

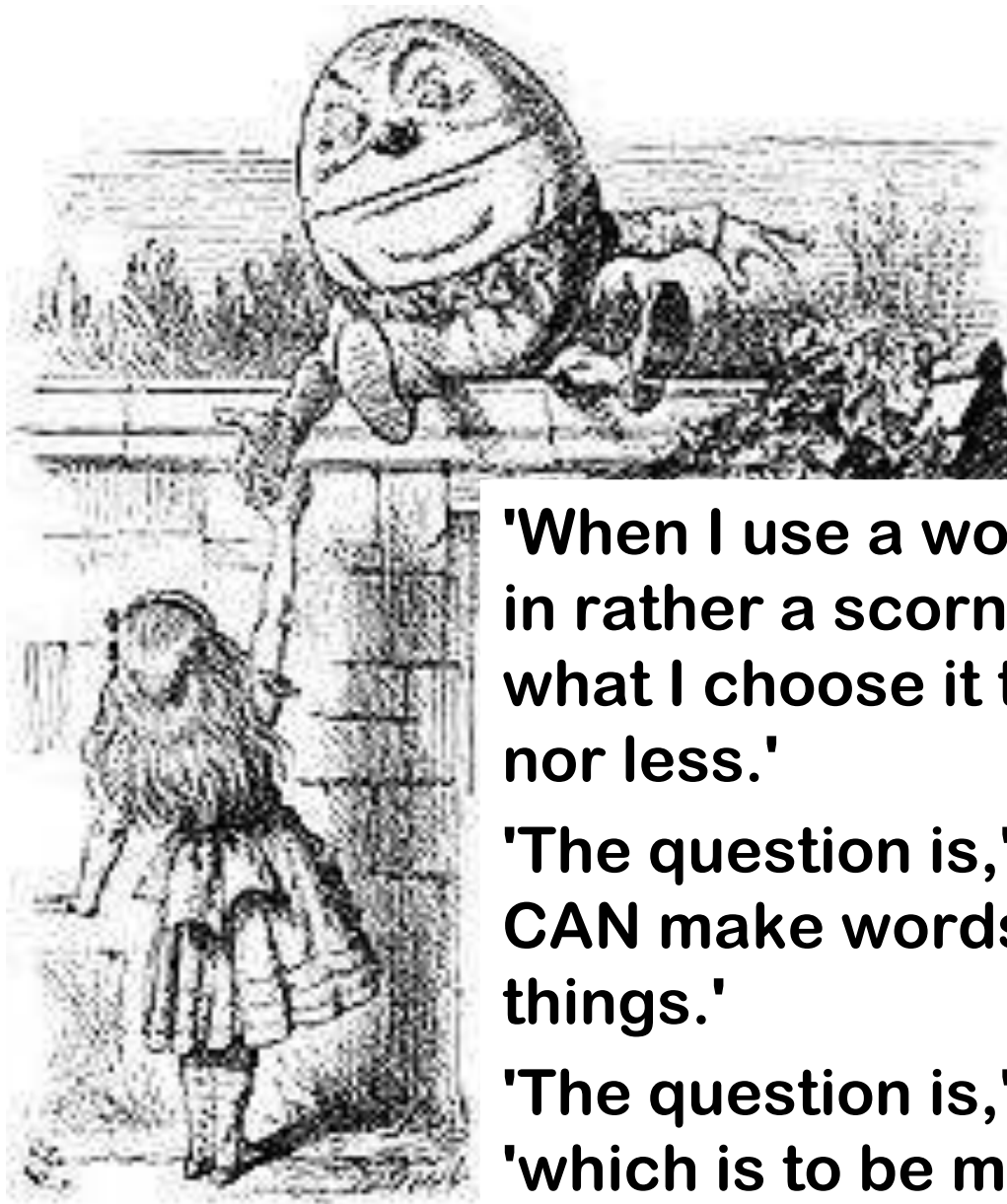
# Nutrient Bioavailability- impacts on health claims and NRVs

Professor Peter J Aggett  
School of Medicine and Health  
Lancaster University, UK

[profpjaggett@aol.com](mailto:profpjaggett@aol.com)

# **Nutrient Bioavailability- impacts on health claims and NRVs**

- What is bioavailability?
- How is it measured?
- Relevance to Nutritional Science
  - Nutrient Intake Values
  - Health Outcomes and Claims
- Evidence Based Mechanistic Reasoning
- Summary and Issues



## **Bioavailability**

(Through the Looking Glass)

'When I use a word,' Humpty Dumpty said in rather a scornful tone, 'it means just what I choose it to mean—neither more nor less.'

'The question is,' said Alice, 'whether you CAN make words mean so many different things.'

'The question is,' said Humpty Dumpty, 'which is to be master—that's all.'

# **Bioavailability**

- The efficiency with which a dietary component is used systemically
- Usually expressed as a percentage of the intake

# Bioavailability

- Used in assessing
  - dietary sources of nutrients and food components
  - nutrient intake values
  - scientific evidence of causality

# **Bioavailability**

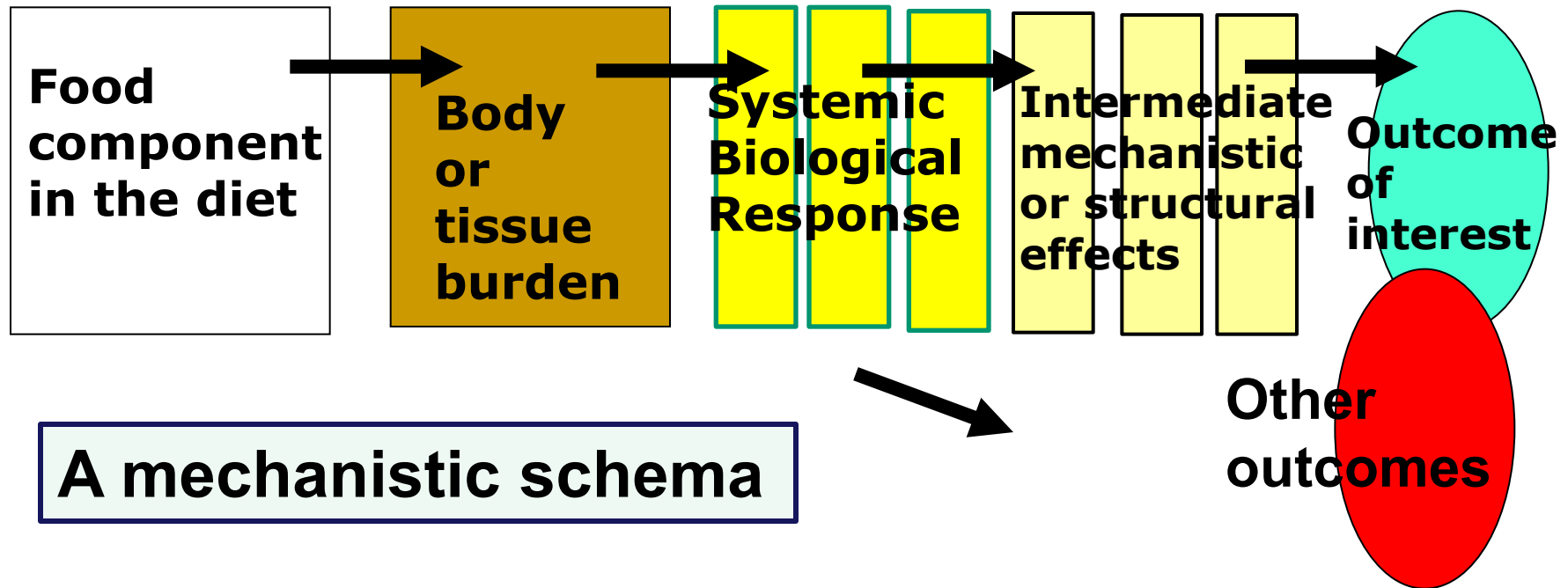
- The efficiency with which a dietary component is used systemically
- Essence of nutritional science

# **The utilisation of a dietary component** **:- components of bioavailability**

- Dietary Factors
- Host Factors

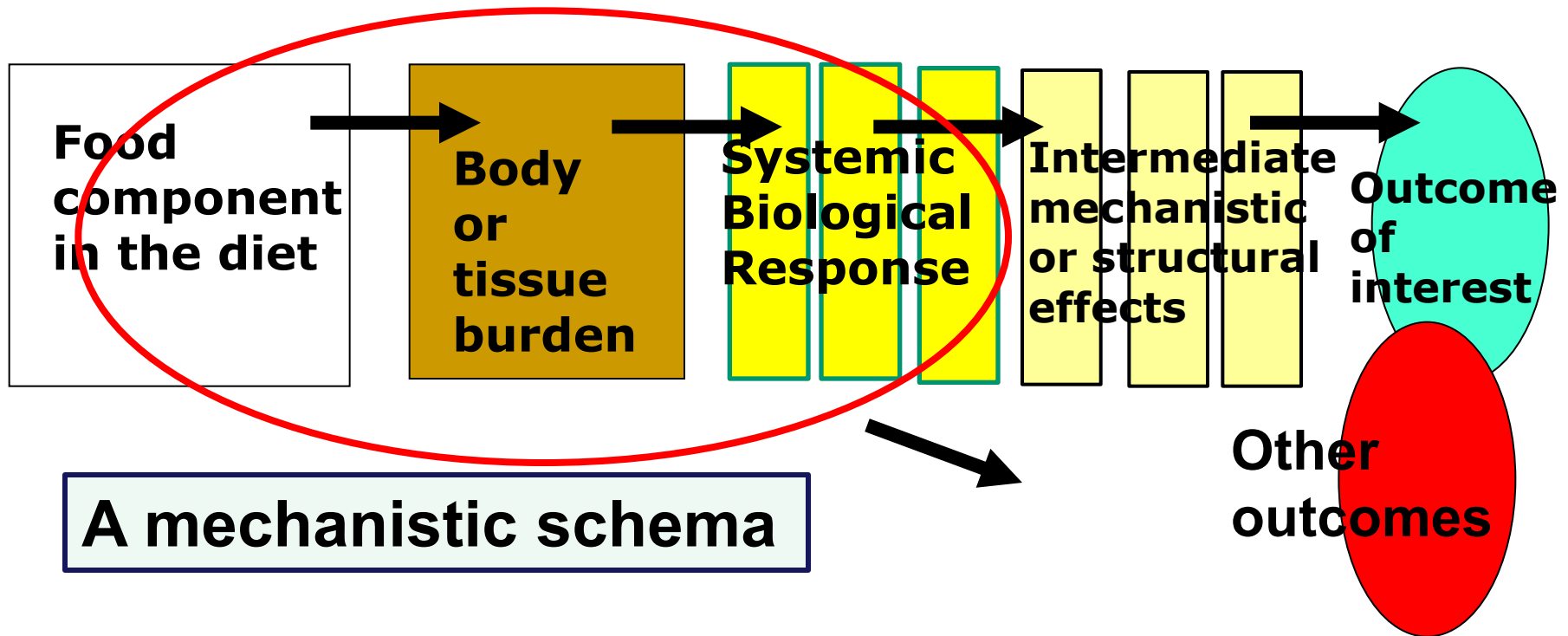
# The Nutritional Chain of Markers: Consumption to Outcomes.

Principle of a causative chain or pathway



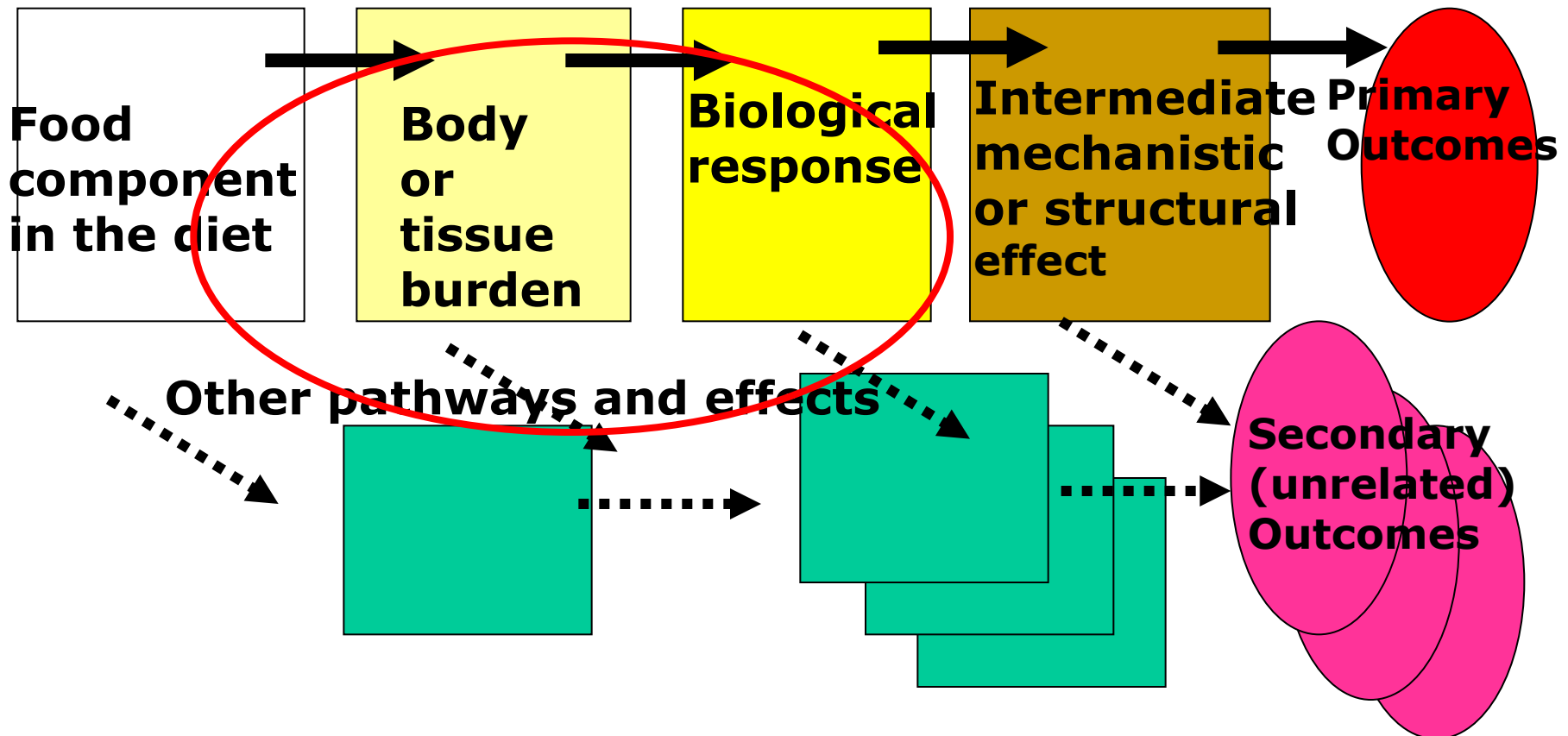
# The Nutritional Chain of Markers: Consumption to Outcomes.

Principle of a causative chain or pathway:  
aspects influenced by bioavailability



# Multiple effects: A Chain of Markers

Principal Stages in the pathophysiological pathway

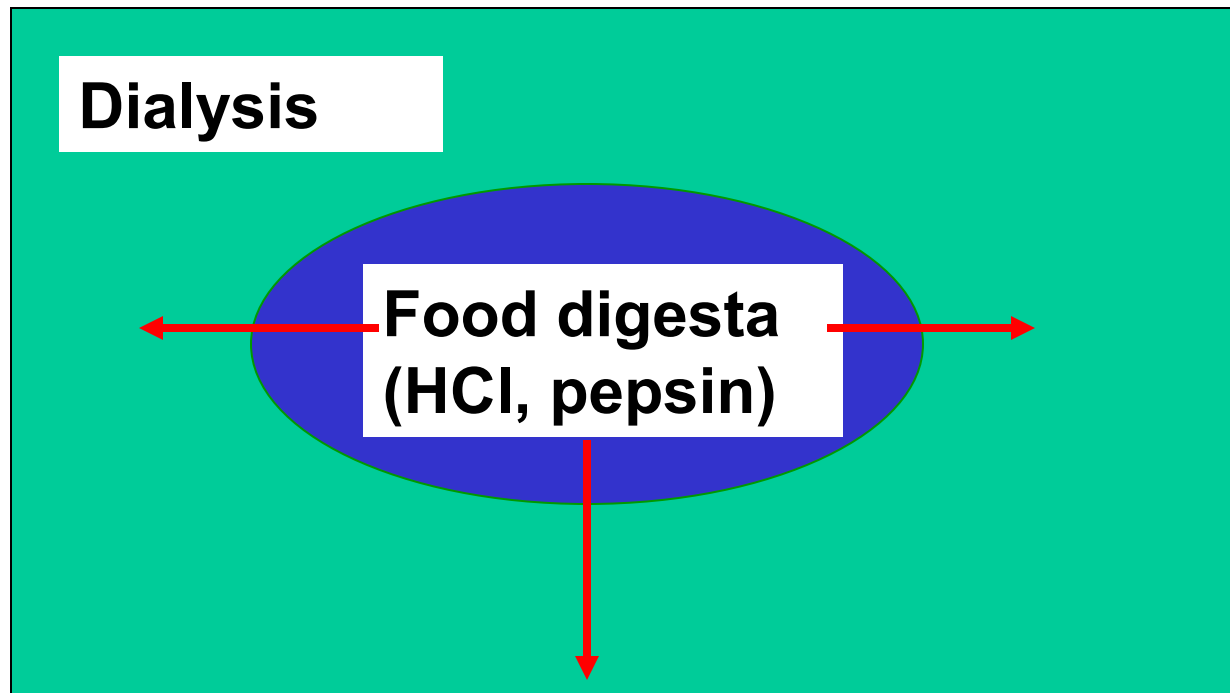


# **Bioavailability**

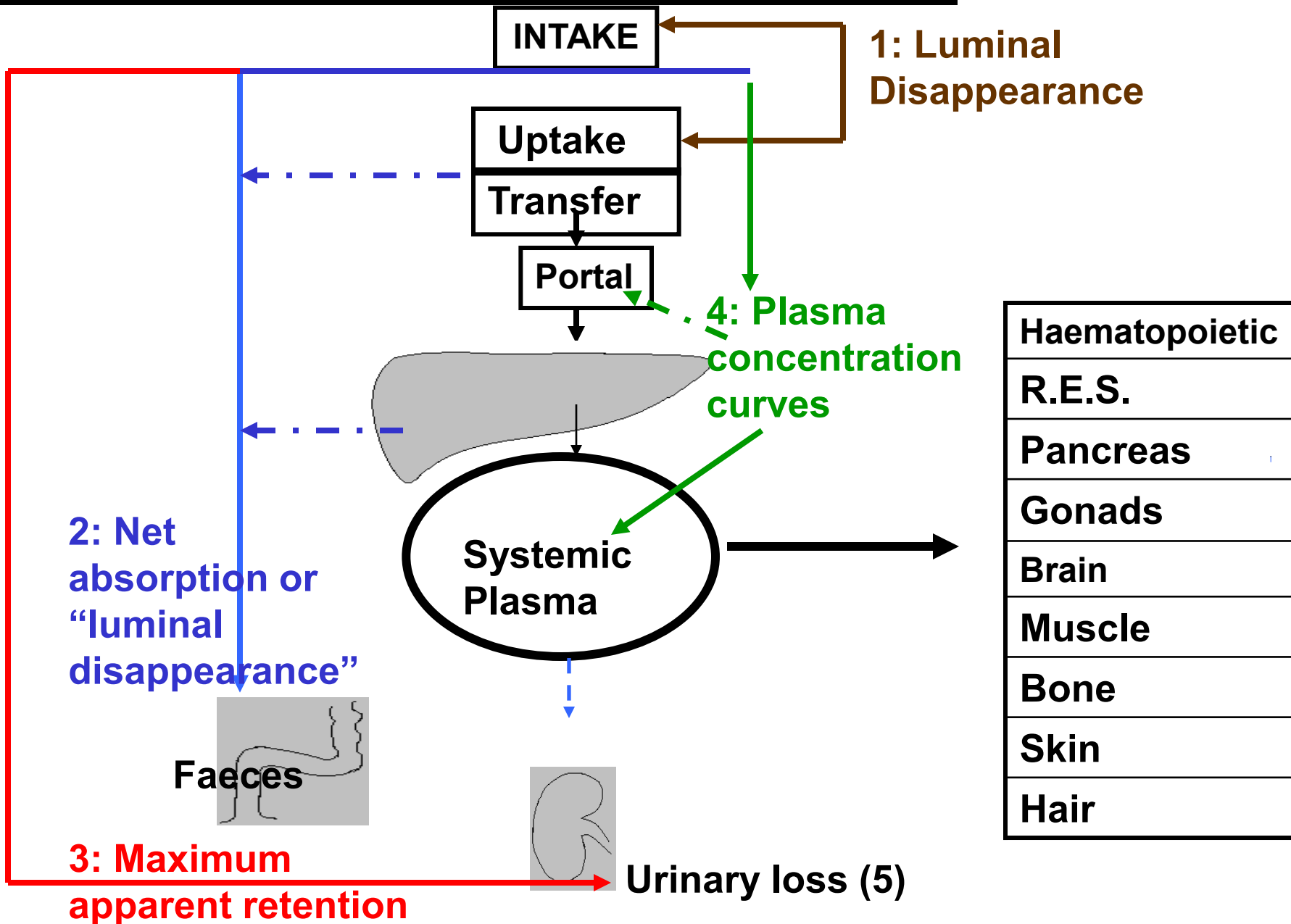
- Challenging concept
- Frequently redefined to fit the assay
- Needs to be used critically
- How is it measured?

# Bioavailability Studies: In vitro

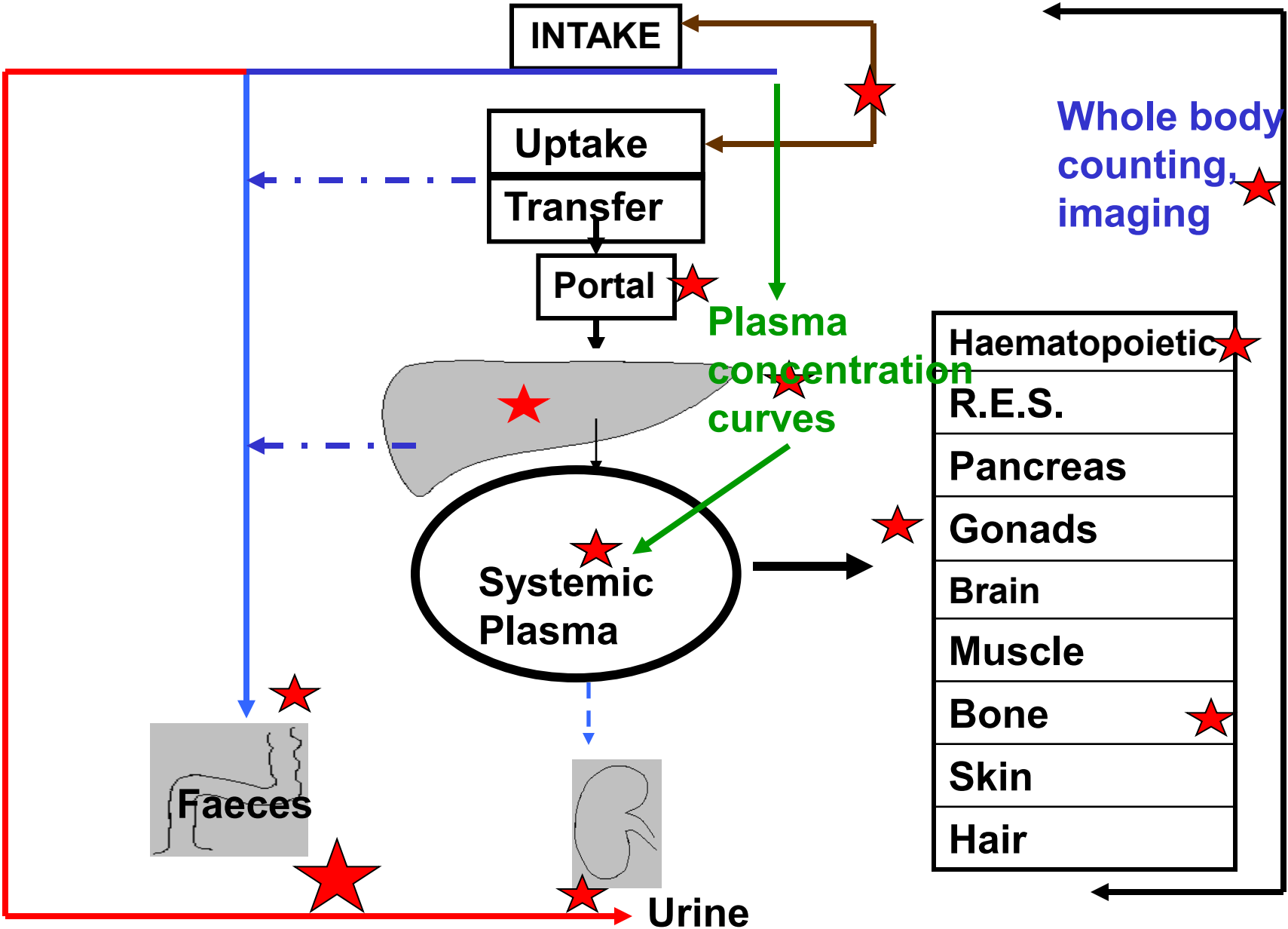
Dialysability: release of component



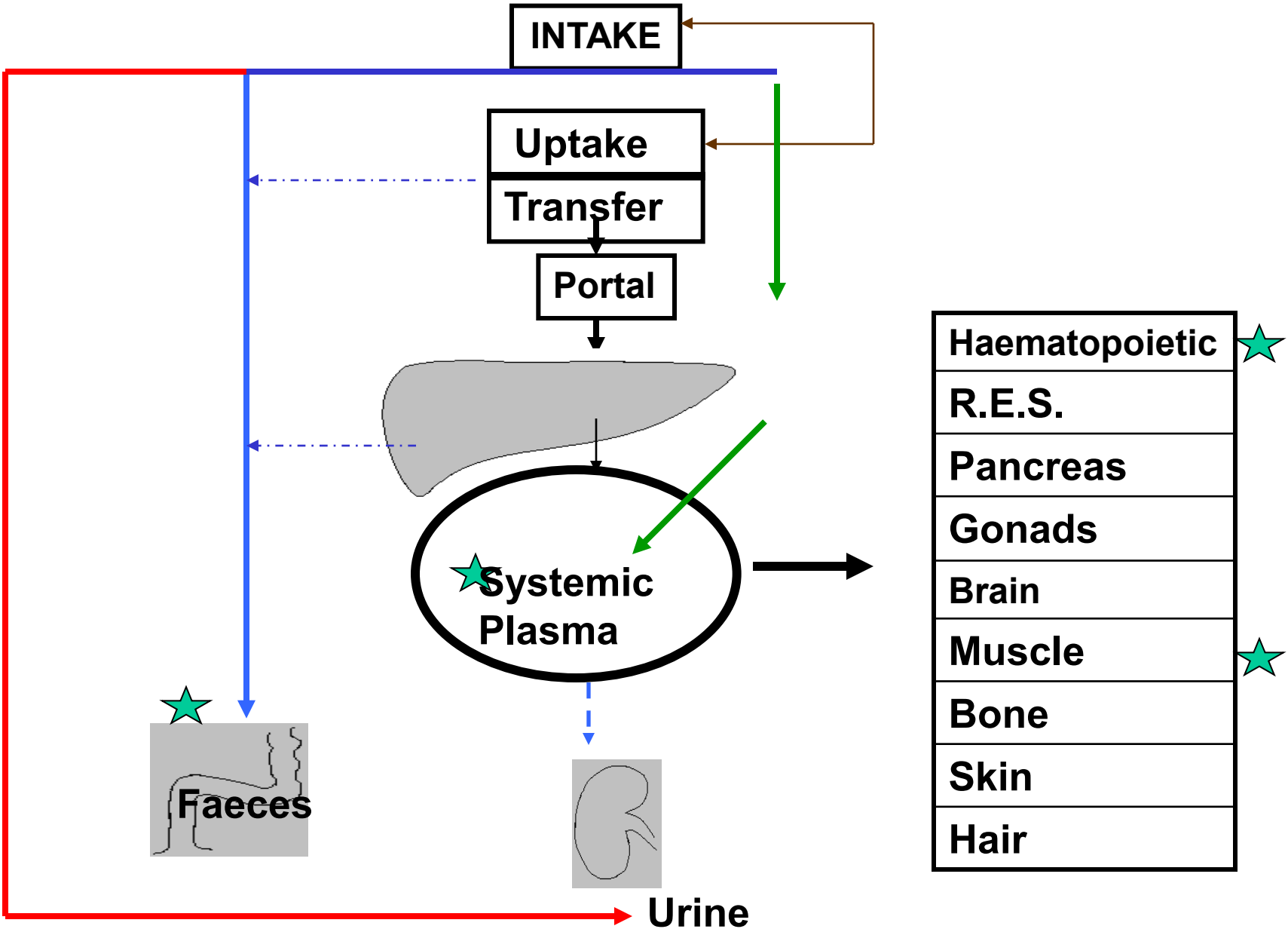
# Bioavailability Studies: in vivo



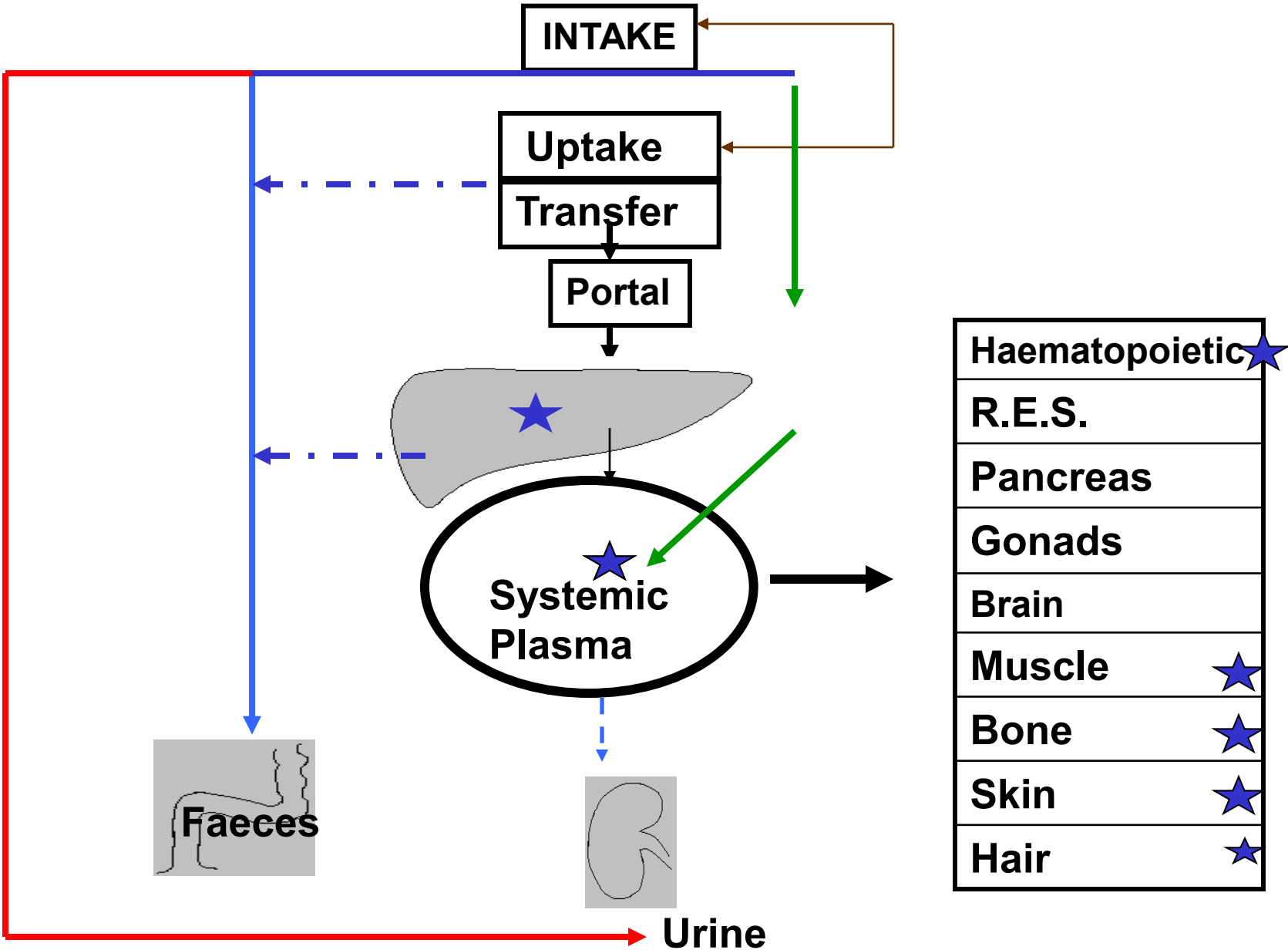
# Bioavailability; Radio-isotope Tracers ★



# Bioavailability: Stable-isotope Tracers



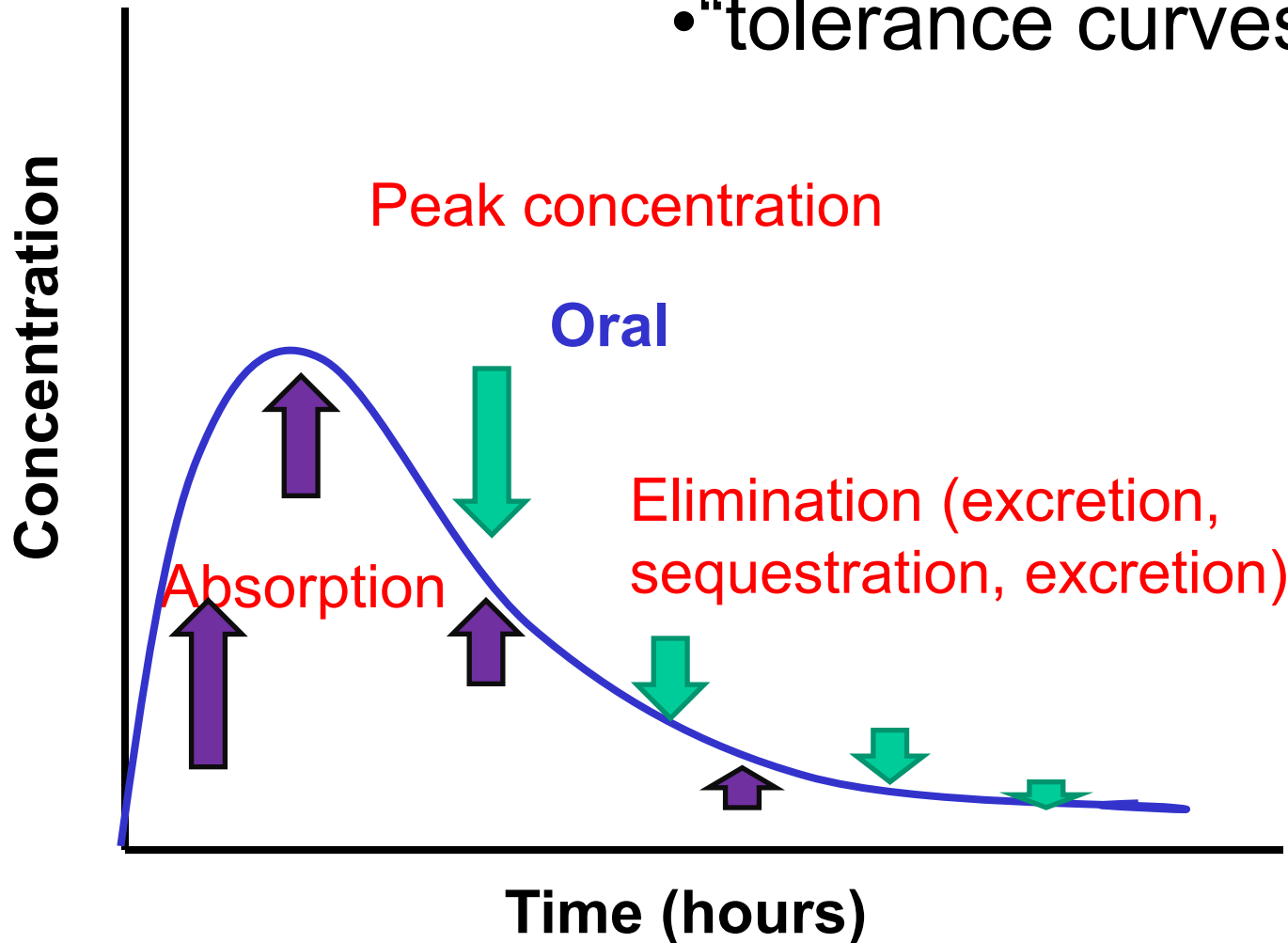
# Bioavailability: Tissue/functional Assays



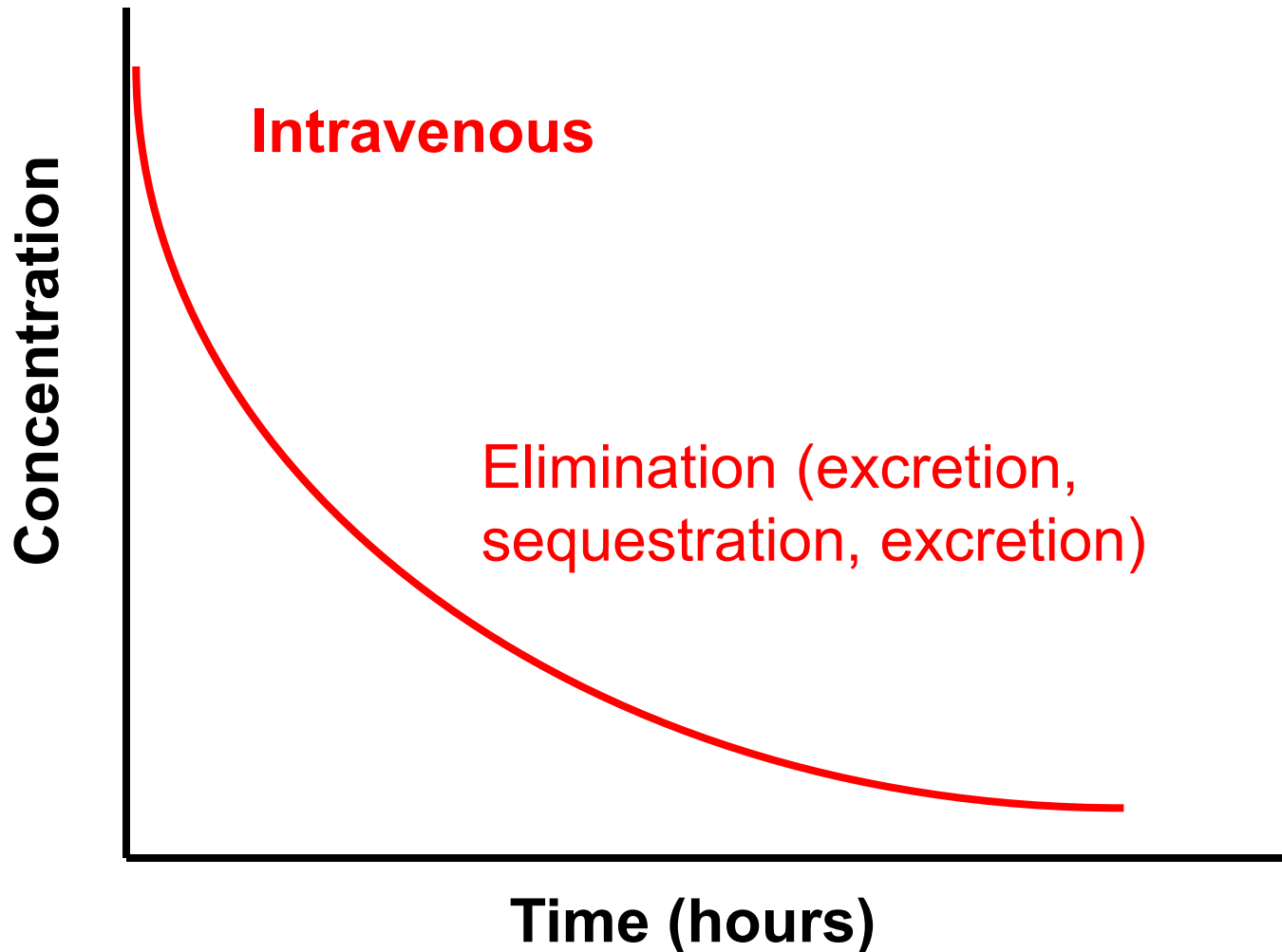
Haematopoietic	★
R.E.S.	
Pancreas	
Gonads	
Brain	
Muscle	★
Bone	★
Skin	★
Hair	★

# Plasma Concentration Time Curves

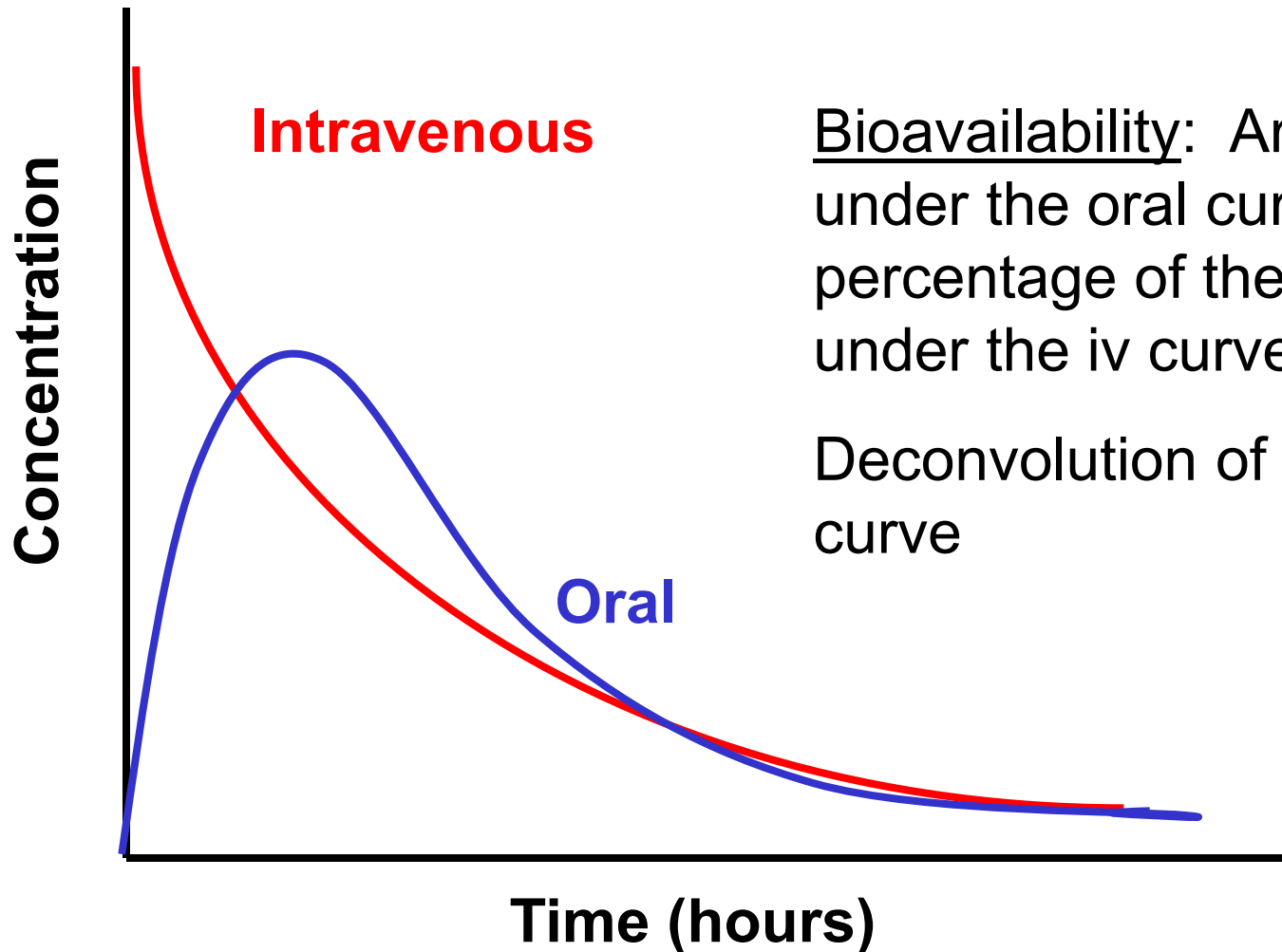
- “tolerance curves”



# Plasma Concentration Time Curves



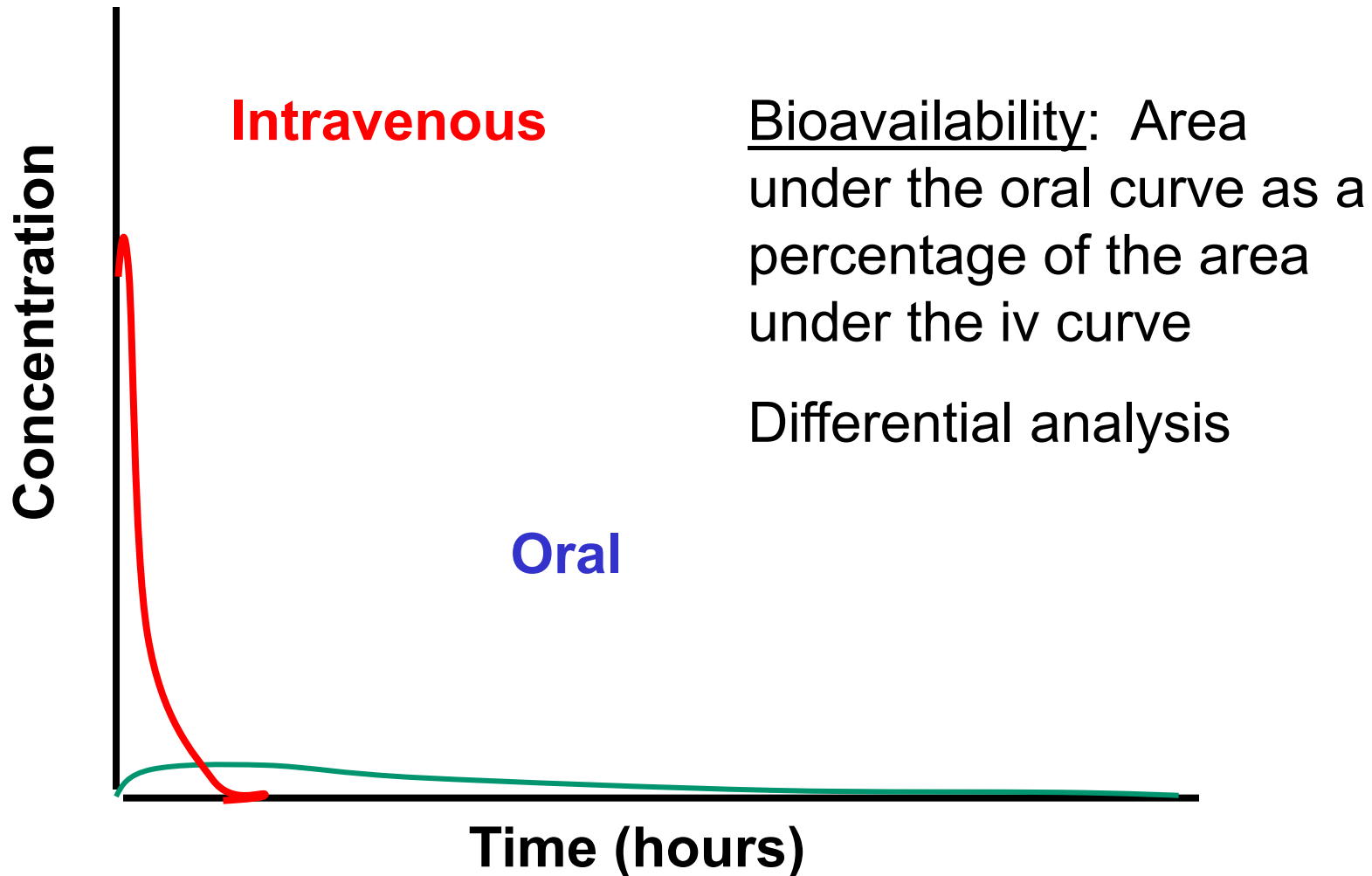
# Plasma Concentration Time Curves (water soluble)



Bioavailability: Area under the oral curve as a percentage of the area under the iv curve

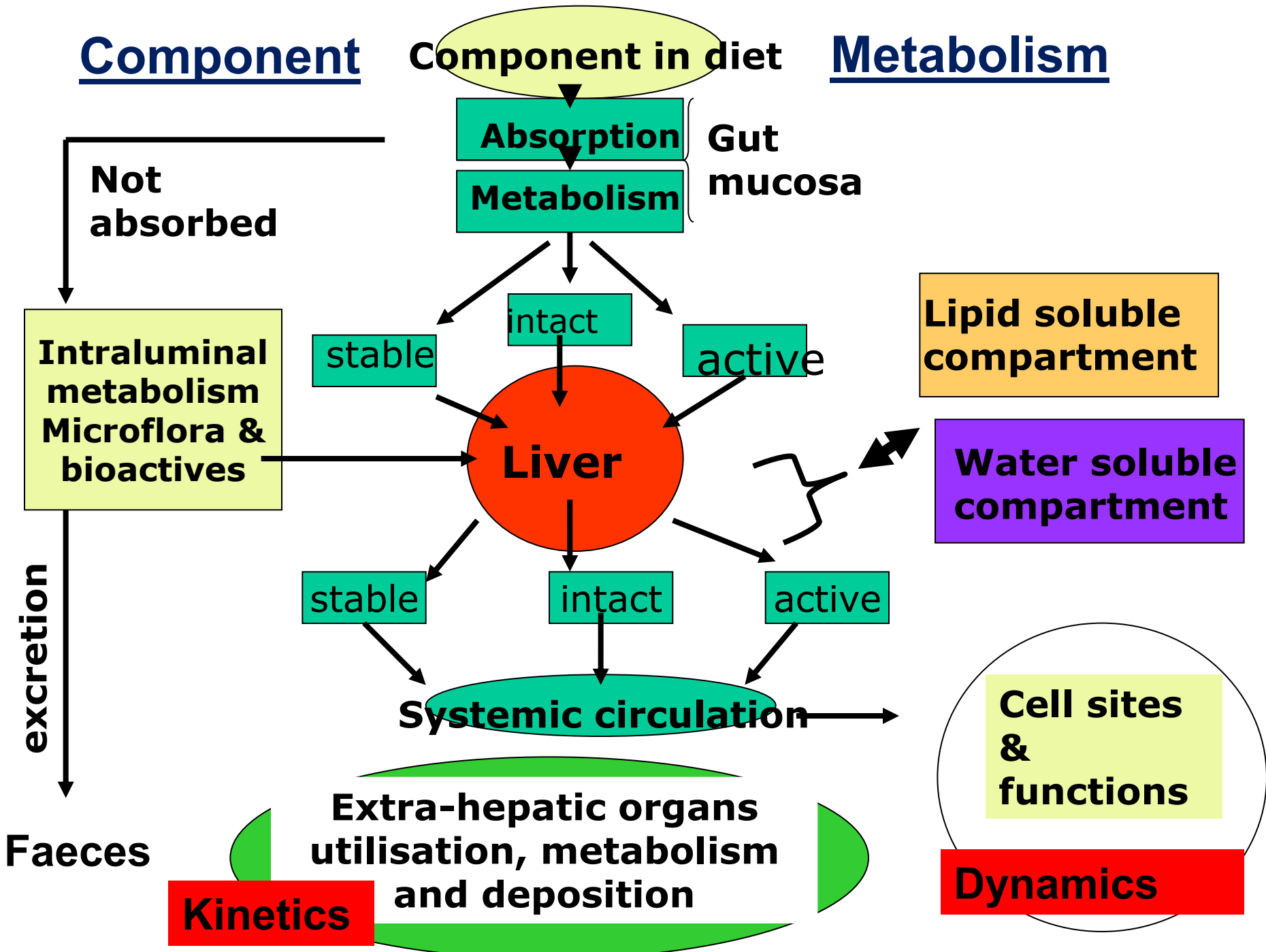
Deconvolution of Oral curve

# Plasma Concentration Time Curves (lipid solubles)



# Factors influencing the utilisation of a dietary component

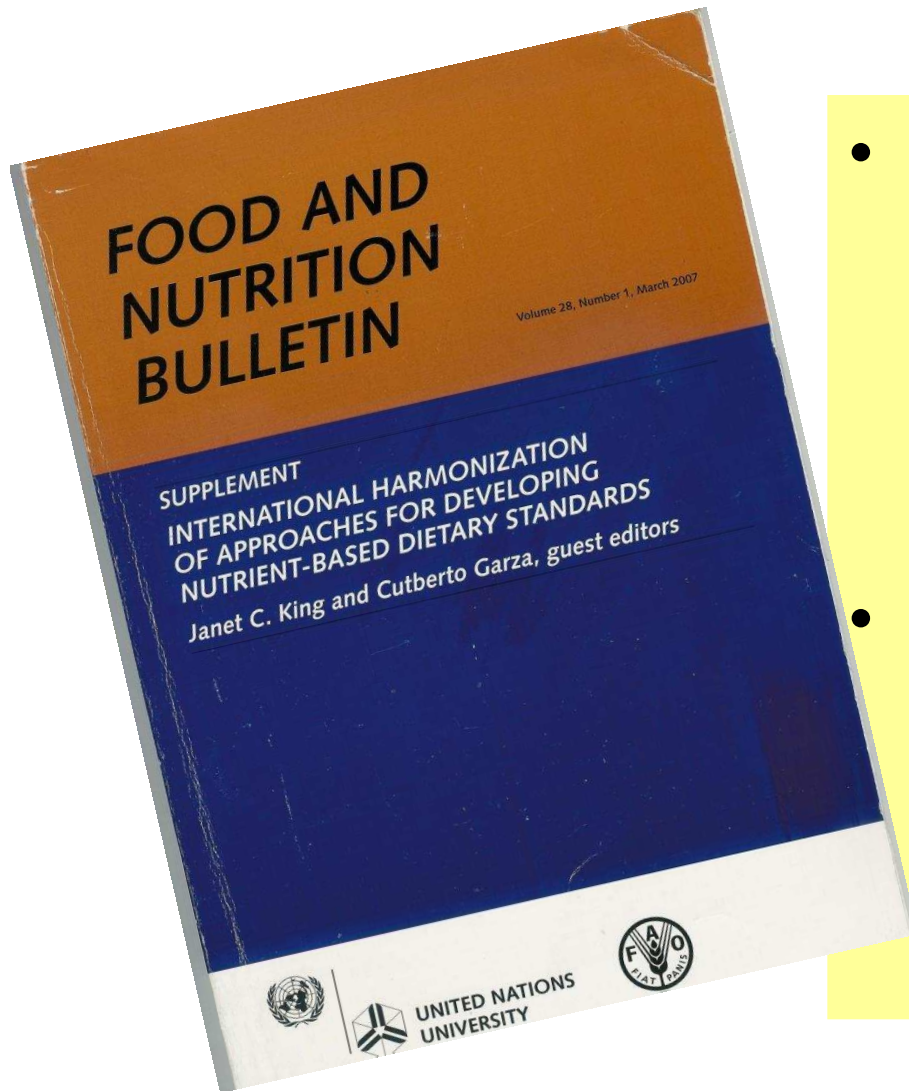
- Characteristics of component
  - Water or lipid soluble; non-metabolised or metabolised; inorganic or organic; cationic or anionic
- Dietary Characteristics: release from the diet
- Host Factors:
  - Intestinal mucosal uptake and transfer; Systemic Distribution and deposition; Systemic Metabolism; Store, sequestration, Functionality of component/metabolites
  - Excretion
- Absorption, Distribution, Metabolism and Excretion



# Bioavailability measurements

- do not necessarily address the full concept of the term
- assess release of the component from the diet
- are limited by host characteristics
- ranks foods and diets but do not give absolute values
- should be applied cautiously to derivation of NIVs.

# Nutrient Intake Values



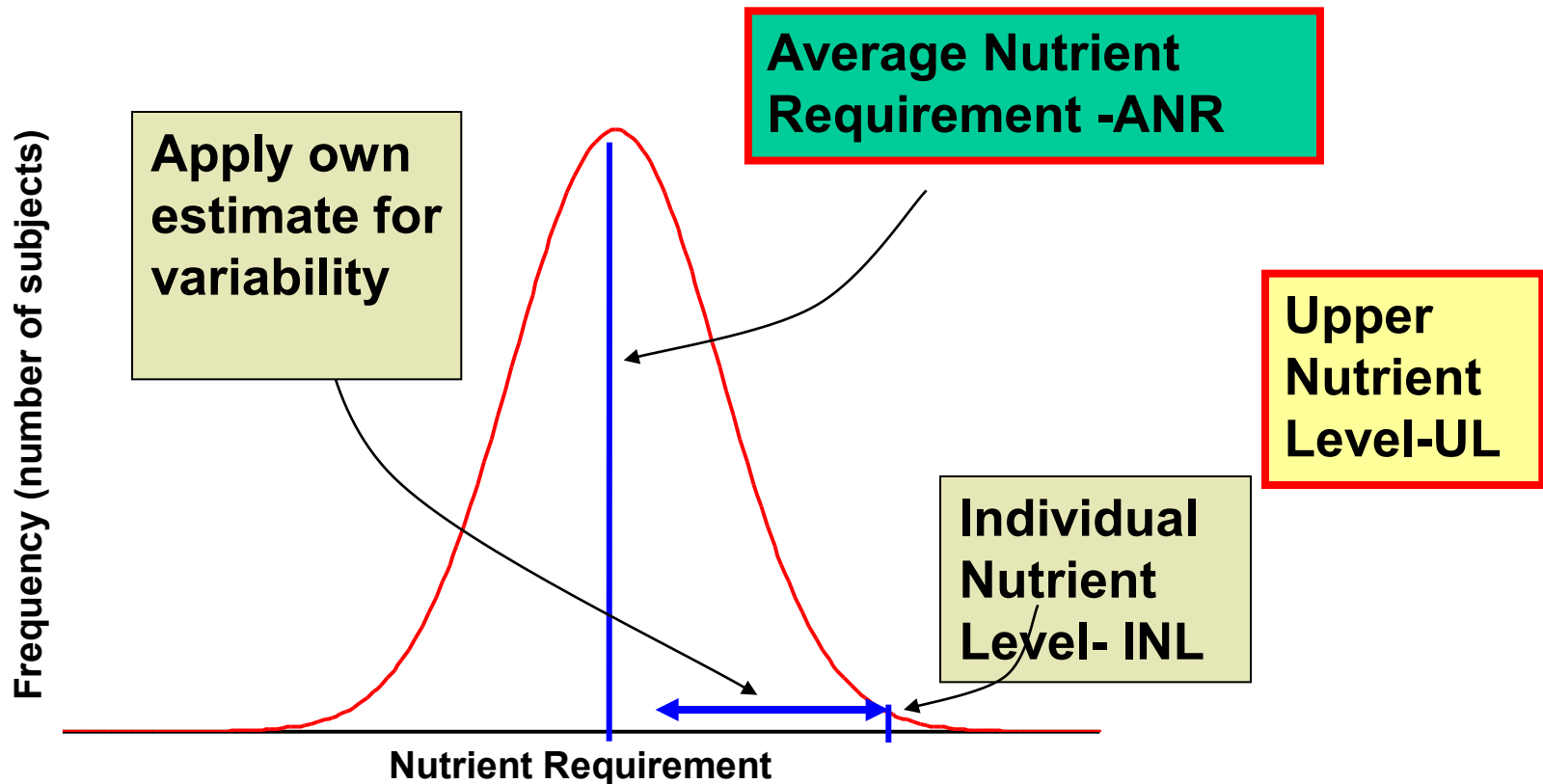
- International Harmonisation of Approaches for Developing Nutrient-Based Dietary Standards
- Food Nutrition Bulletin 2007 (March) 28; 1, S3-S153

# Nutrient Intake Values

- Conceptual exercise
- Advocated Two derived or primary values :
  - Average Nutrient Requirement
  - Upper Nutrient Level

# International Harmonisation of Approaches for Developing Nutrient-Based Dietary Standards

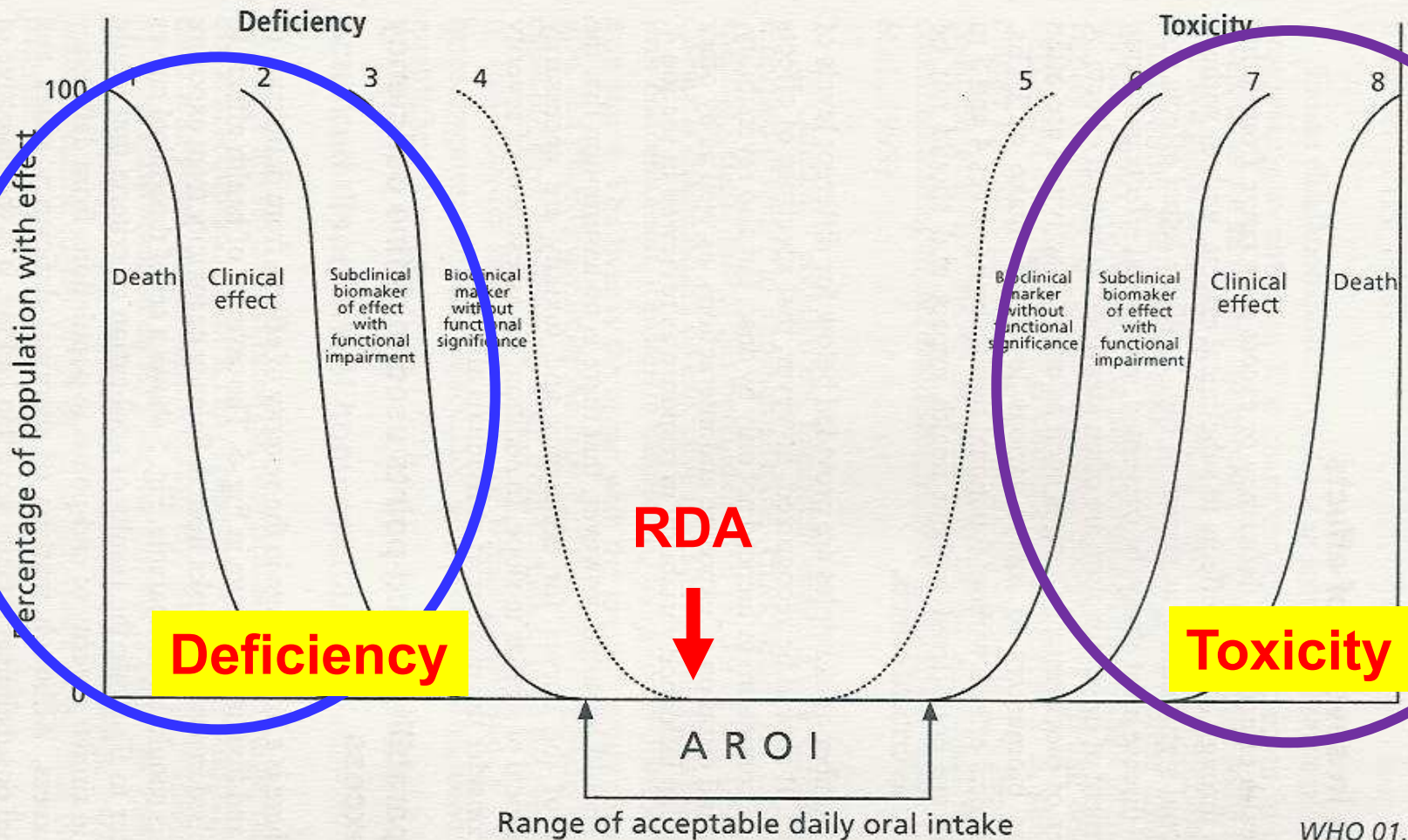
Population distribution of requirements for a nutrient



# Bioavailability and NRVs

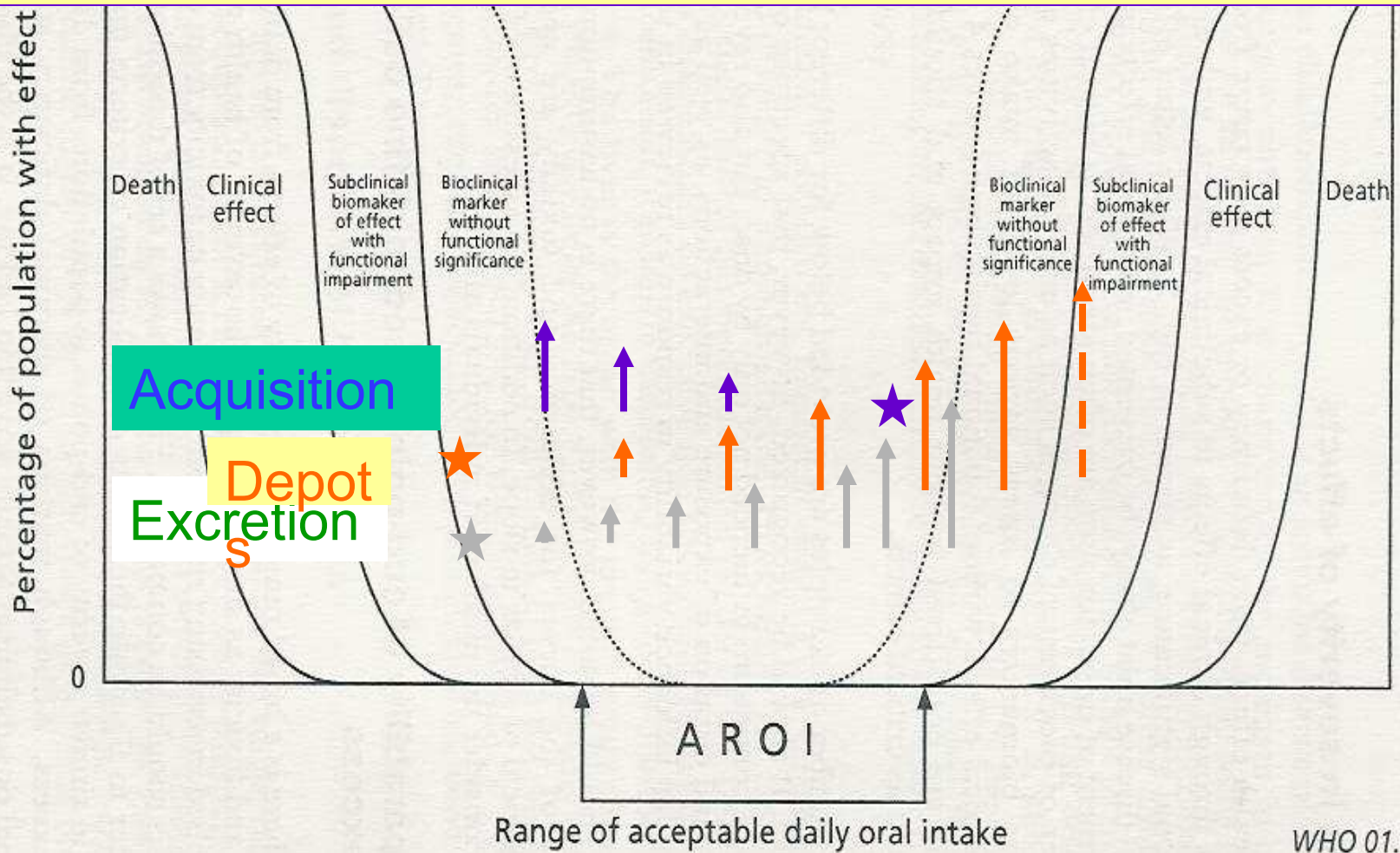
- Average requirement adjusted to a reference intake by factor derived from estimated bioavailability from the diet.
- Cautious values used
  - as such represent “risk management” rather than a sound estimate
  - conservative values used
  - application should be situational and transparent

# Range of Responses to Inadequate and Excess Exposure to a Micronutrient (IPCS, WHO 2002)



- Bioavailability: all elements are inextricably linked

# “Critical Events” (The Homeostatic Swan)



# Health Claim Marker Identification: Marker chain and dose relationship

1. Biochemical changes within homeostatic range and no adverse sequelae

2. **Biochemical changes outside the homeostatic range without known sequelae**

3. **Biochemical changes outside the homeostatic range: a marker of potential adverse effects due to excess**

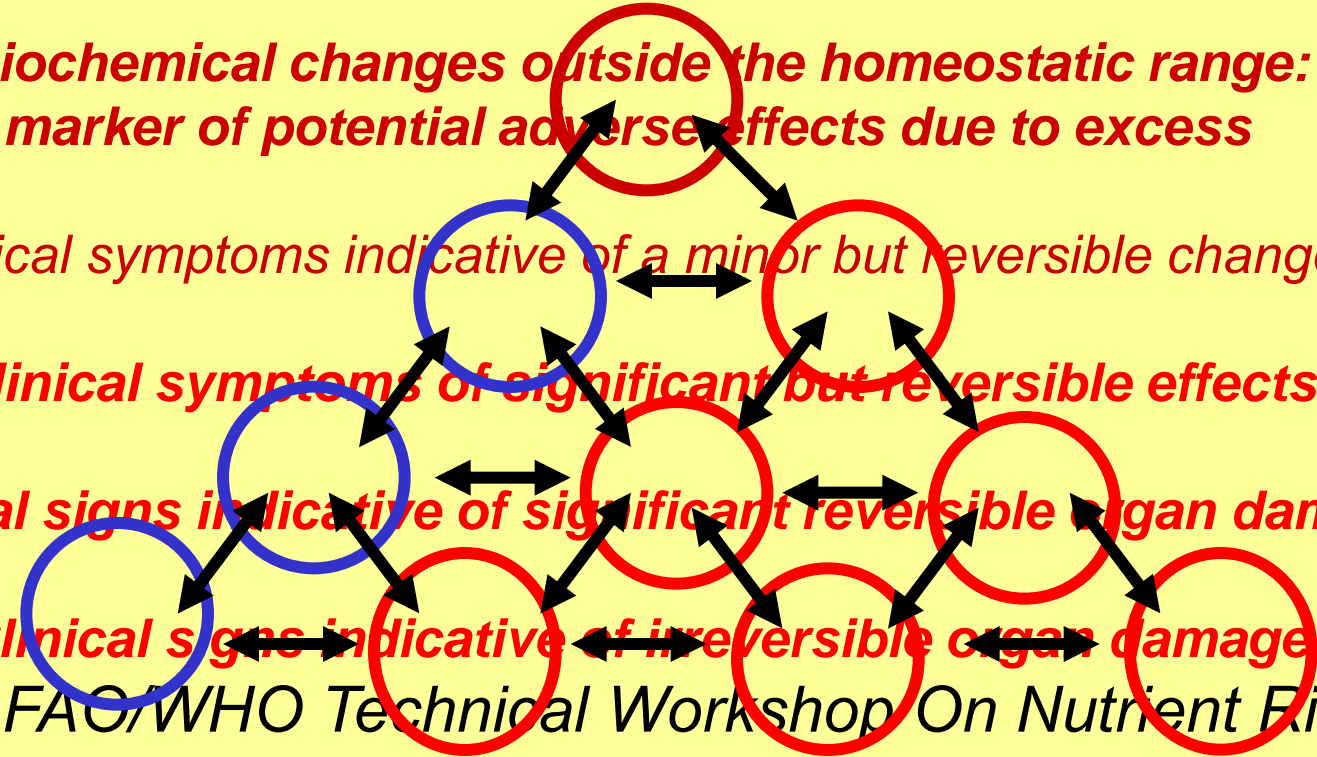
4. Clinical symptoms indicative of a minor but reversible changes

5. Clinical symptoms of significant but reversible effects

6. Clinical signs indicative of significant reversible organ damage

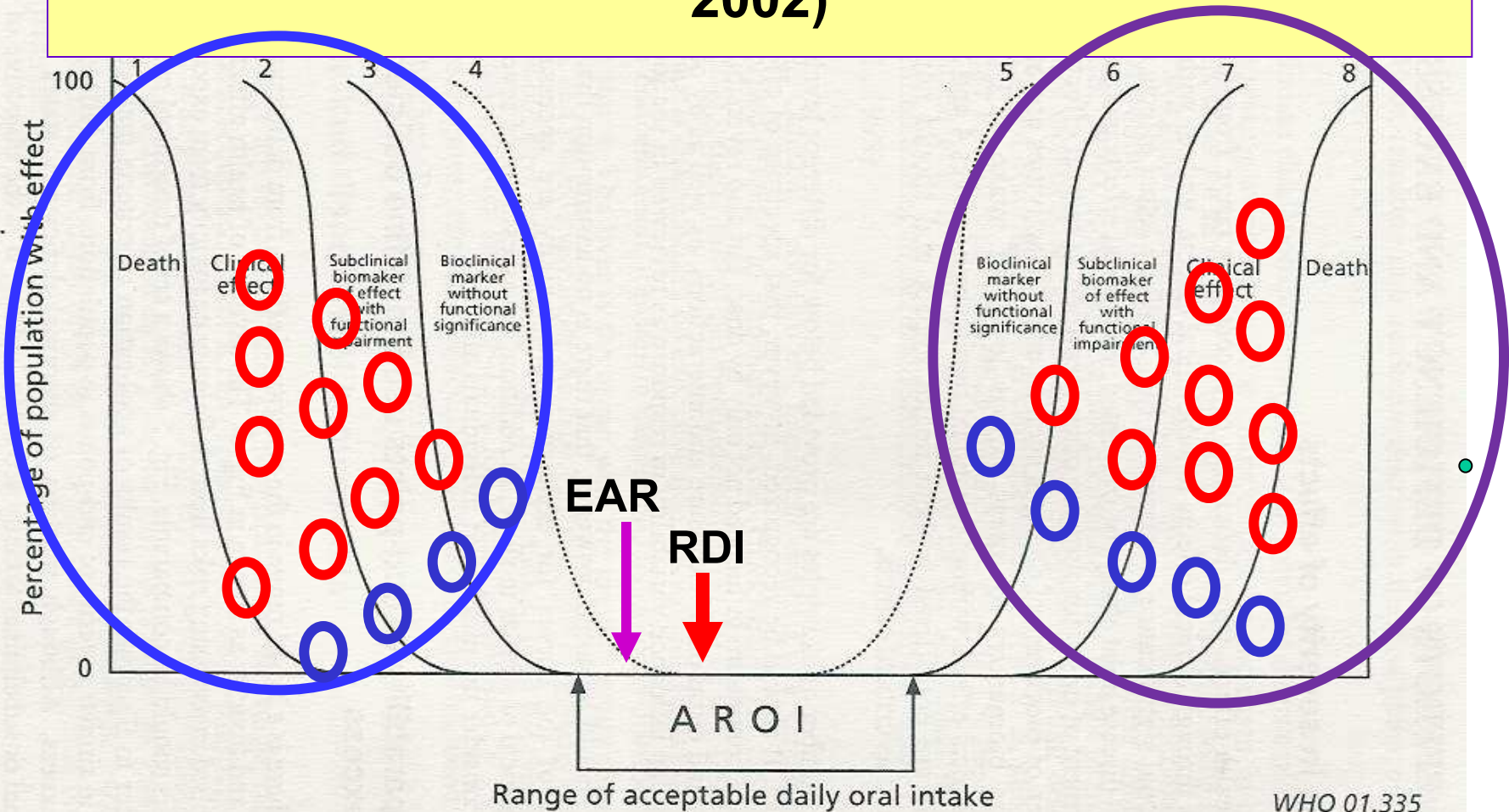
7. Clinical signs indicative of irreversible organ damage

(Joint FAO/WHO Technical Workshop On Nutrient Risk Assessment 2006)



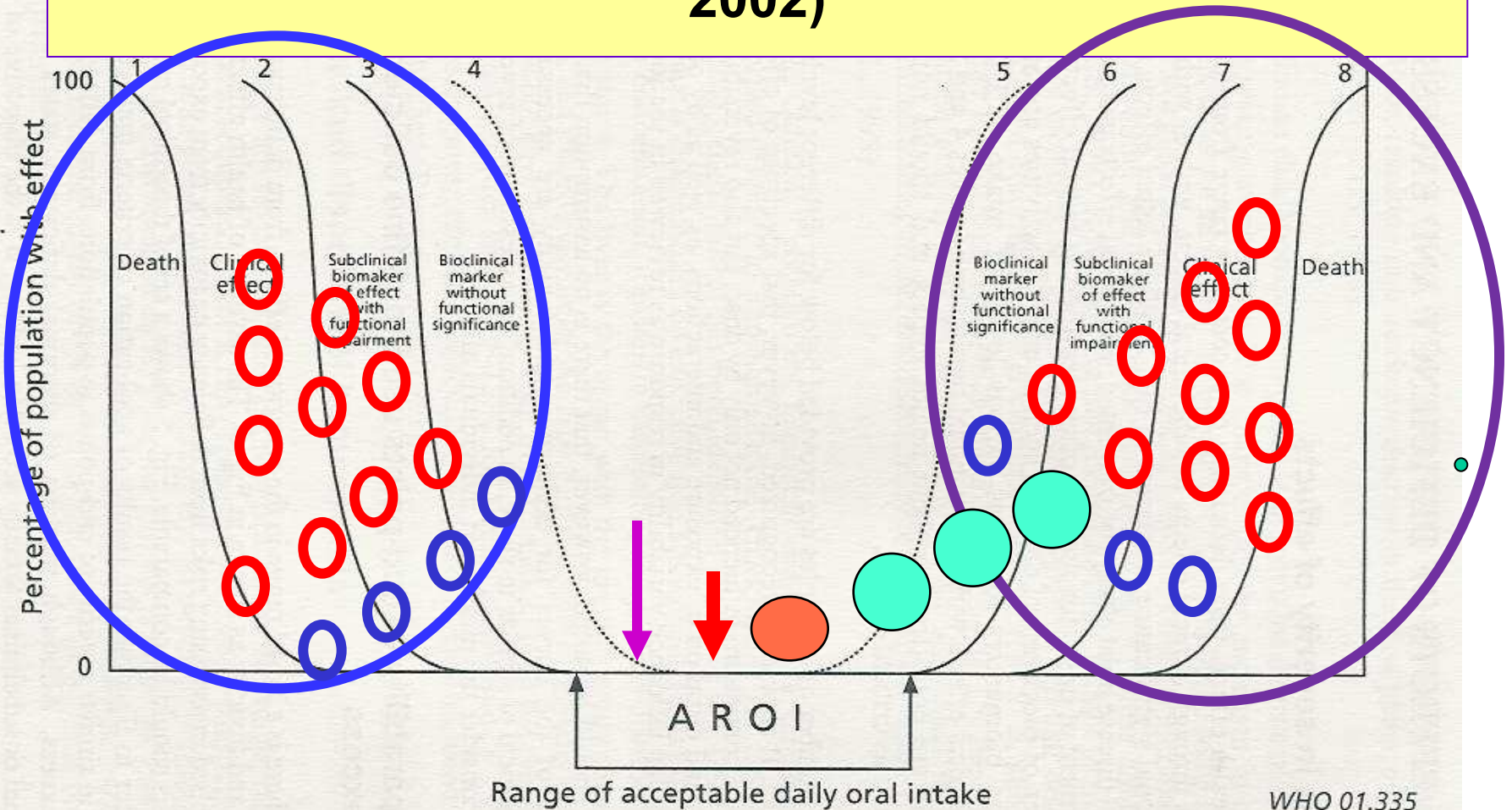
# Responses to **Inadequate** and **Excess** Exposure to a Micronutrient (IPCS, WHO 2002)

Fig



# Responses to **Inadequate** and **Excess** Exposure to a Micronutrient (IPCS, WHO 2002)

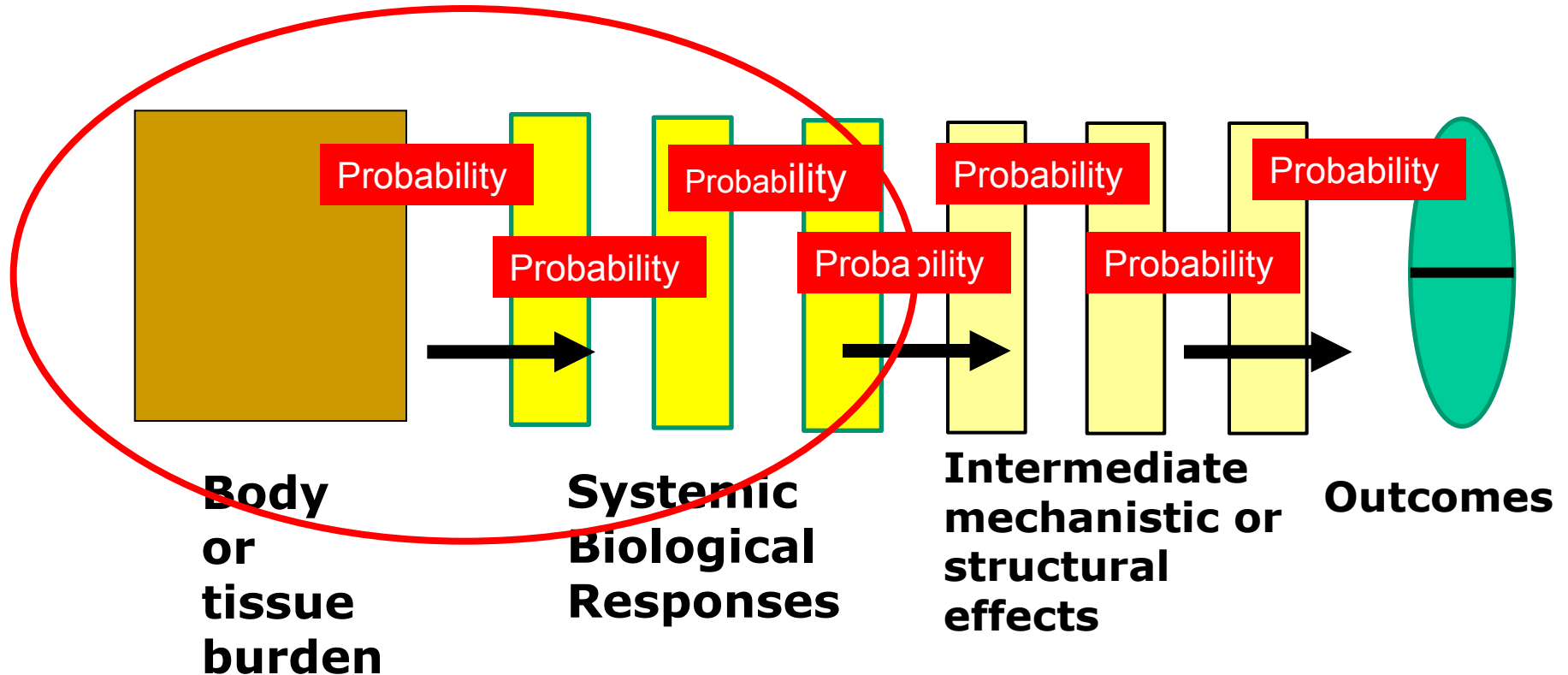
Fig



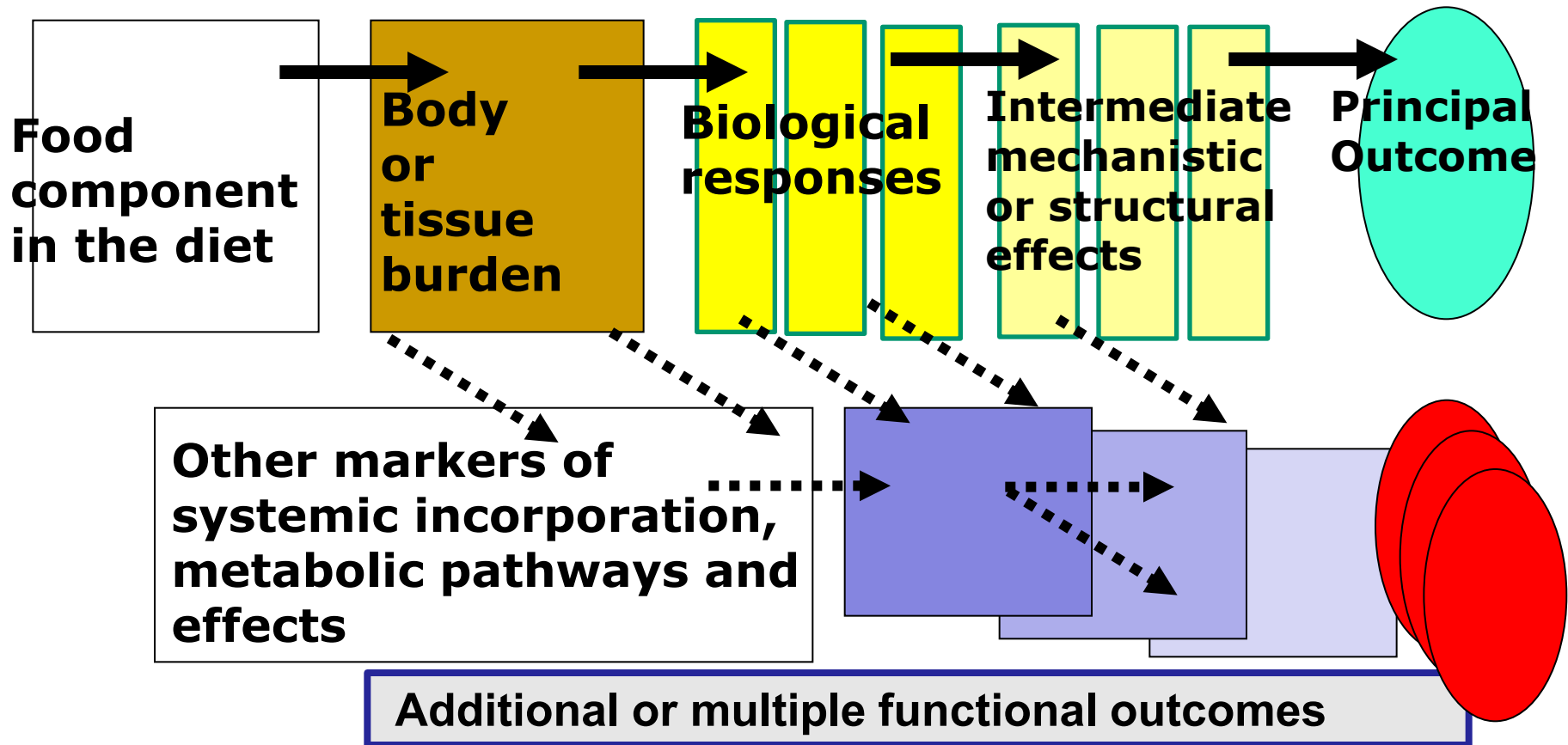
# Evidence Based Mechanistic Reasoning

(Howick et al. JRSM 2010) [www.cebm.net](http://www.cebm.net)

- **Bioavailability's pervasiveness:- Use of intermediate probabilities to deduce overall causal association.**



# The Chain of Markers: Consumption to Multiple Functions or Outcomes.



# Summary

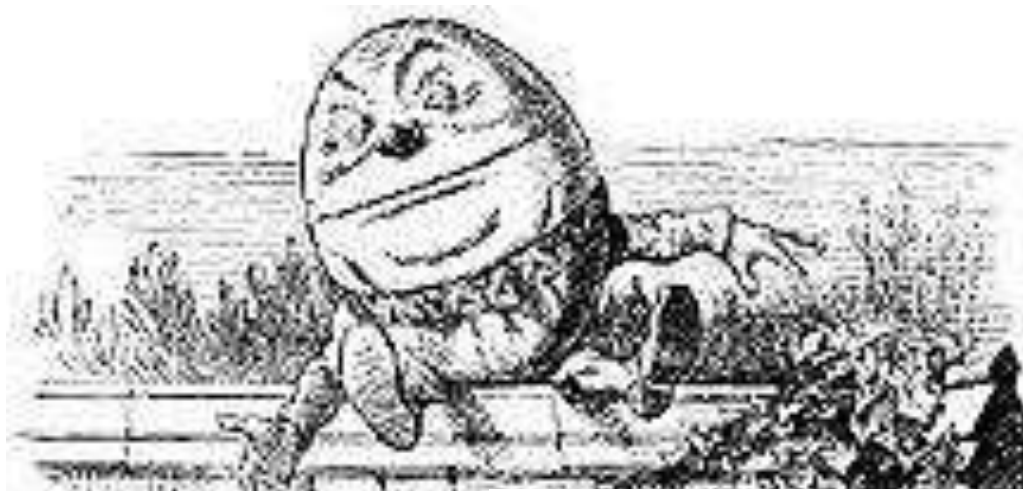
- Bioavailability is a useful concept
- More often misused than honoured
- Concept highly pervasive
- Limited in its assessment and application
- Needs to be used explicitly and precisely without uncritical extrapolation
- Elements should be differentiated

# Summary

- Overestimates of Nutrient Intake Values
- Intrinsic element of establishing true and relevant exposure to single and multiple outcomes/responses to components in developing evidence relevant to demonstrating causal relationships in scientific portfolios for health claims.

# Concluding questions?

- How useful is the term; is it now obsolete?
- Does it obfuscate appropriate scientific analysis?
- Would it be better to address the aspects of the full concept as ADME which is more amenable to EBMR?
- Would this improve the quality of nutritional science e.g. for NRVs and causal inferences?



# **Bioavailability**

**(Through the Looking Glass)**



**'That's a great deal to make one word mean,' Alice said in a thoughtful tone.**

**'When I make a word do a lot of work like that,' said Humpty Dumpty, 'I always pay it extra.'**