified
Population based Recommended Intakes/Food production
Scurvy as an unmet (nutritional deficiency) need largely met

Pleiotropic. Interaction with the genome and omics
Pleiotropic interaction with dietary behaviour, environment-epigenetics, aging populations and chronic disorders

How to understand more fully the broader integrated role of ascorbic acid in human health?

Scale/Complexity/Human Variation & Personalisation
Reductionism to system approaches: Niacin

- Essential nutrient
- Deficiency Pellagra known in the ancient World. Maize introduction in Europe
- Isolated in 1912 by Casimir Funk, structure 1937 Conrad Elvehjem
- Tom Spies et al (1930’s) demonstrated cure. Recommended daily intakes

Additional areas of focus include:
Substrate for key ADP-ribosylation reactions; modifications to histones, genome stability/PARP
HCA2 high affinity GPCR. (Inhibits lipolytic activity/induces vasodilation/apoptotic process/adiponectin secretion)
Lowers serum cholesterol and triglyceride levels
Reductionism to system approaches: Niacin

Historical/Societal observations Ancient World

Unmet need: Pellagra
Human trials/identified foods and intake

Underpinning nutritional science/Bioactive Identified
Population based Recommended Intakes/Food production
Pellagra as an unmet (nutritional deficiency) need largely met

Pleiotropic. Interaction with the genome and omics
Pleiotropic interaction with dietary behaviour
environment-epigenetics, aging populations and chronic disorders

How to understand more fully the broader integrated role of niacin in human health?

Scale/Complexity/Human Variation & Personalisation
Reductionism to system approaches: Butyrate

- Latin “butyrum” for butter
- Chemists seeking the composition of butter
- Discovery 1814/1818 Michael Cheurul/Henri Bracnnot

Additional areas of focus include:
A key histone deacetylase inhibitor, increases histone acetylation
Warburg with cancer cells
Influences acetylation of metabolic proteins
Increases mitochondrial activity
Activates GPCR receptors (FFAR-3 and FFAR-2) highly expressed in the SNS. Activates GPCR109-a the receptor for Niacin, promotes immune tolerance. Neural protection in the CNS
Inhibits angiogenesis
Reduces inflammation (promotes T cell formation). Vasorelaxation (cAMP)
Reductionism to system approaches: Butyrate

Historical/Societal observations in food chemistry

Underpinning nutritional science/Bioactive Identified
Population based Recommended Intakes/Food production

Pleiotropic. Interaction with the genome and omics
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environment-epigenetics, aging populations and chronic
disorders

How to understand more fully the broader integrated role of butyrate in human health?

Scale/Complexity/Human Variation & Personalisation
Reductionism to system approaches: Long chain fatty acids

Fish consumption in the ancient World. Japan, China, ancient Rome, Greece and Egypt
Bang and Dyerberg, omega 3 fatty acids /decreased CVD in an Inuit population, 1972. Subsequently numerous preclinical and clinical outcome trials

Essential fatty acids, desaturation and elongation
Low efficiency of delta -6-desaturase.
Incorporation/membrane phospholipids.
Triglyceride lowering.

Additional areas of focus include:
Membrane stabilisation, suppression of arrhythmias, restenosis, attenuation of atherosclerotic plaques, blood pressure lowering, endothelial function, anti-inflammatory mediators, antithrombotic, activation of gene transcription factors, antioxidative, brain and cognitive development, visual development.
Reductionism to system approaches: Long chain fatty acids

Historical/Societal observations ancient and modern world

Underpinning nutritional science/Bioactive Identified
Population based Recommended Intakes/Food production

Unmet need: Ongoing human trials/identified foods and intake

Pleiotropic. Interaction with the genome and omics.
Pleiotropic interaction with dietary behaviour, environment-epigenetics, aging populations and chronic disorders

How to understand more fully the broader integrated role of long chain PUFA’s in human health?

Scale/Complexity/Human Variation & Personalisation
Reductionism and system approaches

Ascorbic acid
Niacin
Butyrate
Long chain fatty acids

Key lessons?
Reductionism and system approaches: Key lessons

Historical/Societal observations

Unmet need

Human trials/identified foods and intake

Underpinning nutritional science/Bioactive Identified

Population based Recommended Intakes/Food production

Unmet (nutritional deficiency) need largely met

Pleiotropic. Interaction with the genome and omics

Pleiotropic interaction with dietary behaviour, environment-epigenetics, aging populations and chronic disorders

1. Understanding Nutrition at a Molecular level for a single Nutrient will always be fundamentally important.
Reductionism and system approaches: Key lessons

Historical/societal observations

- Unmet need
  - Human trials/identified foods and intake

Underpinning nutritional science/Bioactive Identified

Population based Recommended Intakes/Food production

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Pleiotropic. Interaction with the genome and omics

Pleiotropic interaction with dietary behaviour, environment-epigenetics, aging populations and chronic disorders.

2. Nutrients do not function in isolation*. They are Pleiotropic; multiple system interactions.

*Shao A et al Eur J Nutr (2017) 56 (Suppl 1) :S1-S2
Reductionism and system approaches: Key lessons

Historical/Societal observations

Unmet need

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Underpinning nutritional science/Bioactive Identified

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3. Using a single nutrient approach a relationship exists for example with chronic diseases and bioactive discovery.*

Dietary Fibre  
Catechins  
n-3 Fatty acids  
Anthocyanins  
Vitamin D  
Isoflavones  
Folate  
Carotenoids  
Calcium

Against a background of:

- The Pleiotropic nature of the nutrients,
- Genomic interactions
- Complex pathways of chronic diseases

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Reductionism and system approaches: Key lessons

Historical/societal observations.

Unmet need
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4. A need to shift to a broader dietary focus and broader scientific disciplinary input in nutrition:
   - Scale
   - Complexity (complex science)
Historical perspectives

Two key lessons from the history of successful innovation

Creativity + Application → Scale (Complexity)

Complexity + Sophistication → Personalisation
Personalisation From Complexity at Scale?

Complex science
(Linked and Integrated disparate data
{Big Data} at scale)

Consumer/public/end-users/industry

Scale/complexity-sophistication/personalised
Personalisation from complexity at scale

Consumer/public/end-users/industry
- Deriving benefit from Variability
- Personalised predictors in nutrition
- Clarity.
- Convenience.
- Reliability.

Linked and integrated disparate data (Big Data) at scale and may include inputs from:
- The Genome/Epigenome/Transcriptome/Proteome/Metabolome/Microbiome
- Nutritional Bioinformatics, Biomarkers, Pleiotropic interactions
- Dietary Behaviour/Metabolic Flexibility/Phenotypic Measures
- Environment/Age/Lifestyle/Family history/Chronic disorders/Drug-Diet interactions
- Personalisation and reduction to practice using machine logic and algorithms
Personalisation from complexity at scale

“Invention, it must be humbly admitted, does not consist in creating out of void but out of chaos.”

Mary Wollstonecraft Shelley
Personalisation from complexity at scale


To foster seamless collaboration between nutrition and other disciplines.

Possible global research collaboration to harmonize complex science as it applies to nutrition.

To learn from other disciplines that have faced similar challenges.

Transitioning; reduction to practice
Personalisation from complexity at scale

Nutrition is not alone – Pharmaceuticals

From the traditional one drug one target model we now have:

- Beneficial Pleiotropy, Repurposing, Repositioning and Therapeutic Switching
- Synthetic lethality
- Pharmacogenomics
Reductionism to system approaches

- Humans understanding the unmet need. Problem solving
- Societal observations
- Nutrient deficiency molecular discovery
- Complex Systems Science
- Approaches to personalisation from complexity at population scale
Reductionism to System Approaches
Thank you
Personalisation from complexity at scale

Dense urbanisation

Concentrated workforce

Systems thinking

Urban Engineering/Public Health

Cholera Outbreaks

Search for antimicrobials

John Snow