Submicron Systems in Functional Foods

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Unilever: 400 brands worldwide

Key Consumer Benefit Areas

Weight Management :

- Satiety enhancement
- Sustained energy delivery
- Muscle mass preservation
- Fat loss

Mental Development & Performance :

- Mental performance and cognitive development
- Growth and physical enhancement





Cardiovascular Health :

- Lipid lowering
- Homocysteine lowering
- Blood pressure lowering
- Improved blood circulation

Resistance to Disease :

- Optimised immune function
- Increased resistance to infection
- Gut health

Background

- Functional foods – the most dynamically developing sector of food industry, with a clear match between consumer demand and business attractiveness.
- Formulation aspects of functional foods are still underestimated. Pharma explores them more seriously, but mainly considers simplified effects of food matrix (fasted vs. fed state).
- In foods we always operate in a fed state situation, and in addition we can influence the diet. Foods are enormously complex systems with huge variation of in-use and in-body properties, but our challenge is to turn this complexity to our benefit!
- Generic approaches do not always exist; mostly there are "horses for courses".
- Combination of traditional (physical and microbial stability, mouthfeel, flavour release) and novel (enhanced bioavailability, targeted delivery, in-body functionality) food attributes is a prerequisite for a successful FuFo product.
- **Submicron systems in functional foods: just a few examples**

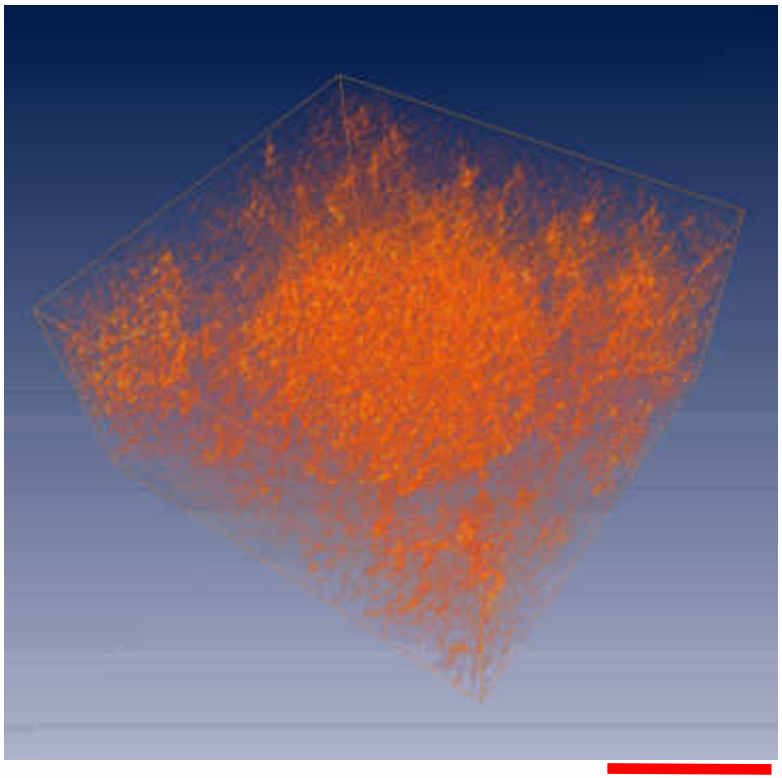
Nanotechnologies: How do we define them?

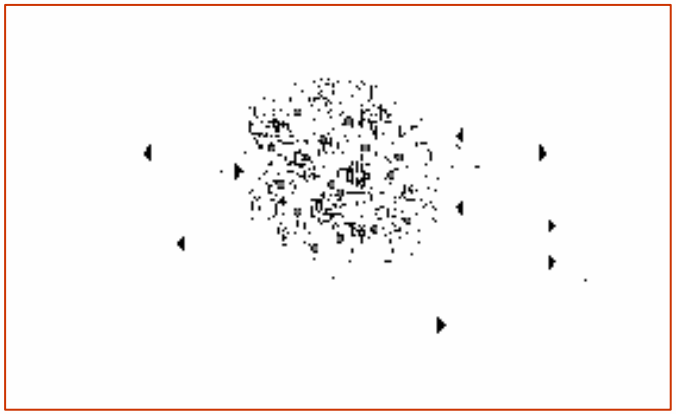
Nanotechnologies should probably best be understood as a *conceptual and intellectual framework* that enables the design of more complex macroscopic structures using nanometer scale building blocks.

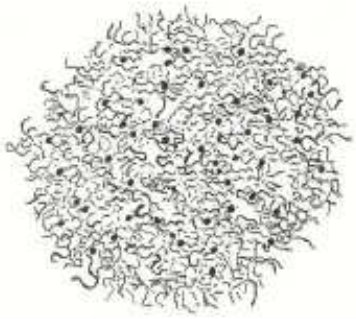
Weiss, Takhistov, McClements, "Functional Materials in Food Nanotechnology", J. Food Sci. (2006) 71, R107-R116

Milk

Casein Micelles







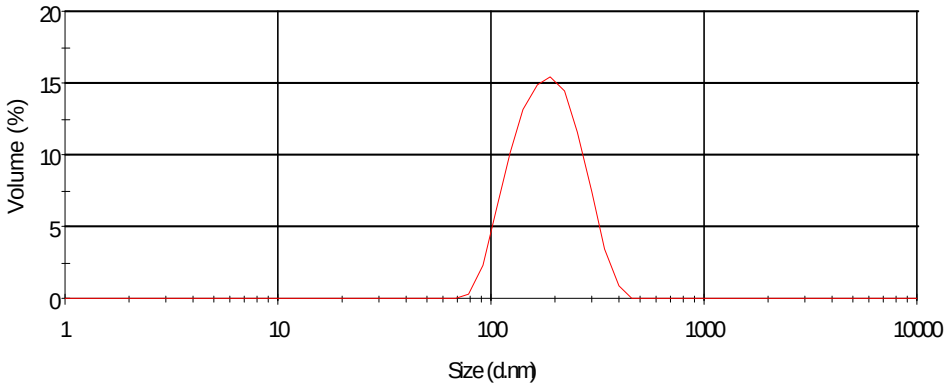
- **Milk is a well known food material**
- **Submicron casein micelles have evolved by Nature to provide nutrition and molecular calcium for growing young (scale bar is 100 nm)**

Liqueur

True submicron emulsion based on droplet size

- **Average droplet size 190 nm**
- **Max droplet size < 500 nm**

Droplet size measurement with NanoZetasizer

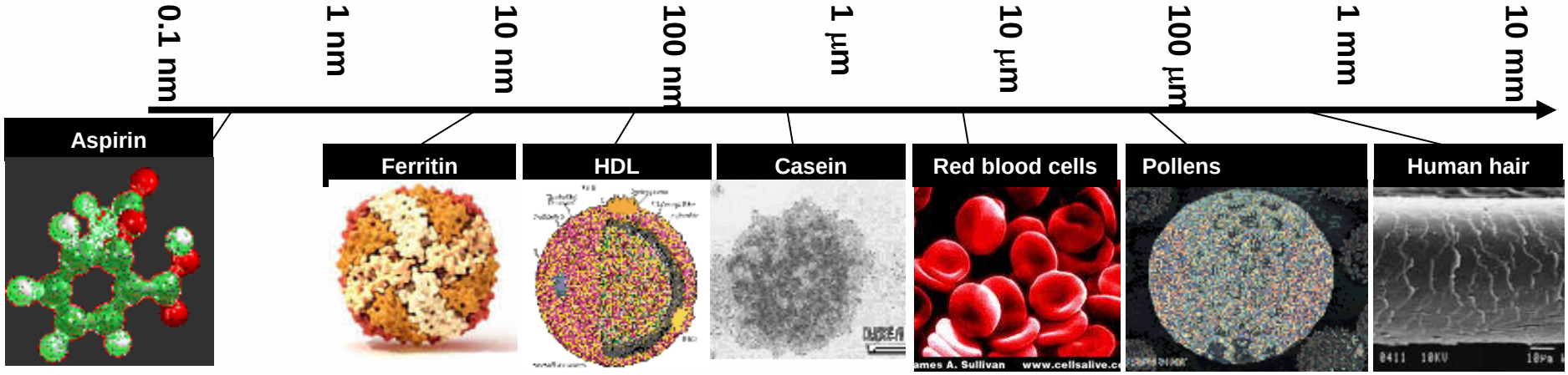


Submicron Structures in Foods

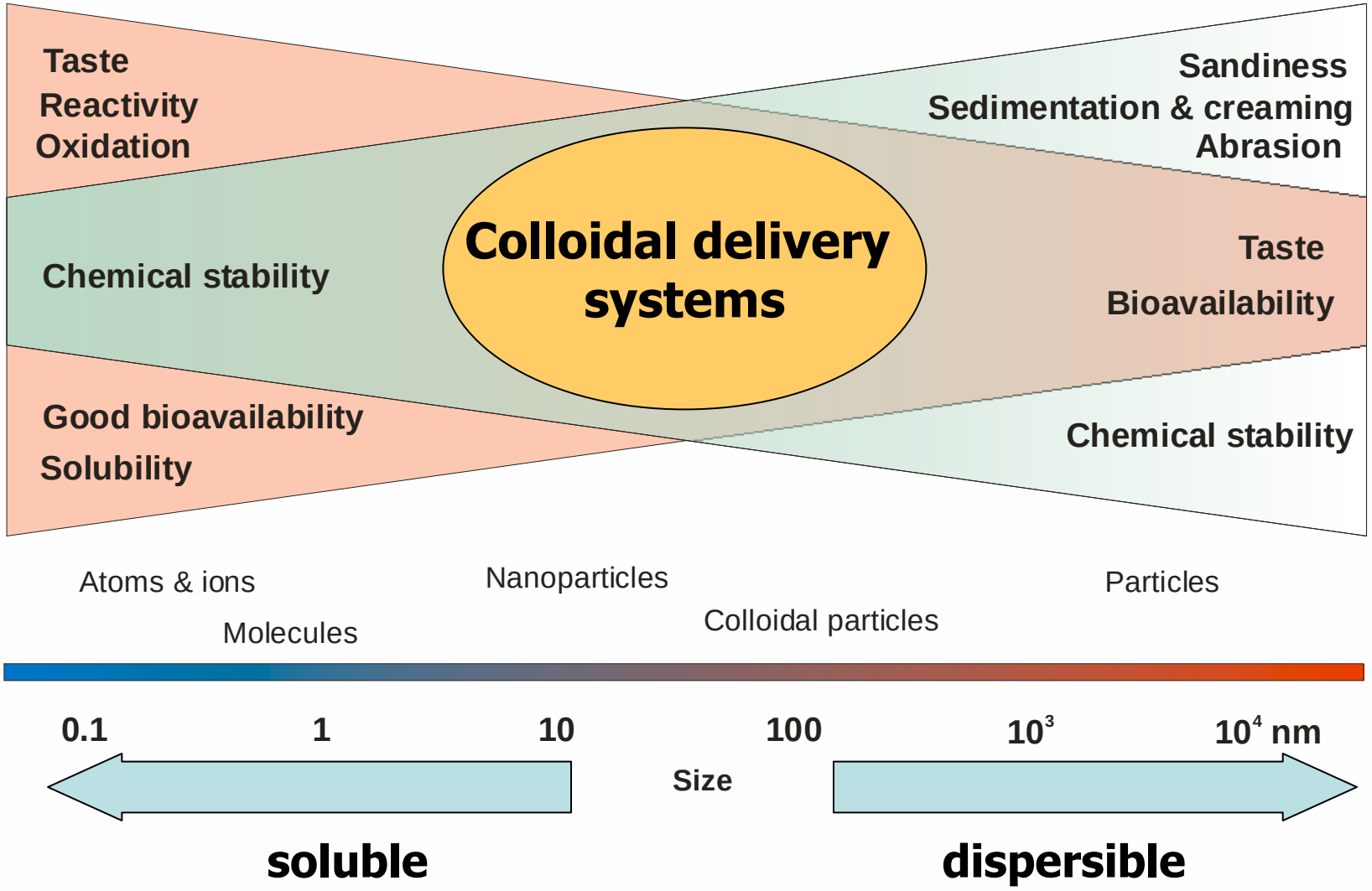
< 100 nm
- **Polyphenolic particles:**
  - **tea, wine, coffee**
- **Proteins**
  - **milk proteins: casein, lactoglobulin, …**
  - **soy proteins: glycinin, conglycinin, …**
  - **sport drinks: whey - mineral particles**

< 300 nm
- **Protein particles**
  - **soy protein**
  - **egg proteins**
- **Cream liqueurs (e.g., Irish Cream)**

< 800 nm
- **Oil**
  - **homogenized milk**
  - **clinical nutrition emulsions (e.g., Intralipid™)**
- **Protein particles**
  - **soy**
- **Broken plant cells**

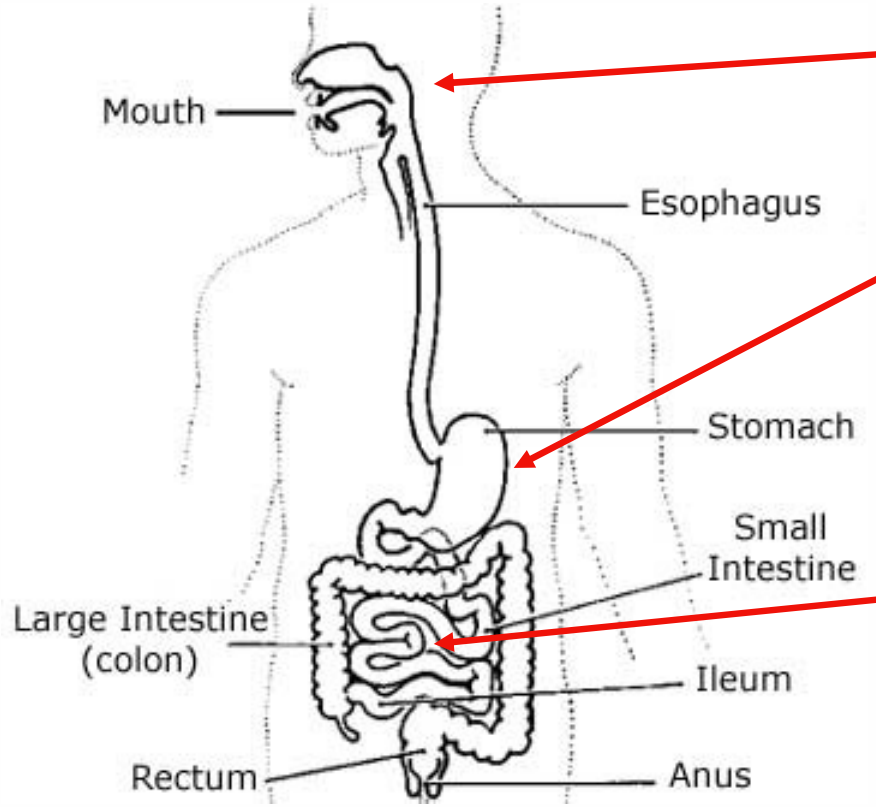


Colloidal Delivery Systems



Food-Body Interaction Sites

Numerous physico-chemical processes are taking place in human body during food intake, digestion and absorption



homogenization

absorption

emulsification

phase transitions

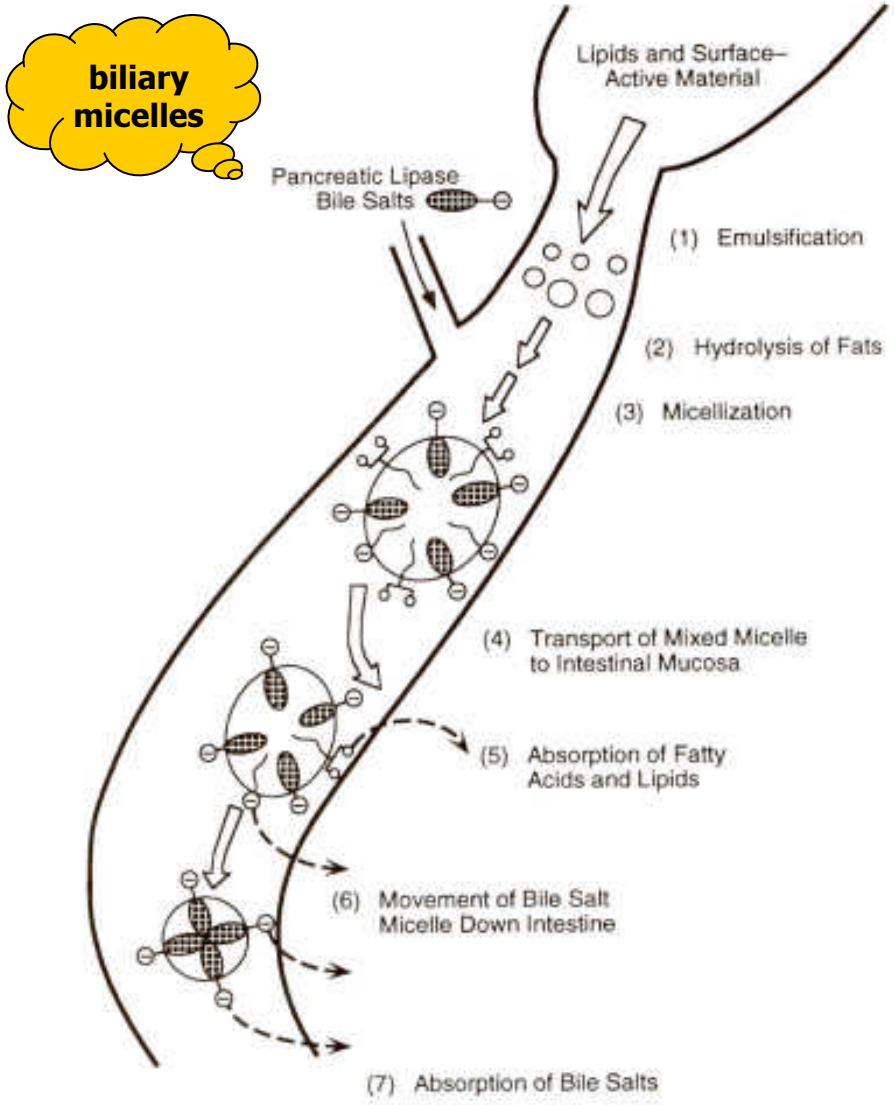
enzymatic hydrolysis

amphiphilic self-assembly

micellar solubilization

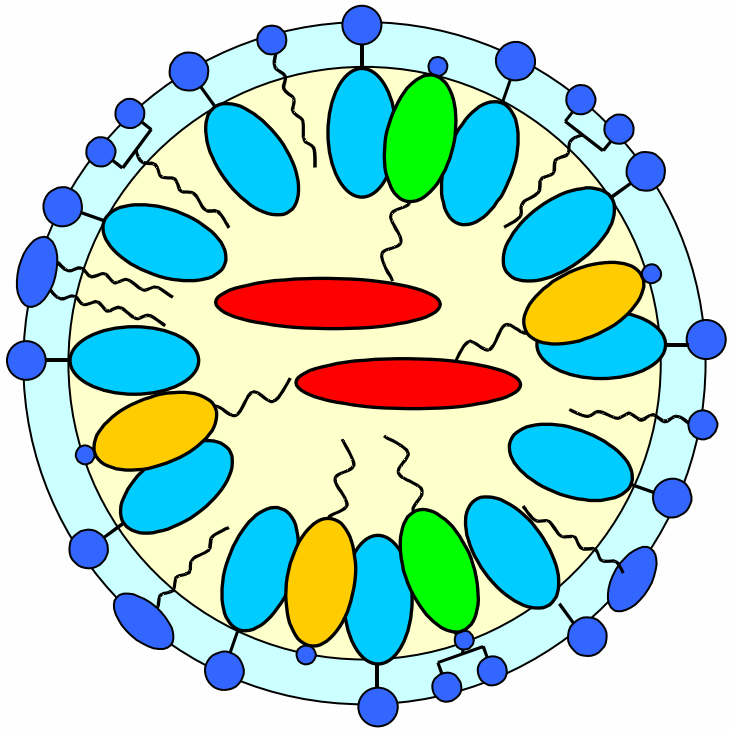
diffusion-mediated absorption

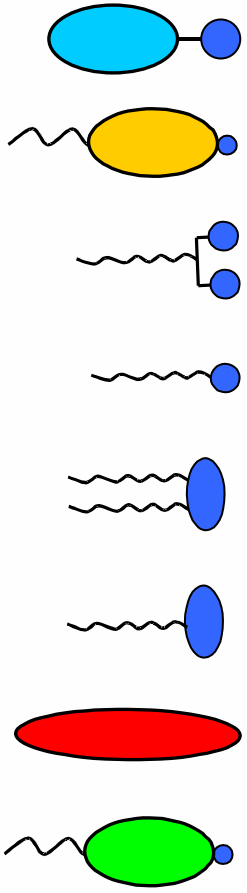
Physical Chemistry of Human GI Tract



From "The Colloidal Domain" by D. Fennell Evans & Håkan Wennerström, VCH Publishers, New York (1994)

Dietary Mixed Micelle





bile acid salt

cholesterol

monoglyceride

fatty acid

phospholipid

lysophospholipid

lipophilic nutrient

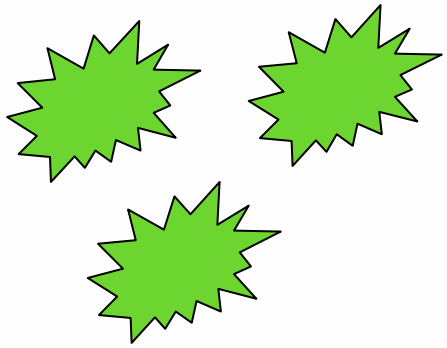
plant sterol/stanol

"peach" model

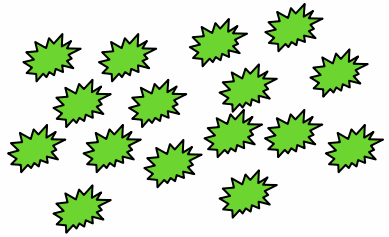
Melnikov et al, Eur. J. Lipid Sci. Technol. 105 (2003)171–185

Tailoring Bioaccessibility of Actives Using Colloidal Systems

Macroscopic particles of functional actives



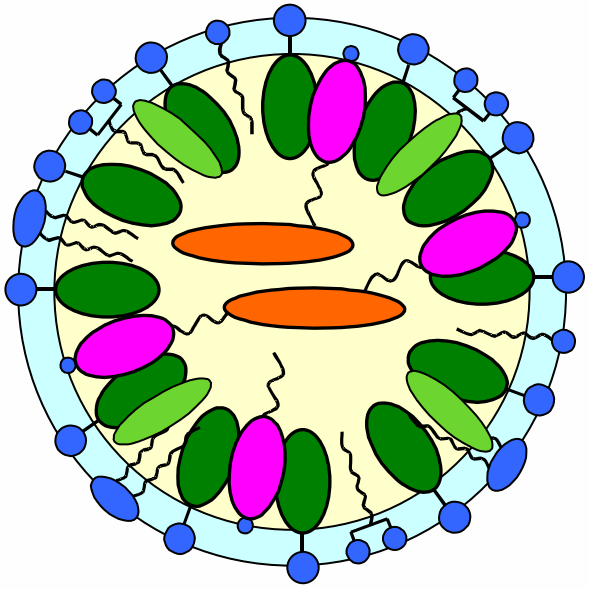
Colloidal particles of functional actives



slow process

rapid process

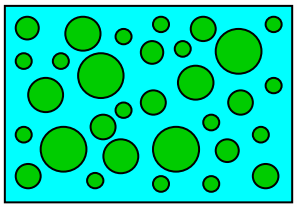
active molecule



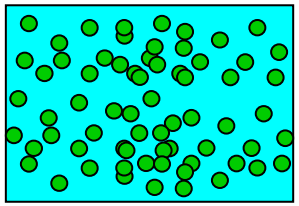
dietary mixed micelle

Tailoring Bioaccessibility of Actives Using Colloidal Systems

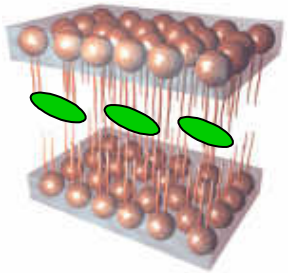
Food emulsions with functional actives



Submicron emulsions with functional actives



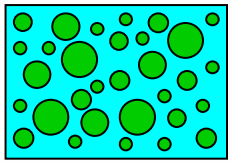
Lipid mesophases with functional actives

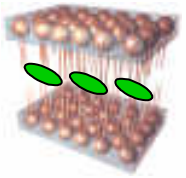


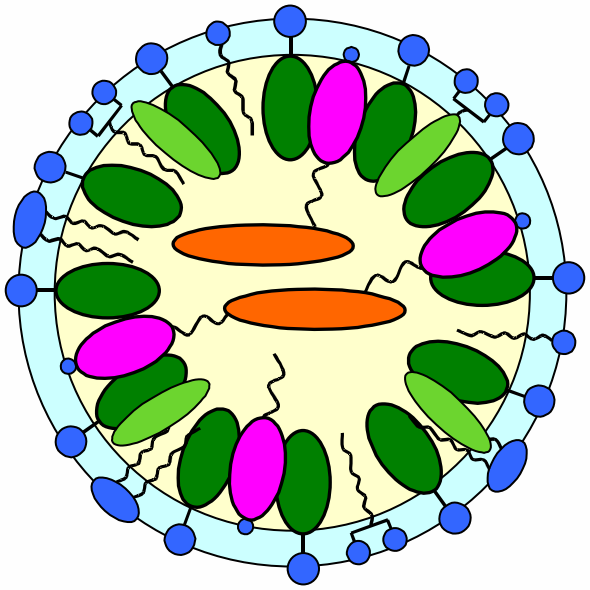
low rate

medium rate

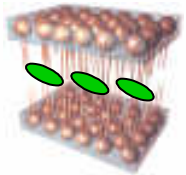
high rate







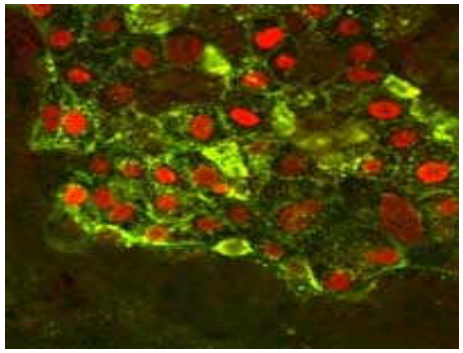
dietary mixed micelle



Predictive Modelling

In vitro lipolysis model

+

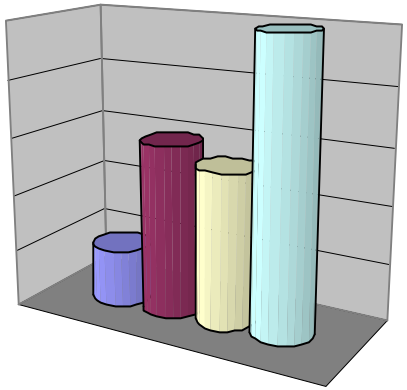


CaCo2 cell model

NUTRITION INFORMATION Typical Values	Per 100g bottle
Energy	367kJ/87kcal
Protein	2.6 g
Carbohydrate	12.5 g
of which sugars	12.5 g
Fat (excluding sterols*)	2.9 g
of which -saturates	1.1 g
-monounsaturates	0.8 g
-polyunsaturates	1.0 g
Fibre	Trace
Sodium	0.05 g

* sterols do not contribute to the energy value

CH-lowering efficacy

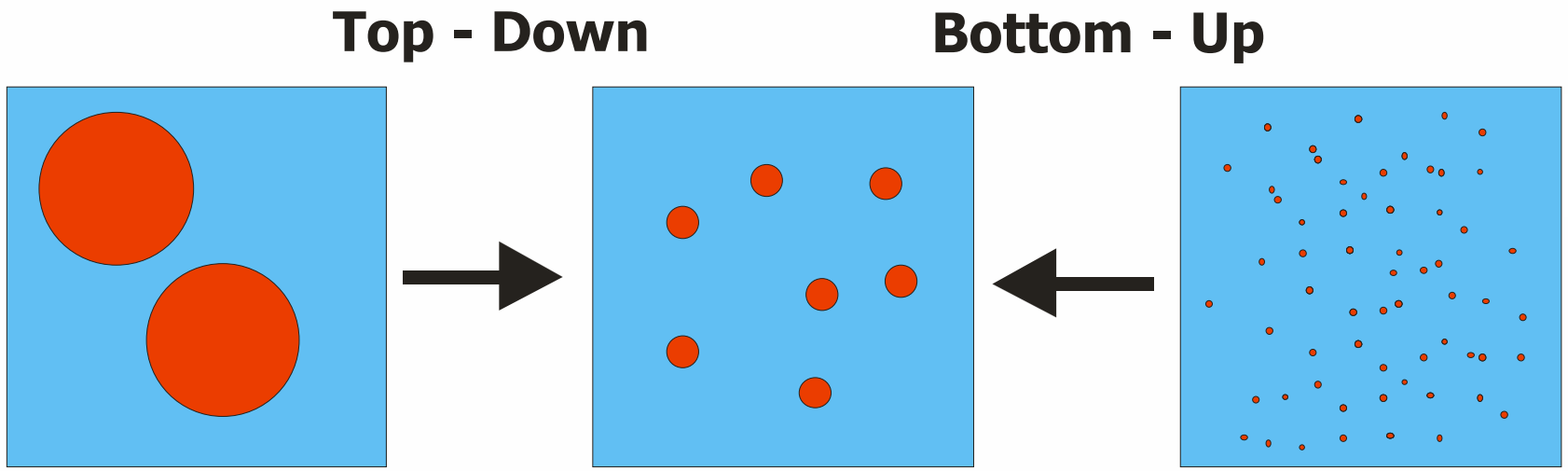


PSE, skimmed milk
PSE, semiskimmed milk
PSE, skimmed milk + meal
PSE, semiskimmed milk + meal

Cholesterol reductions can start within 2 weeks.
For optimal cholesterol lowering results:

- Use **one bottle per day** (contains 2g plant sterols)
- Consume with meals
- Use as part of a healthy diet including fruit and vegetables
- Use everyday to continue the cholesterol lowering effects
- Consume no more than 3g plant sterols per day

Fabrication of Colloidal Particles



Top-down approach: submicron lipid emulsions

food-grade lipid emulsifier

↓

heating above melting point

↓

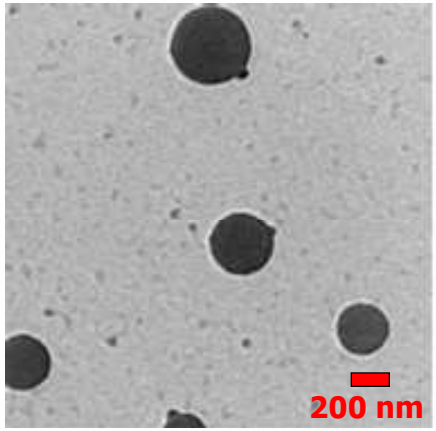
high pressure homogenization → macroemulsion

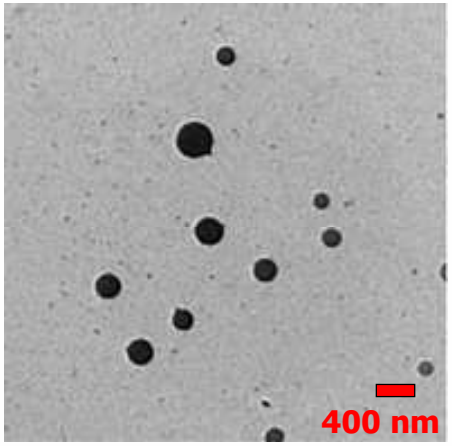
↓

microfluidiser → submicron emulsion

↓

cooling → colloidal particles





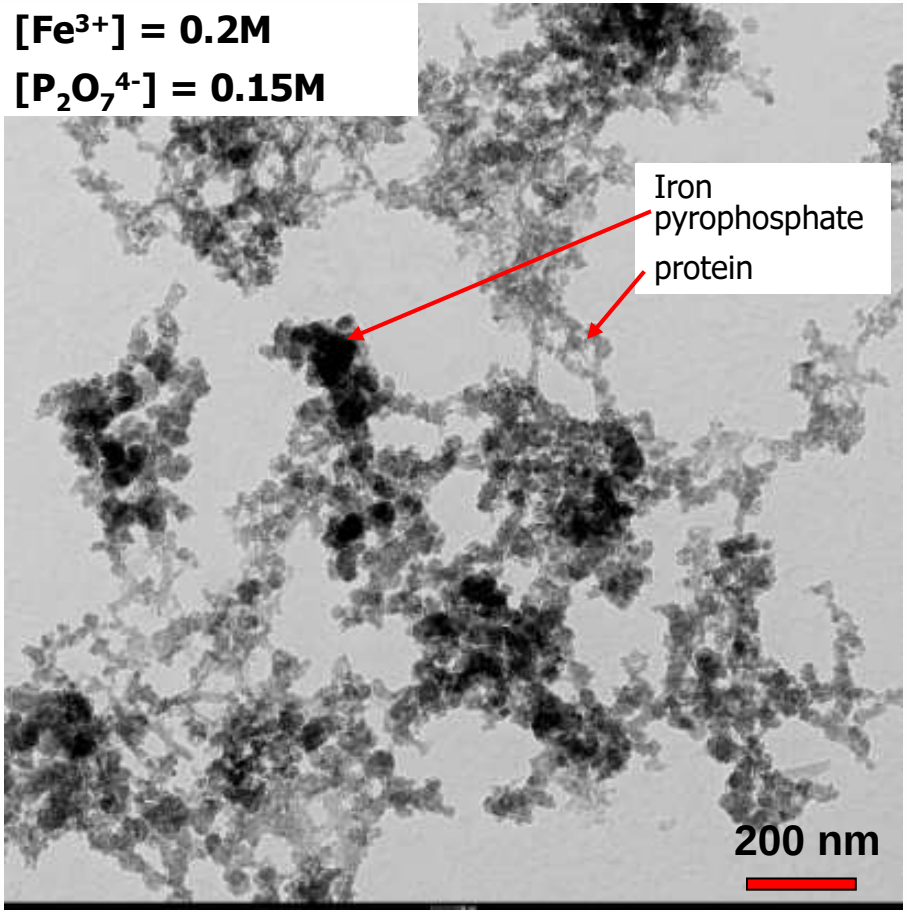
Bottom-up approach: Fe(III) pyrophosphate – protein particles

TEM images

protein = 1.0 wt%

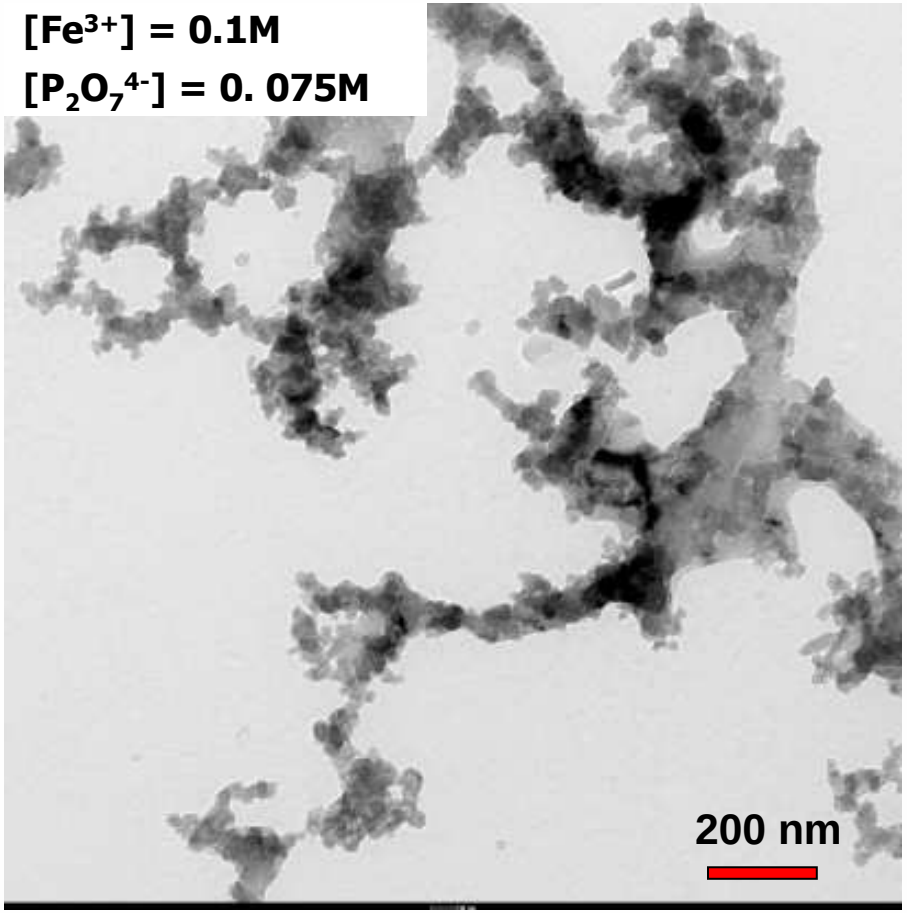
$[Fe^{3+}]$ = 0.2M

$[P_2O_7^{4-}]$ = 0.15M



$[Fe^{3+}]$ = 0.1M

$[P_2O_7^{4-}]$ = 0. 075M



Chemical analysis - approximate formula $Fe_4(P_2O_7)_3$

Product Functionality Control

- Composition
- Structure
- Appearance
- Stability (microbiological, physical, chemical)
- Texture
- Taste & Flavor
- Digestion & Bioavailability
- Targeted Delivery

Design of Functional Foods

From the structural design for

- **Physical stability and appearance**
- **Microbiological stability**
- **Flavour release and mouthfeel**

To tailoring of *in-body functionality*

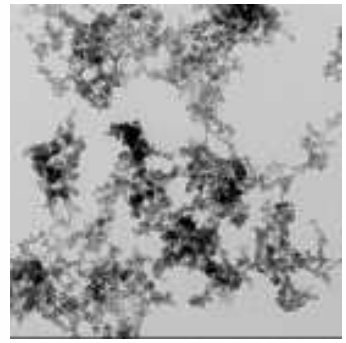
- **Enhanced bioavailability**
- **Controlled release**
- **In-body structuring**

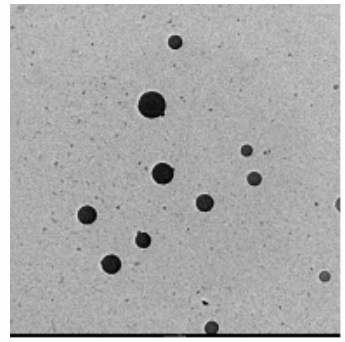
Via new approach to "old" technologies

- **Emulsions and foams**
- **Colloidal particles**
- **Hydrocolloids and composites**
- **Biomimetic systems**
- **Others**

Summary

- Submicron colloidal dispersions - suitable delivery systems for (bio)active compounds and (micro)nutrients in various functional food formats
- Expected benefits
  - solubility - dispersibility balance
  - physical stability
  - product compatibility
  - morphology control - amorphous vs. crystalline
  - size control
    - dissolution/digestion rate
    - bioaccessibility/bioavailability
- Bottom-up and top-down syntheses of colloidal particles

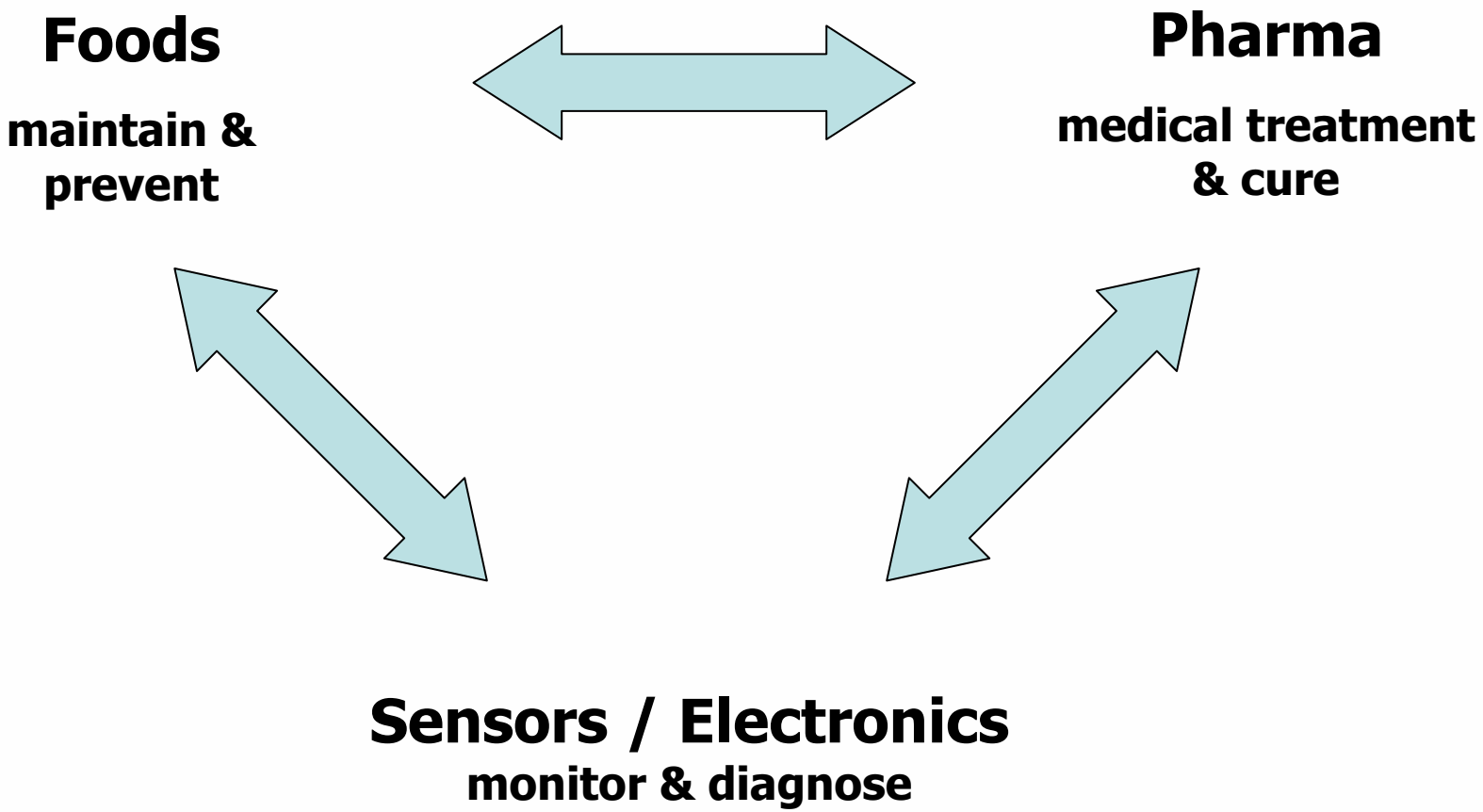




Conclusions

- **Submicron colloidal systems offer an unlimited choice of innovative approaches to the design of functional foods products**
- **Colloidal dispersions are proven as successful delivery system for active molecules and micronutrients in foods**
- **Knowledge in the area develops very rapidly, and the only way to innovate successfully is to actively use *Open Innovation* with academic partners, ingredient suppliers and other businesses: *let's create new functional food propositions together!***

Cross-Industry Synergies



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- Unilever R&D Shanghai (H. Li, Dr. A. Tan)
- Unilever R&D Vlaardingen colleagues

THANK YOU FOR YOUR ATTENTION!

Backup Slides

Communication Aspects

- Colloidal particles are very well-known building blocks of all foods products (e.g. casein micelles or egg yolk granules)
- Health concerns are predominantly related to the direct uptake of nanoparticles (e.g. via endocytosis) and uncontrolled bioavailability of poorly-soluble actives (particle size <100 nm)
- The challenge for foods companies is to educate consumers and clearly explain the difference between inorganic nanoparticles and all-natural submicron colloidal food systems (e.g. milk, eggs, honey, grains, etc.)
- Application of natural/biomimetic submicron particles is clearly beneficial from the communication perspective
- Additional clinical examination and demonstration of safety of food-grade colloidal systems is required for the creation of public opinion