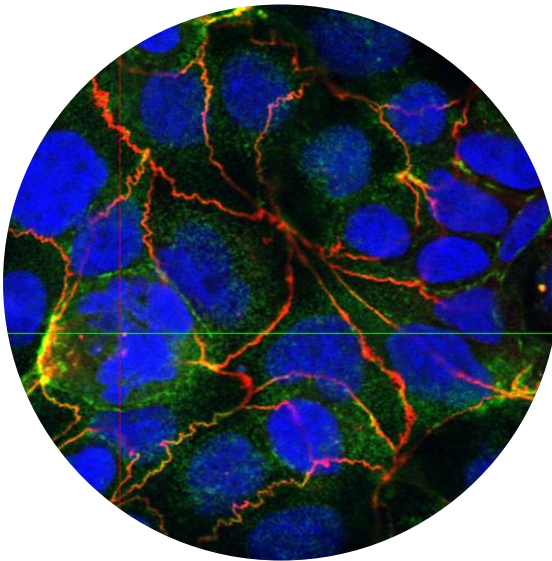


# Human gut-on-a-chip as a model for bioavailability and biotransformation studies

Hans Bouwmeester

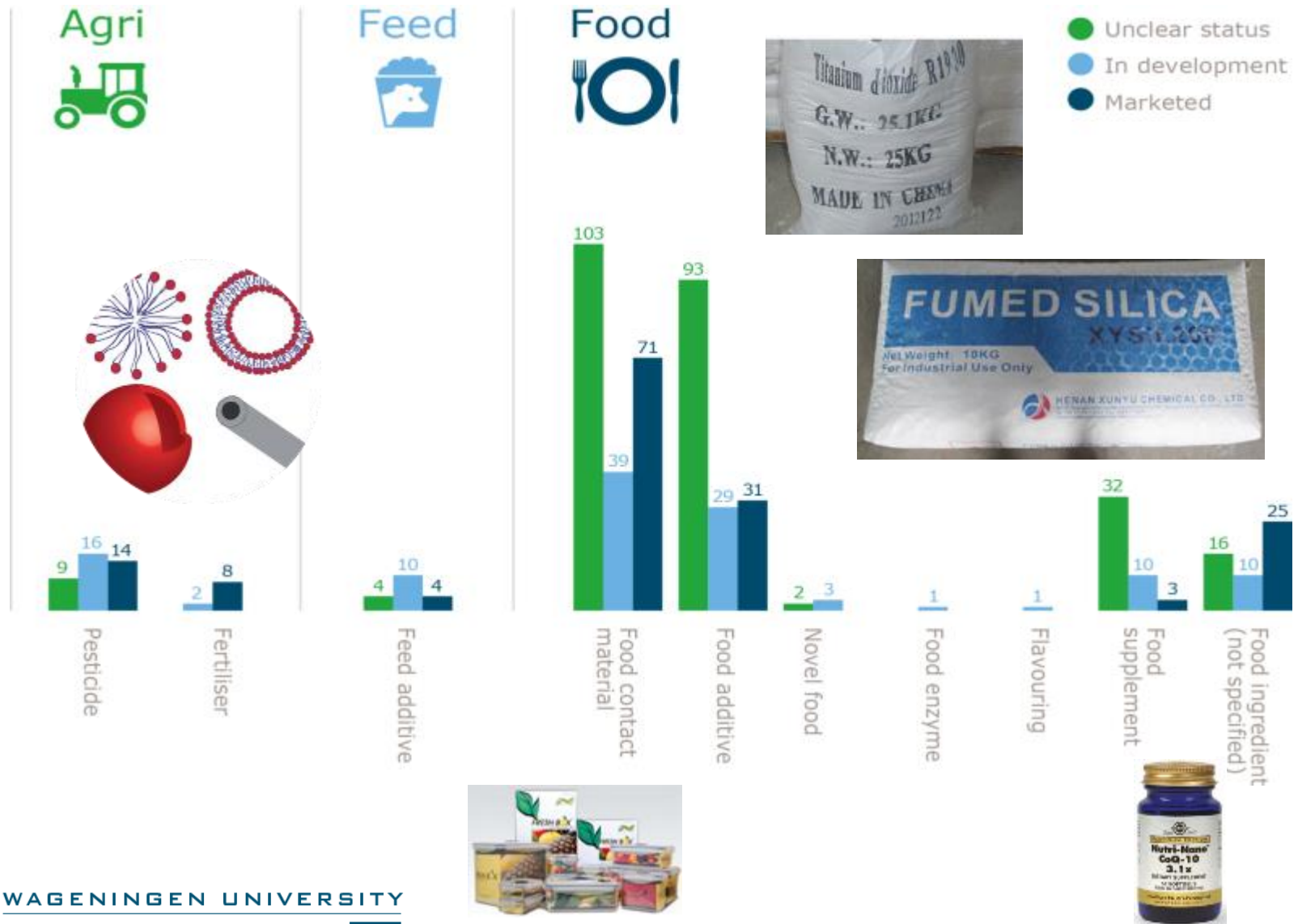
Senior scientist; *special* associate professor

Nanotoxicology - RSC Toxicology Award Seminar - 19 April 2016

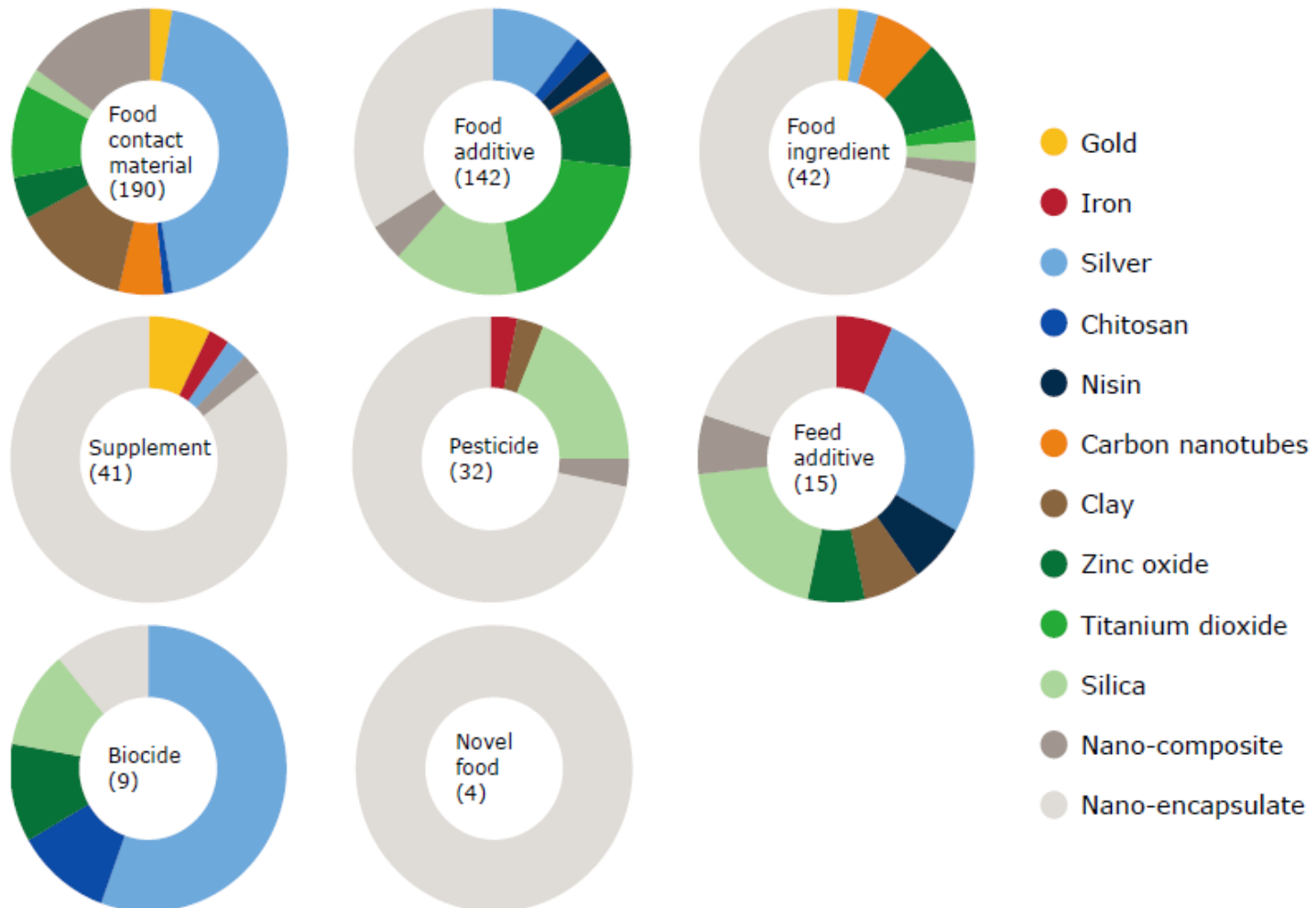


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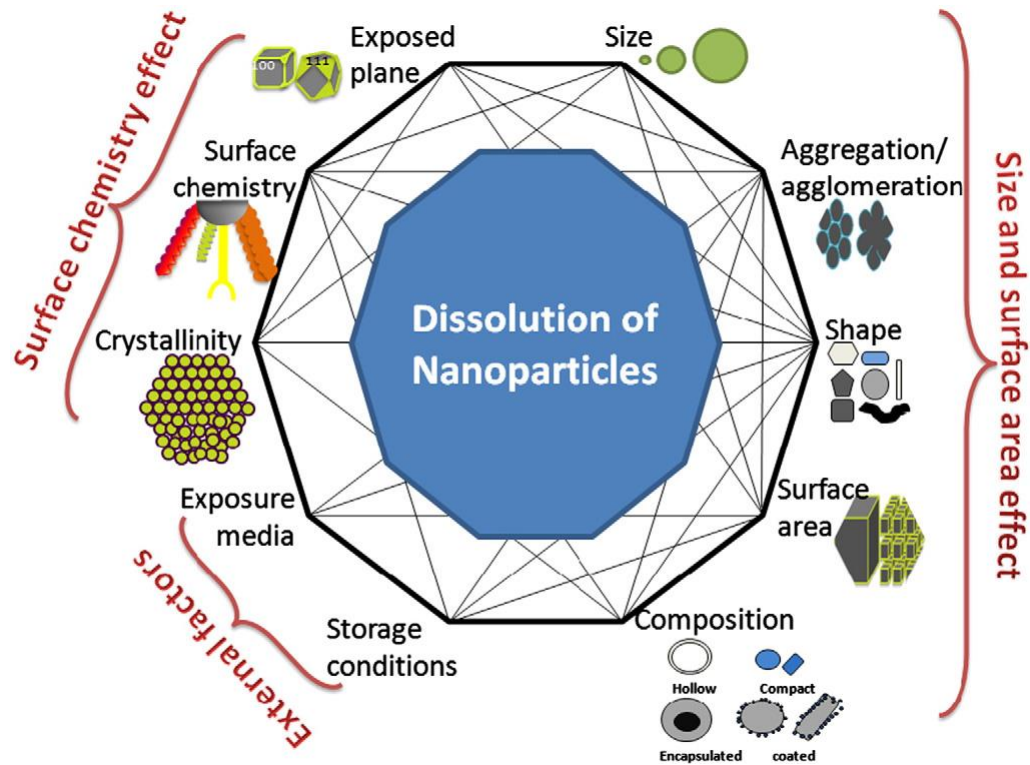
# Nanoparticles in the food chain



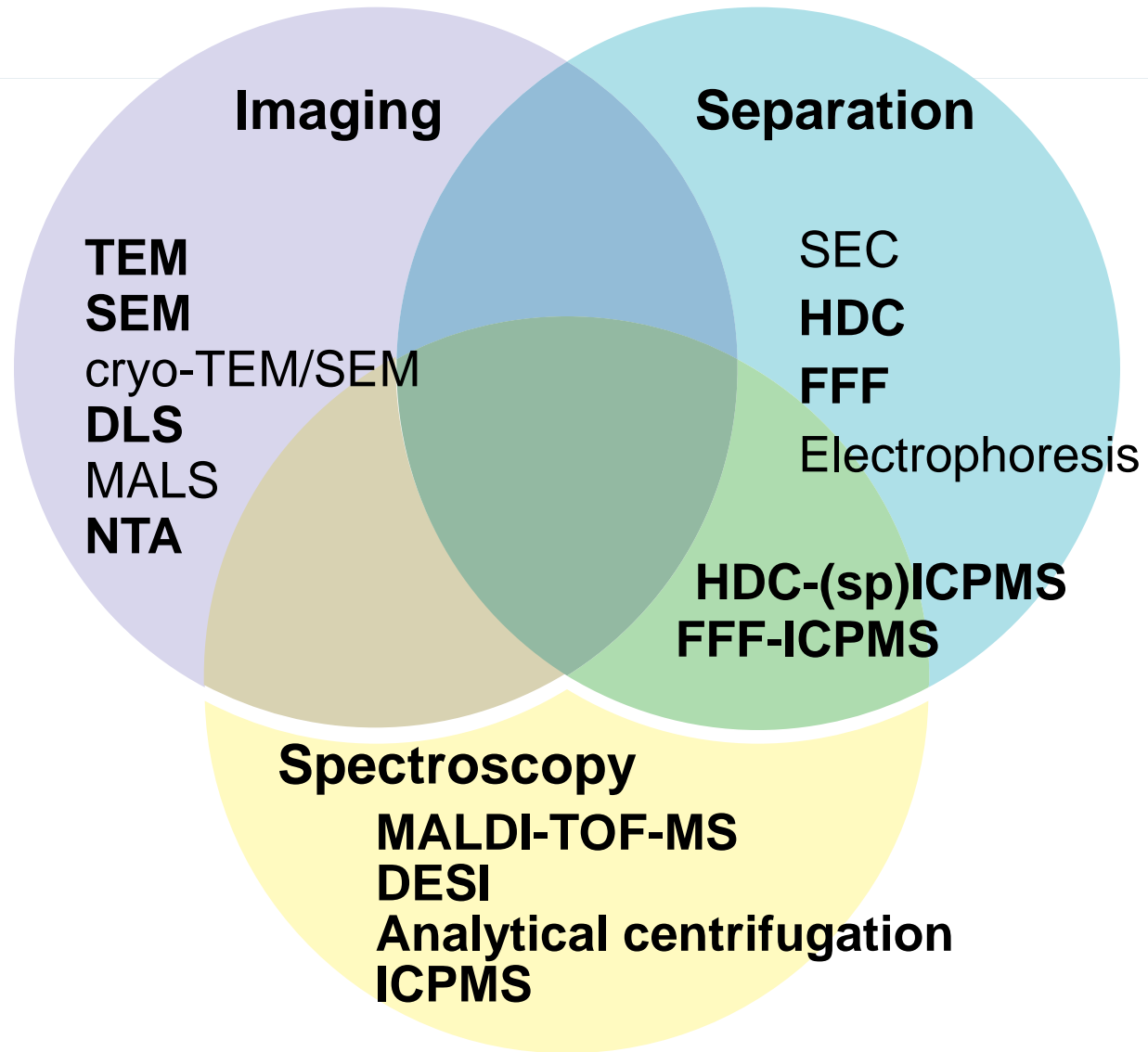
# Nanomaterial applied in agriculture, feed and food



# Nanoparticles characterization

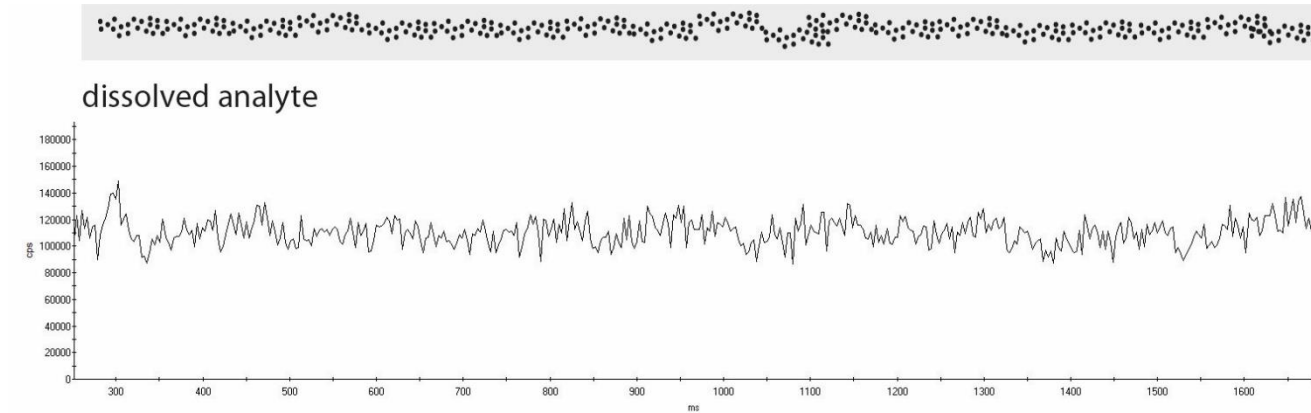


# Nanoparticles characterisation

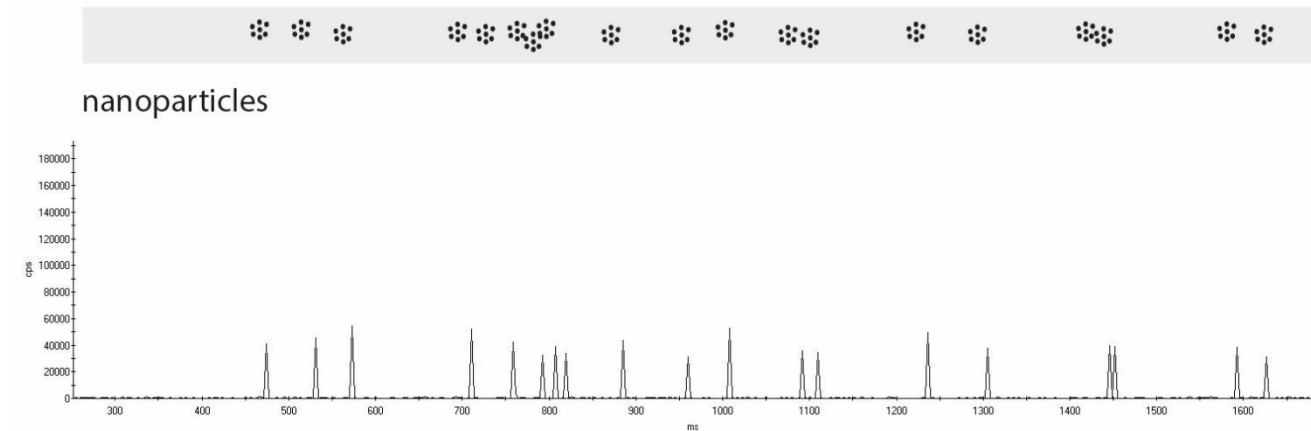


# single particle – ICP-MS

- *single particle inductively coupled plasma mass spectrometry*



ICP-MS



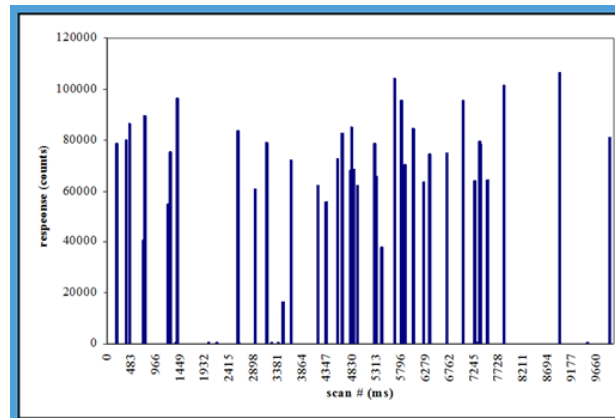
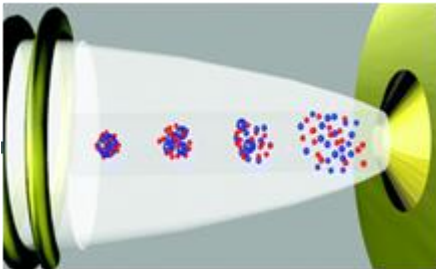
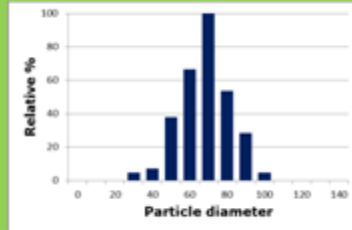
spICP-MS



# spICP-MS

## Benefits of spICP-MS

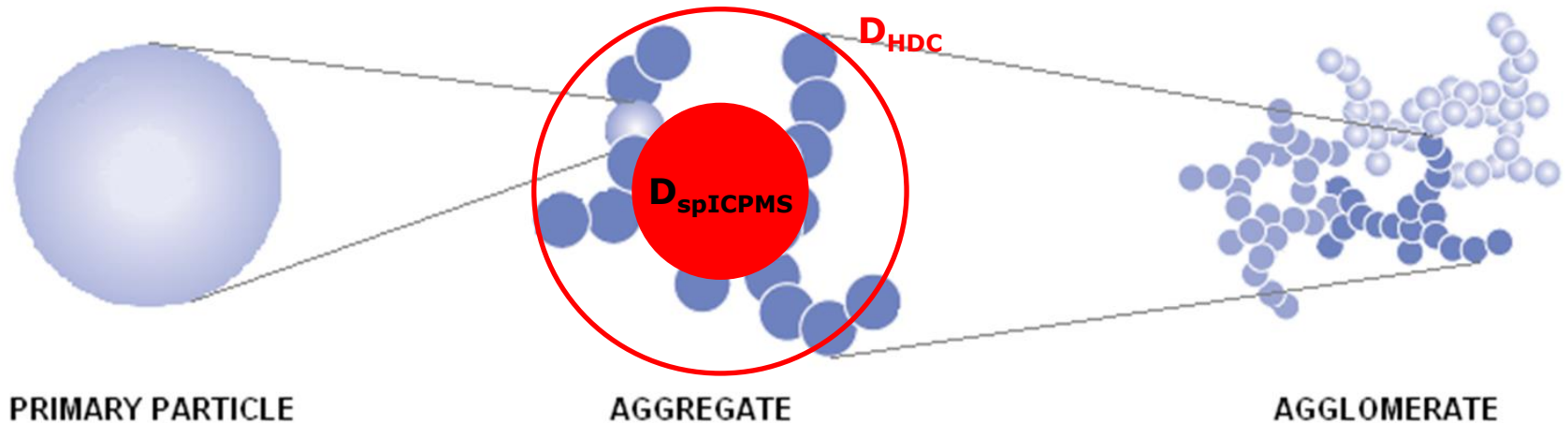
- Measures size distribution and concentration
- Quick analysis
- Very limited sample preparation needed
- Equipment present on many routine labs
- Can be combined with chromatography methods (HDC, FFF)





# HDC or FFF coupled with spICP-MS

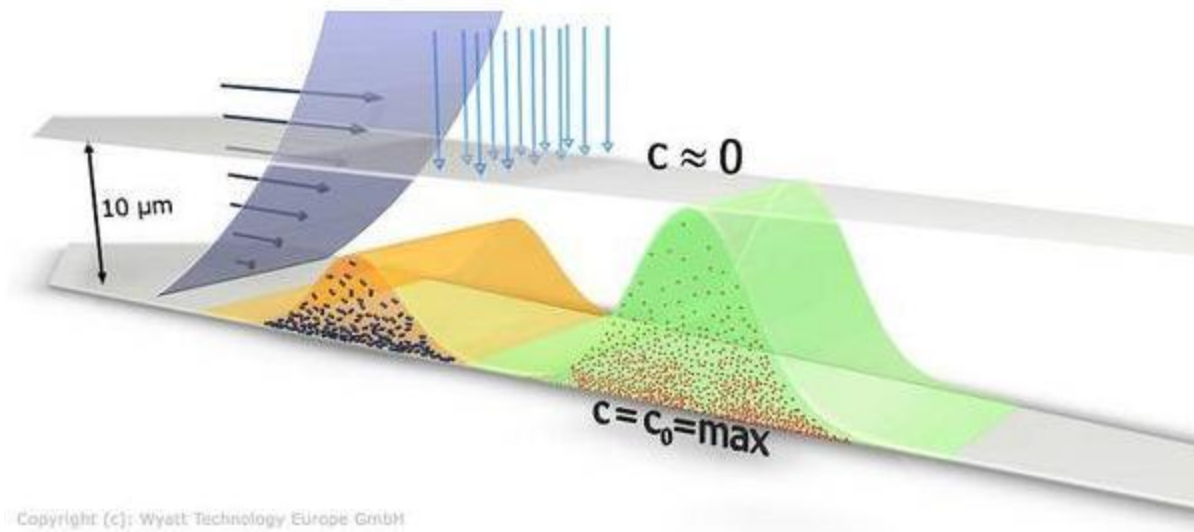
- aggregation, agglomeration and dissolution studies





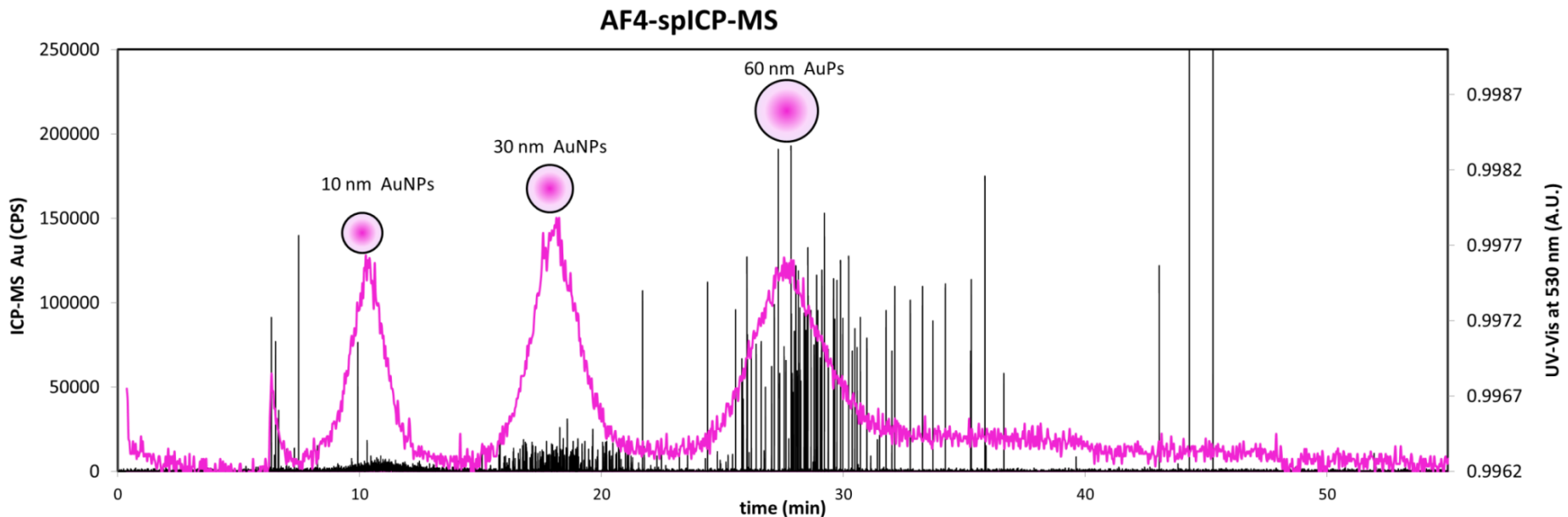
# Flow Field Flow Fractionation

(AF4, FFF, fIFFF)



# AF4 coupled with spICP- MS

- the first hyphenated platform, proof of principle

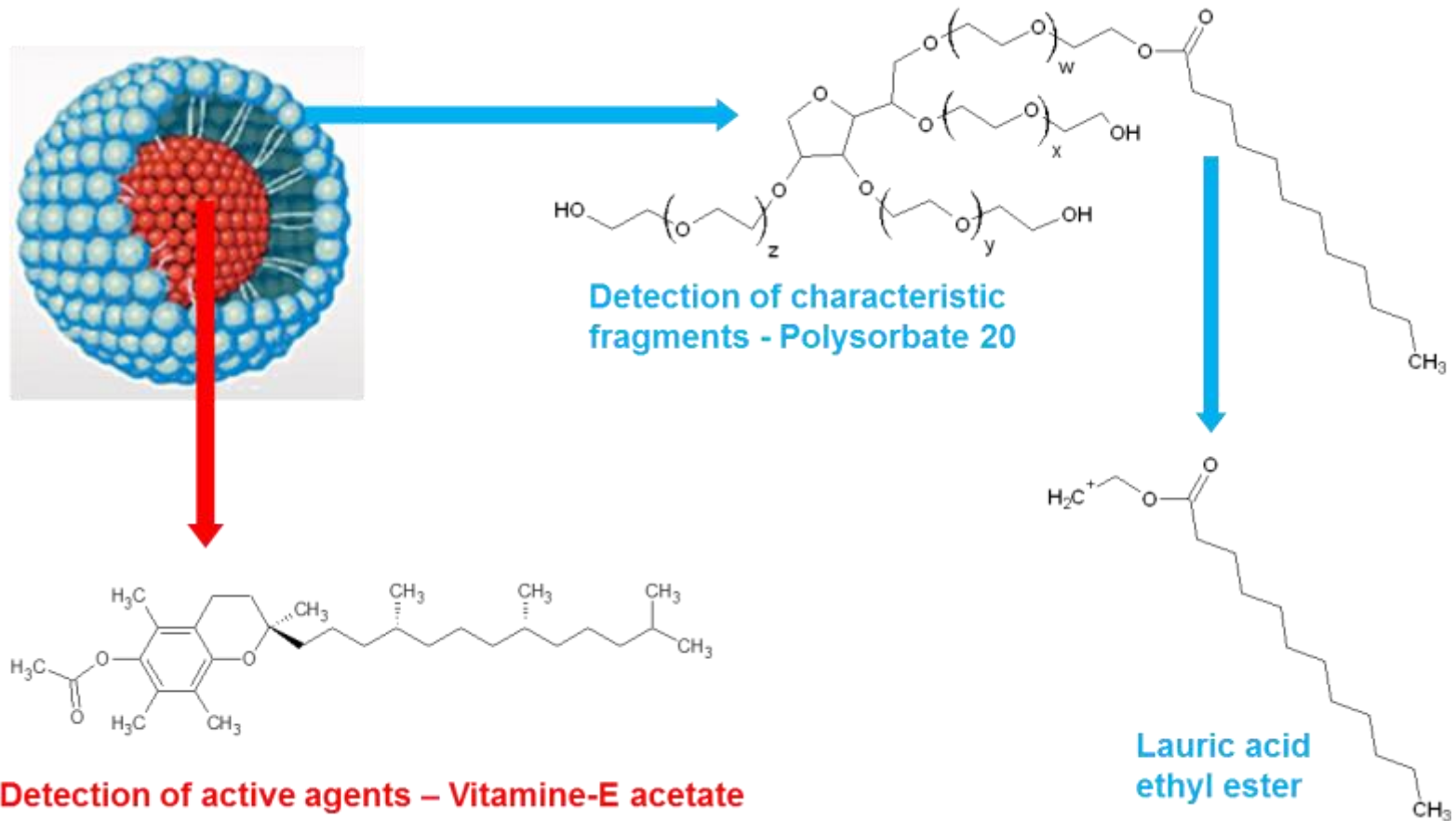


C. Cascio et al.

MSFooDay Conference, Foggia 7-9th October 2015

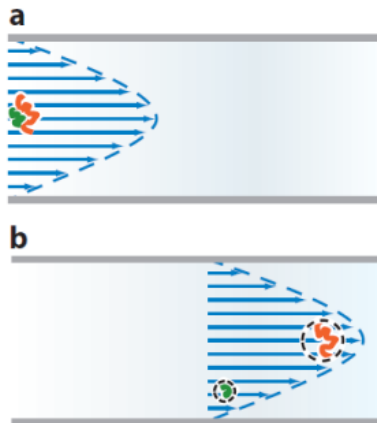
# Organic nanoparticles in food:

## Measure shell or active ingredient

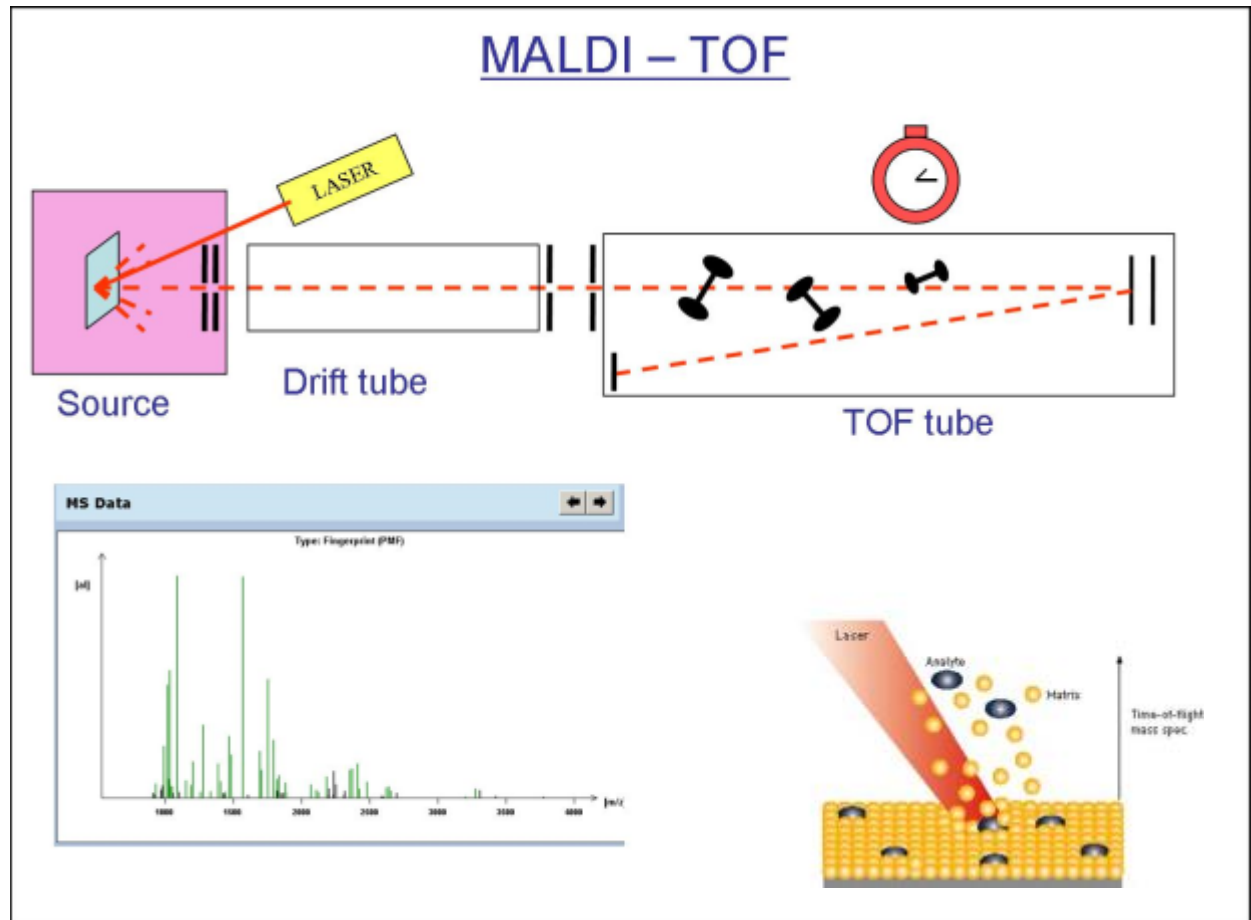


# Collected HDC fractions are analysed with MALDI-TOFMS

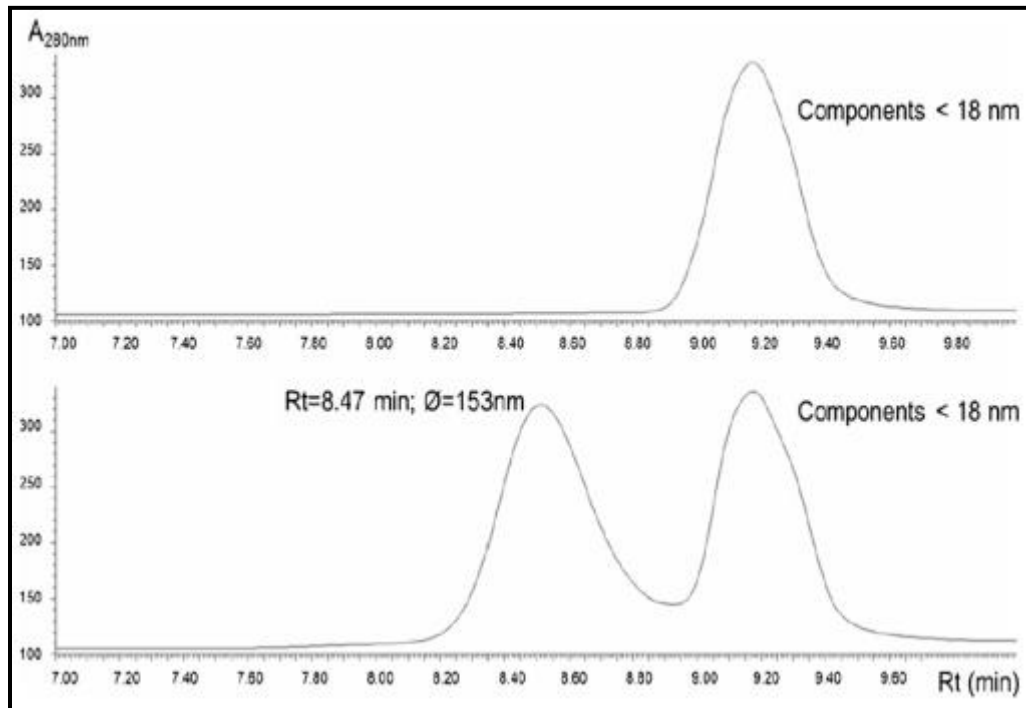
## HDC



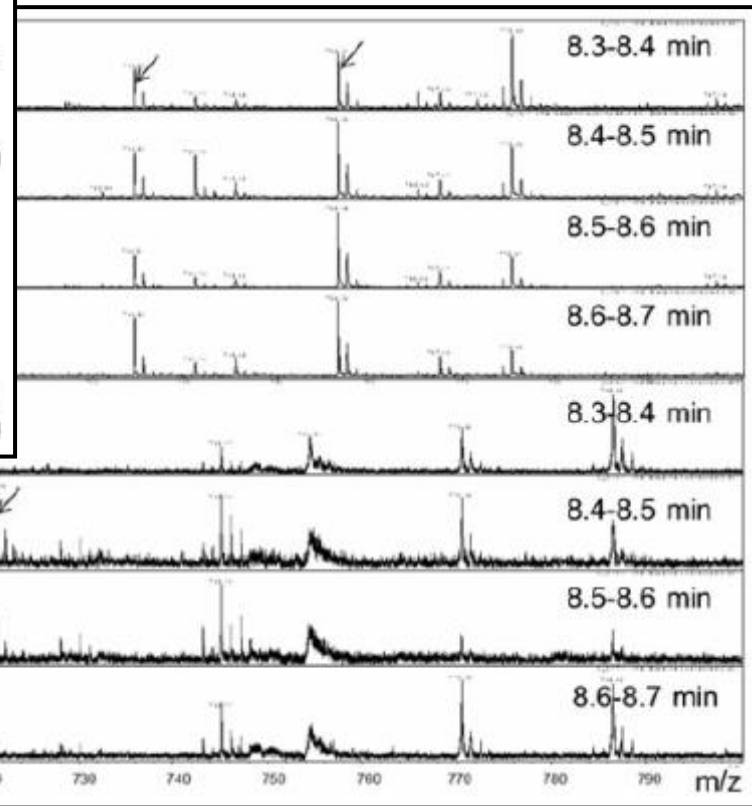
## MALDI – TOF



# Coatsome nanoparticles in orange juice



HDC separation of particle and matrix

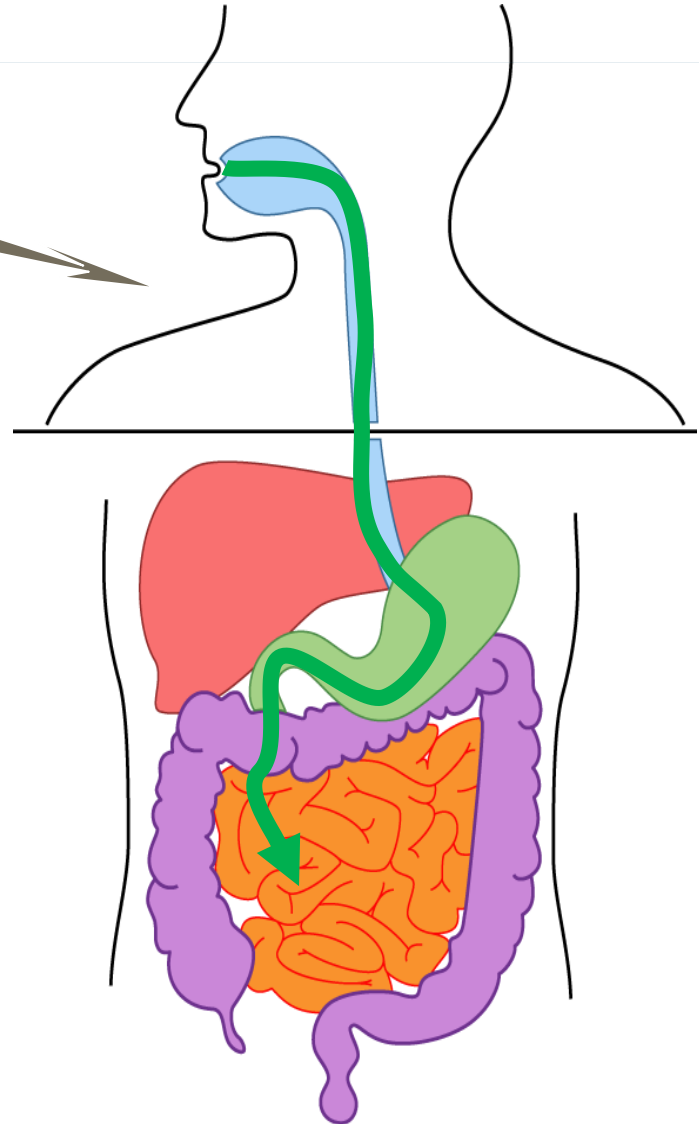
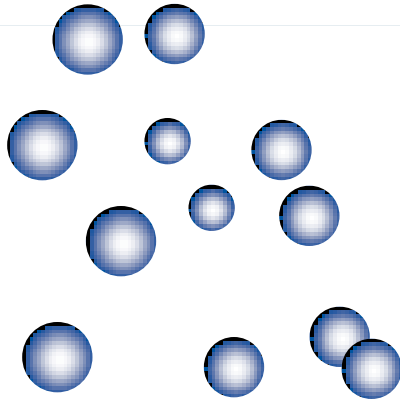


MALDI-TOFMS identification of particle

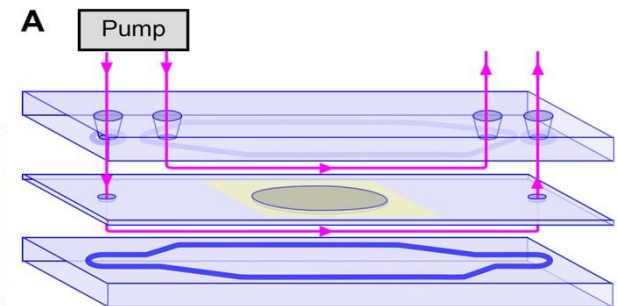
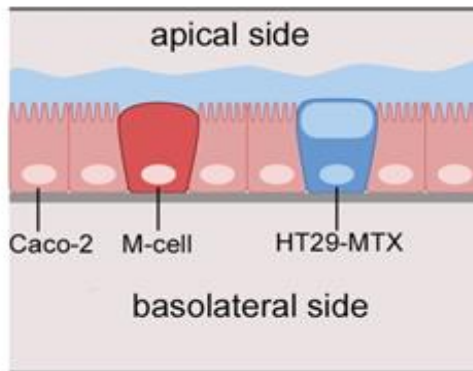
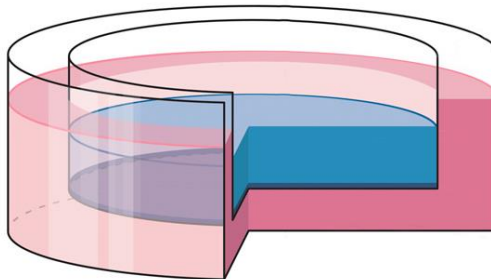
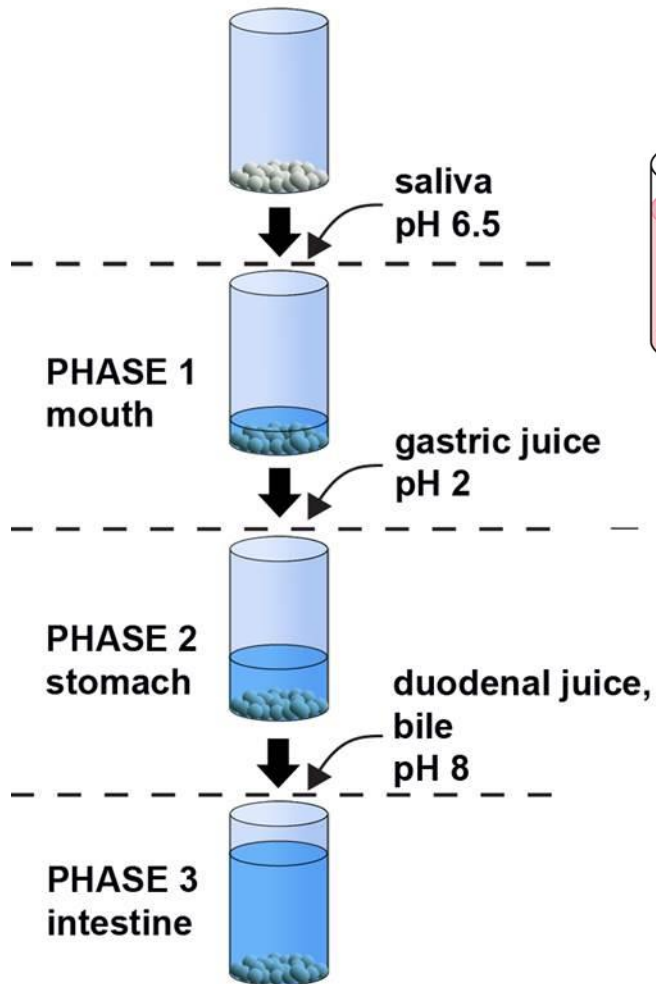


# Oral exposure route

Passage of barriers that affect NPs

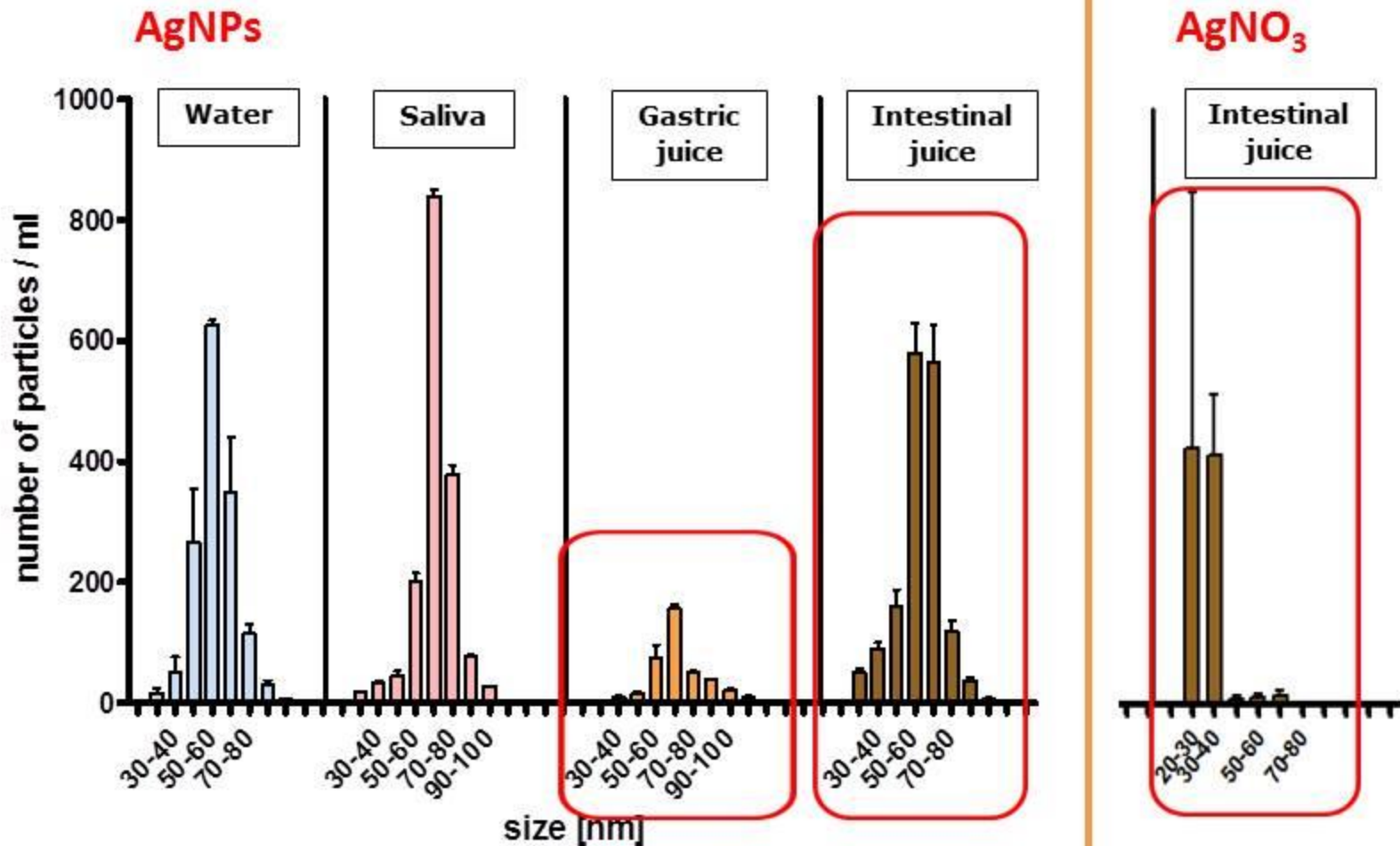


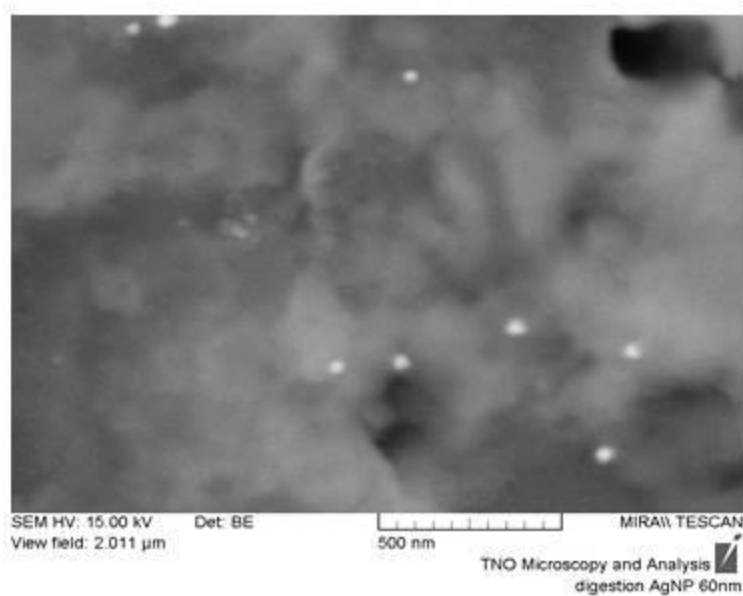
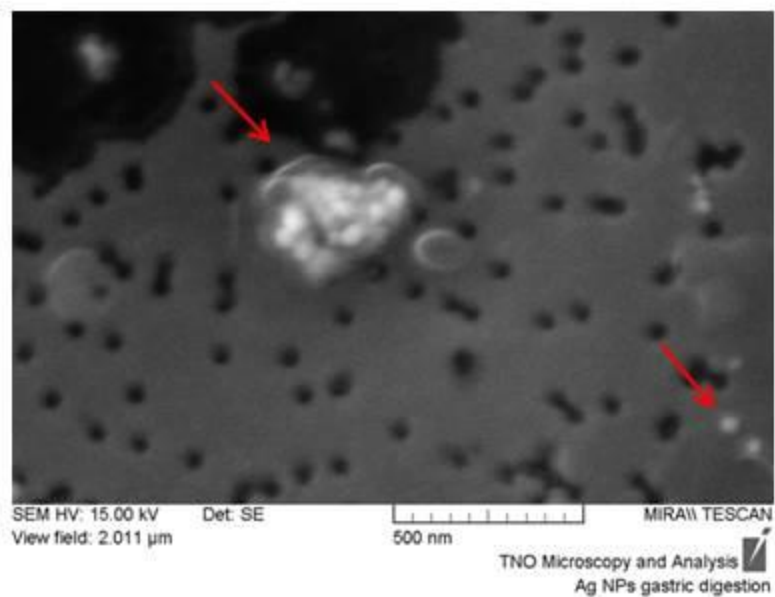
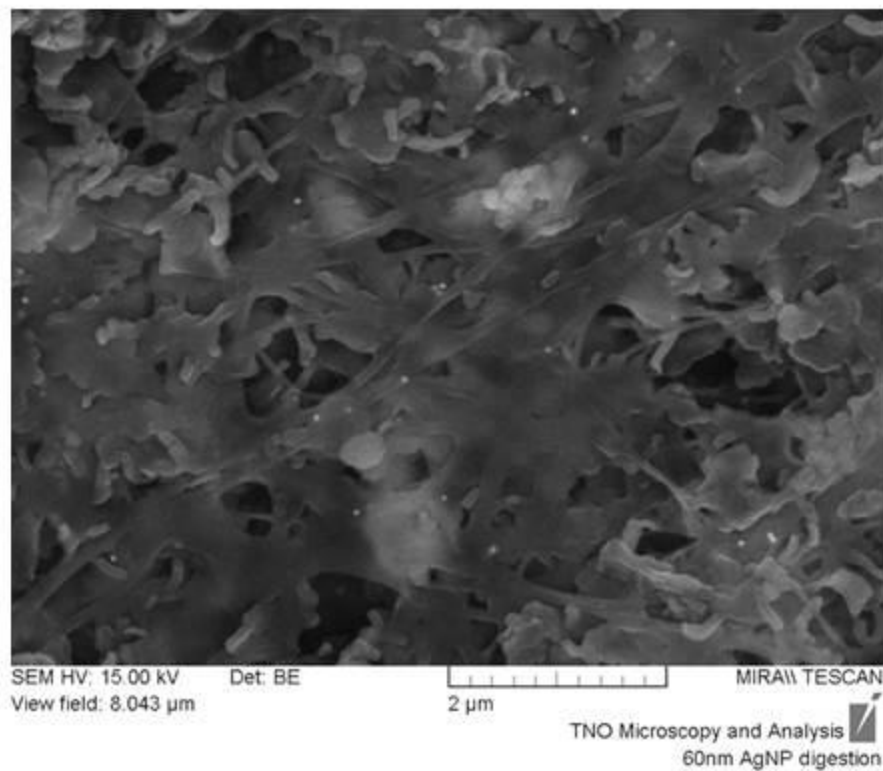
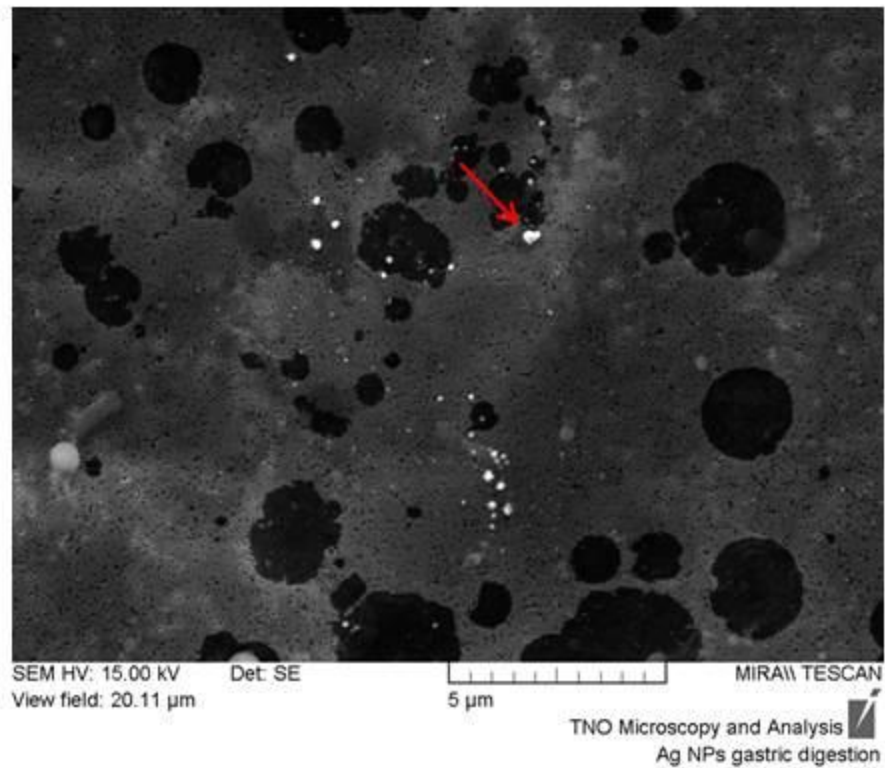
# Model systems



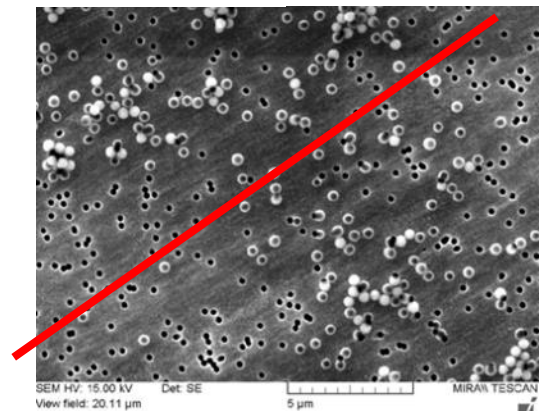
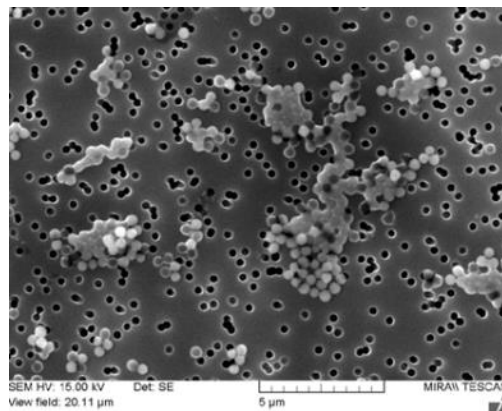
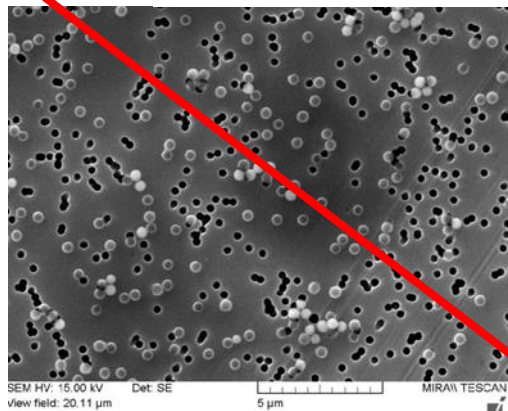
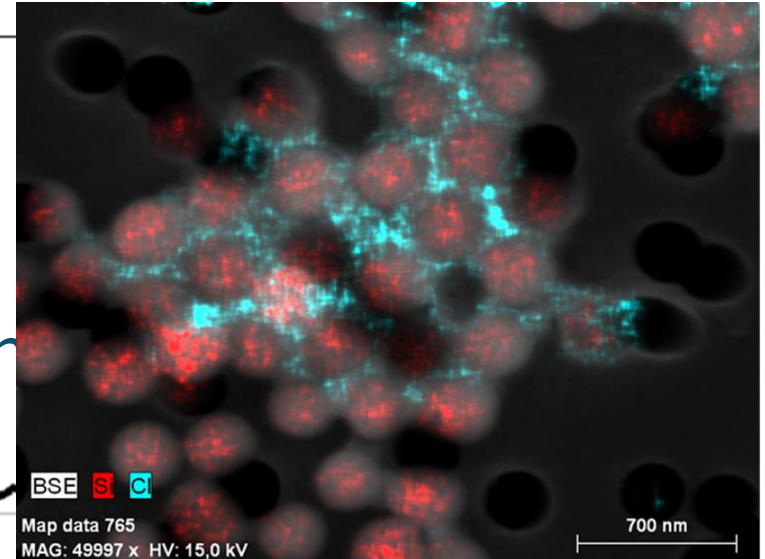
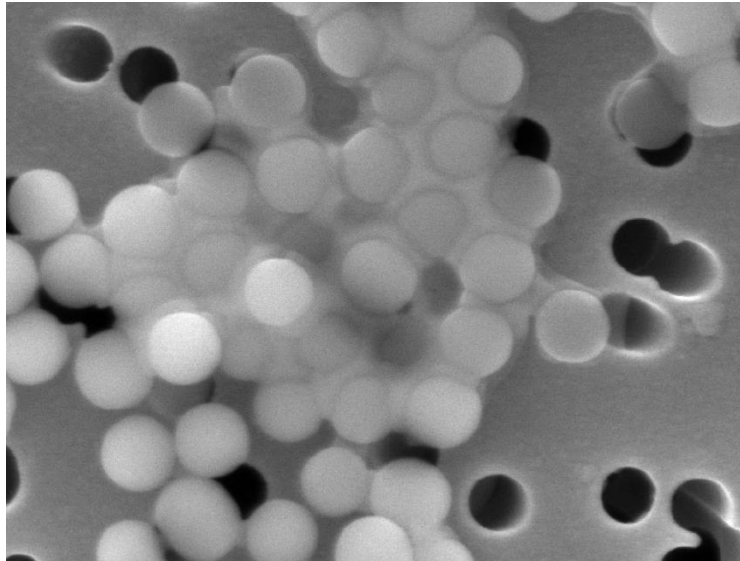


# Digestion with proteins



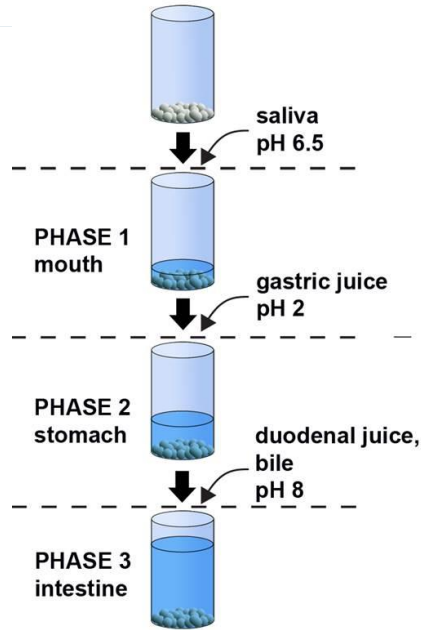


# Silica: E551 and model NPs

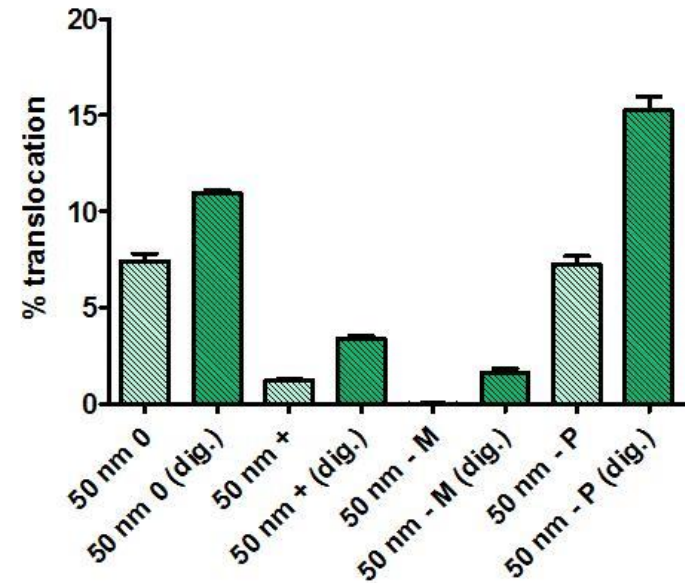




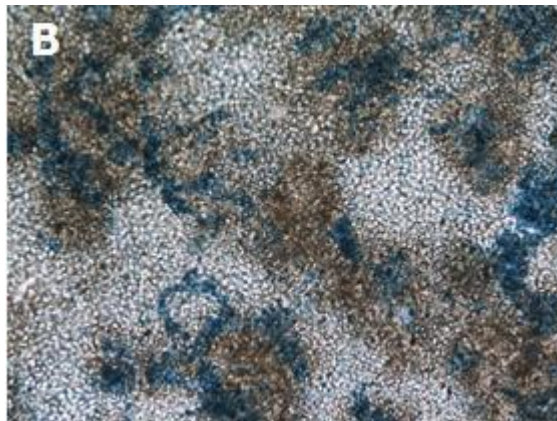
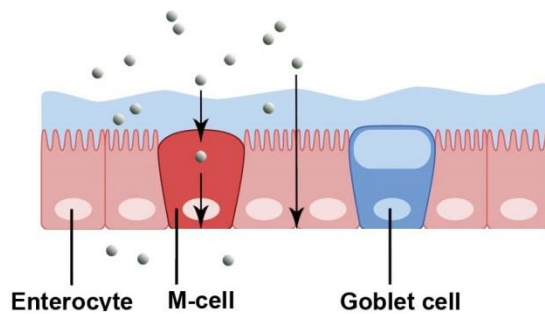
# Translocation



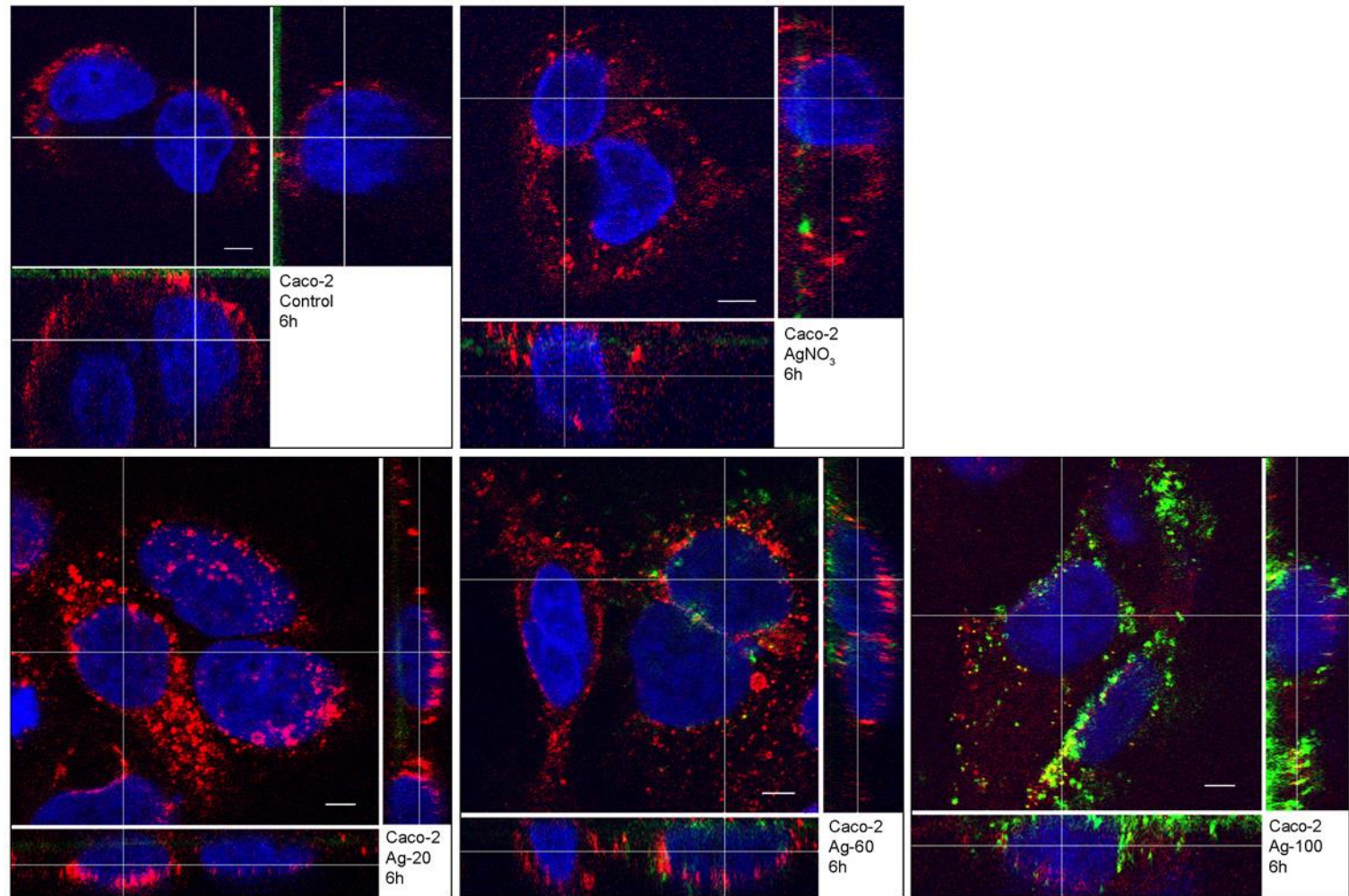
Pristine vs. digested PS-NPs translocation



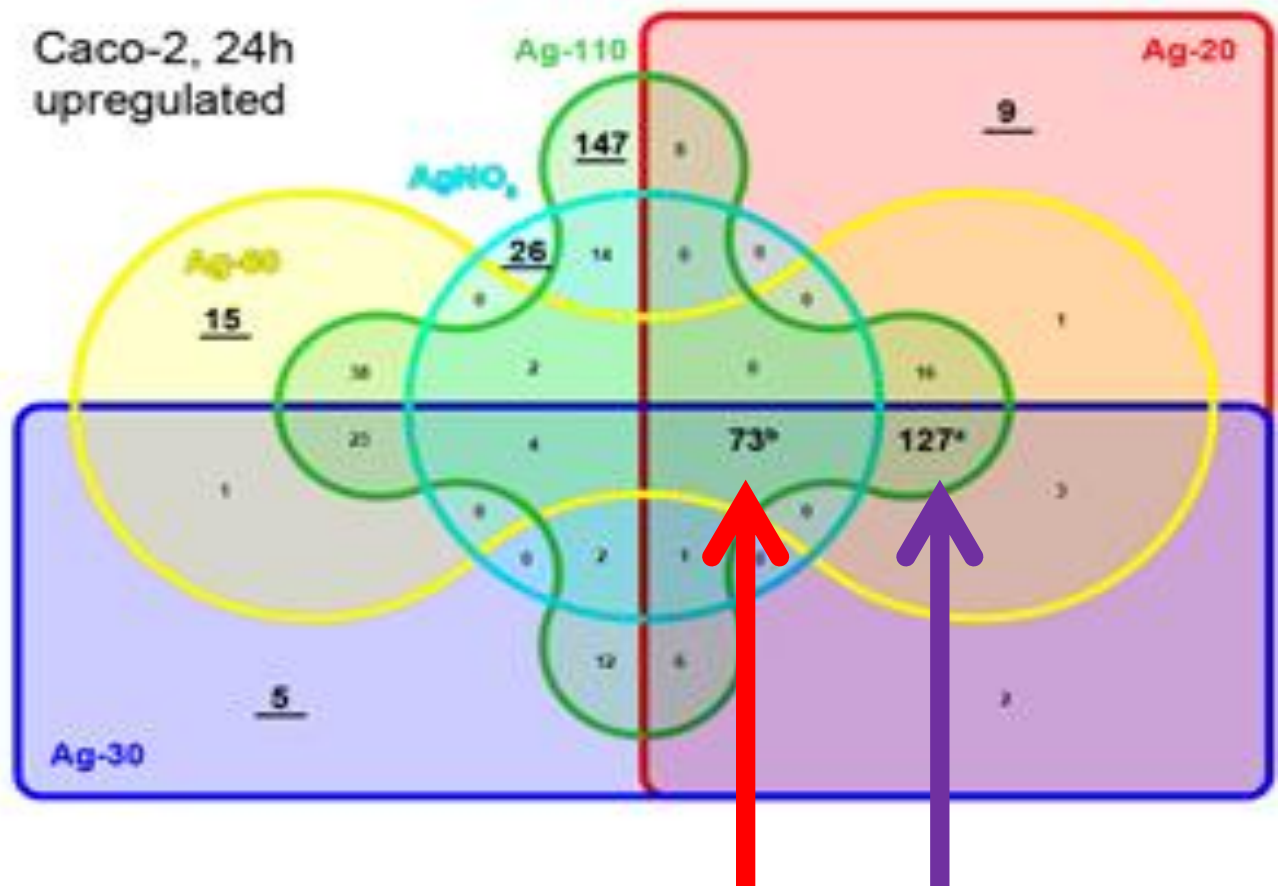
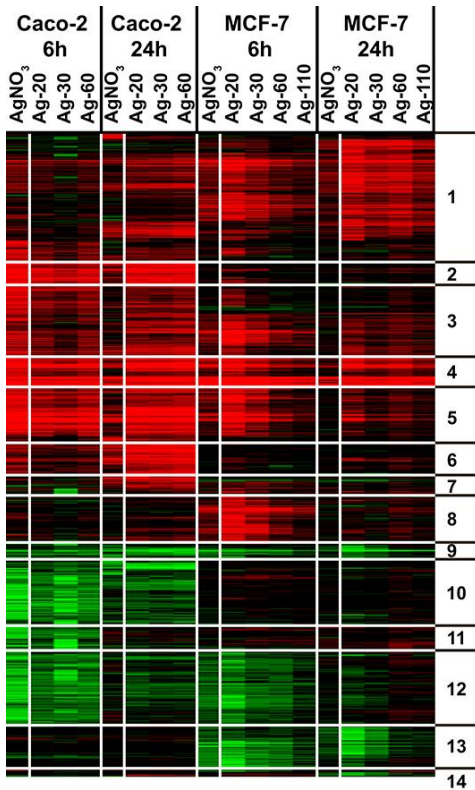
Intestinal barrier



# Uptake of AgNPs: Caco-2



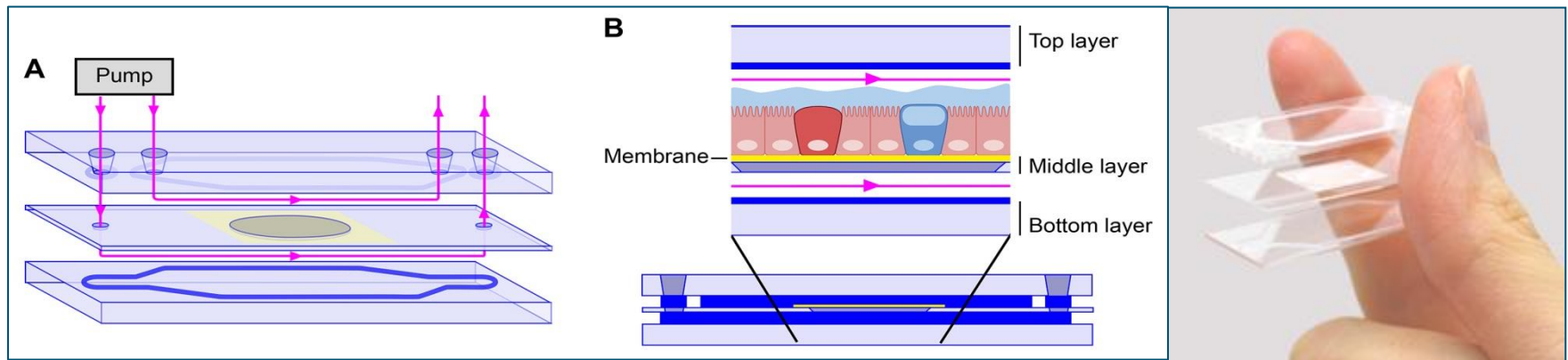
# Toxicogenomics: Ag NPs vs Ag-ions





# To adequately resemble human biology

Wyss institute: organ on chip



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GUTTEST



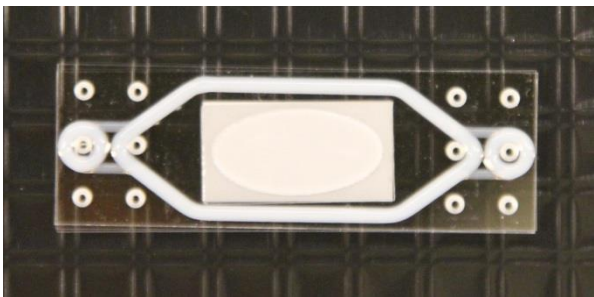
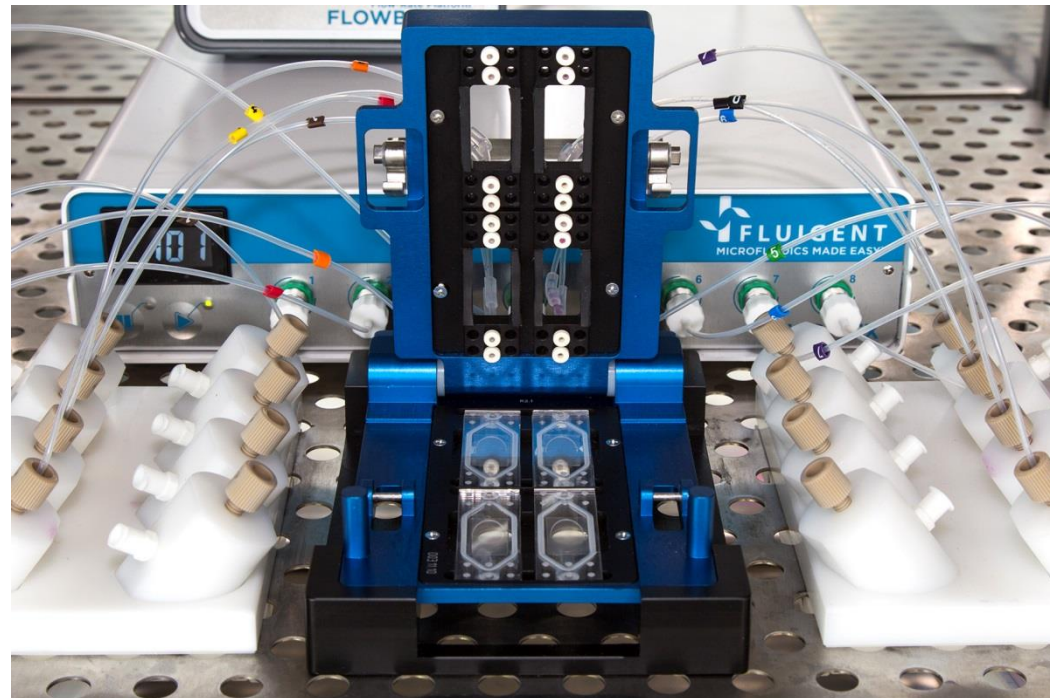
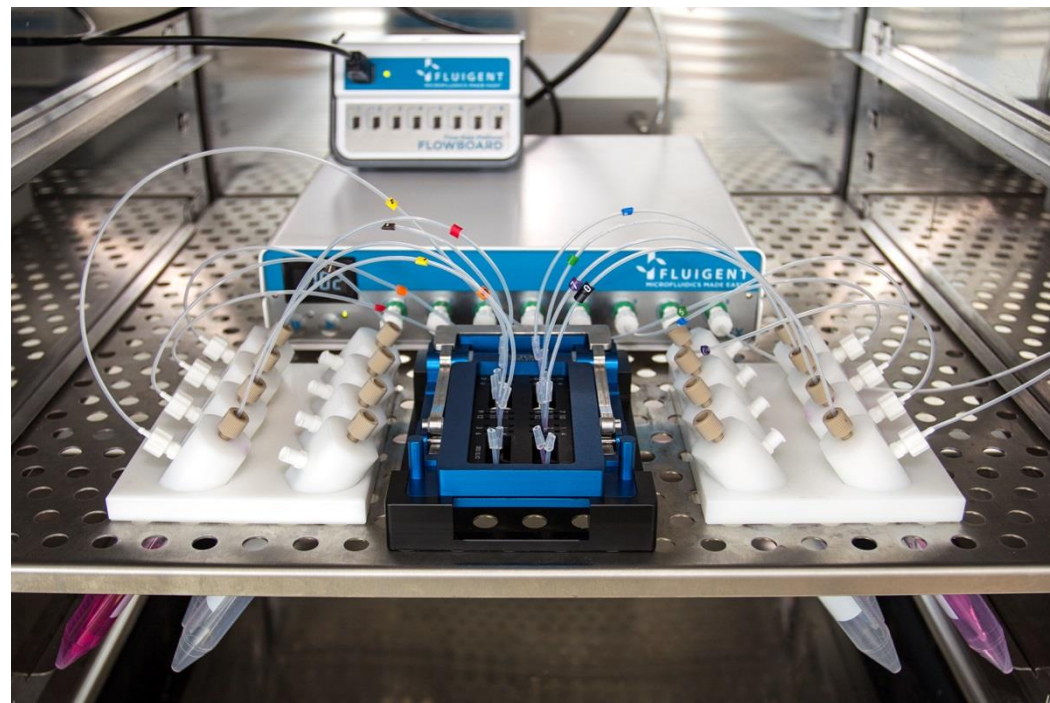
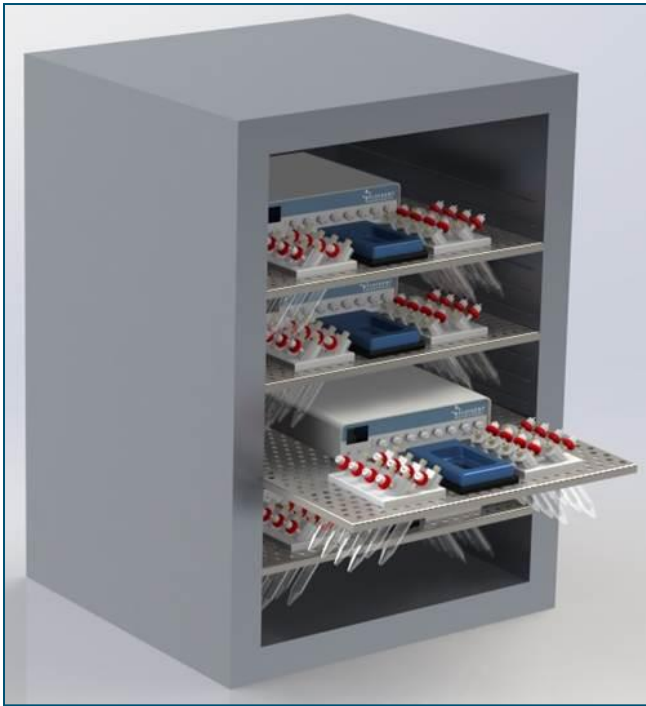
Rijksoverheid

Gut-on-a-chip



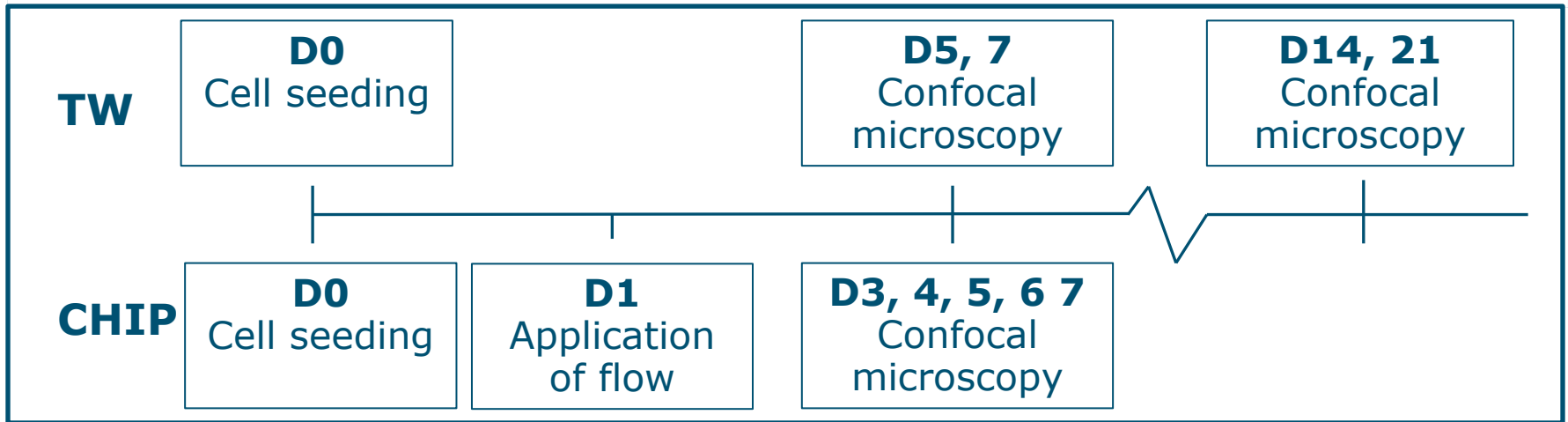
Integrated gut models





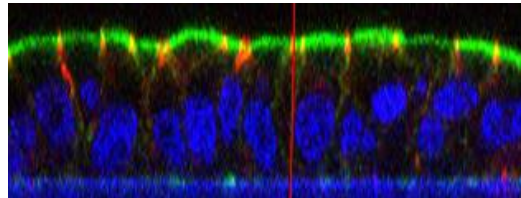
# Cell growth and differentiation

## CHIP *versus* Transwell



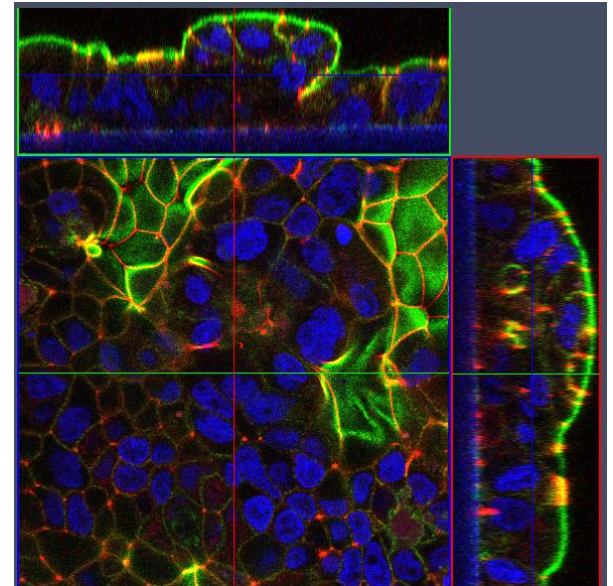
### Staining

- Nucleus (blue)
- Tight junctions (red)
- Cytoskeleton (green)



### Parameters

- Height
- Proliferation (cell numbers/area)
- Differentiation (polarisation)

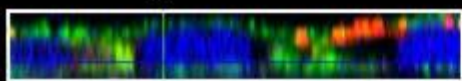




Day 5

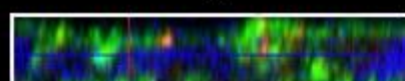
Day 7

Day 14

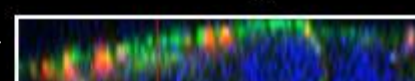


$\sim 6 \mu\text{m}$

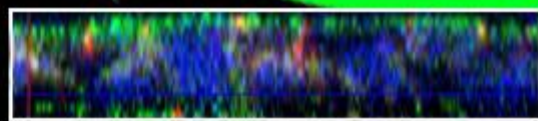
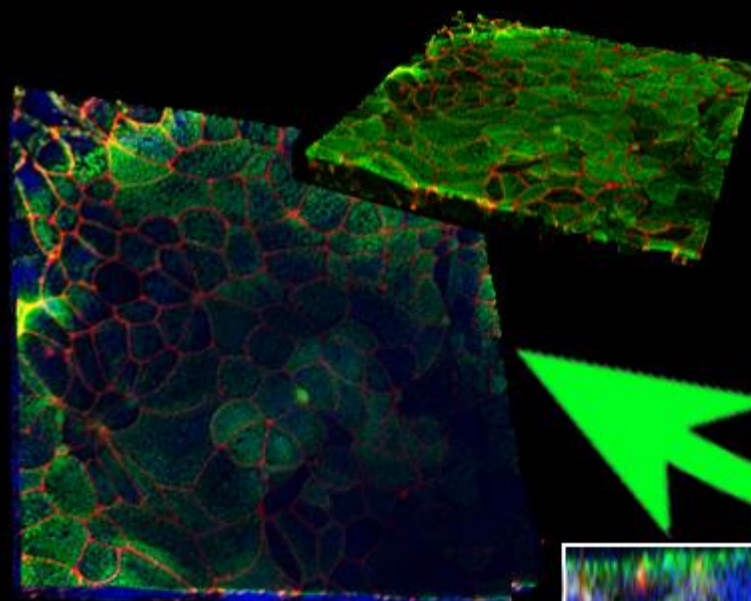
$\sim 11 \mu\text{m}$



$\sim 12 \mu\text{m}$



Caco-2 in Transwell



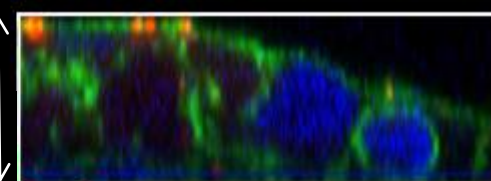
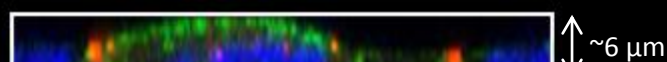
$\sim 12 \mu\text{m}$

Day 21

Day 3

Day 4

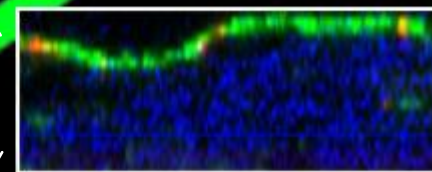
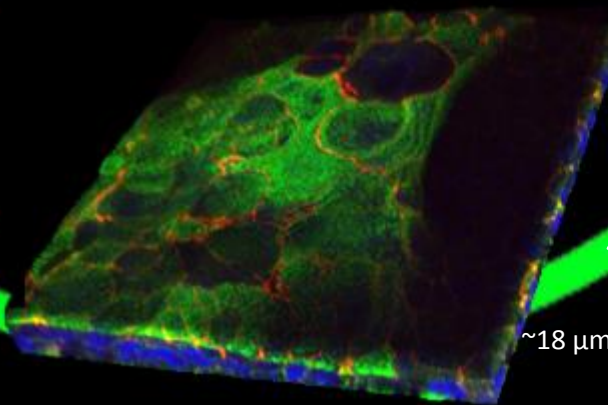
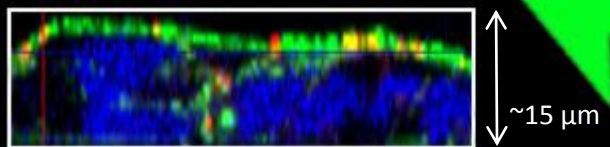
Day 5



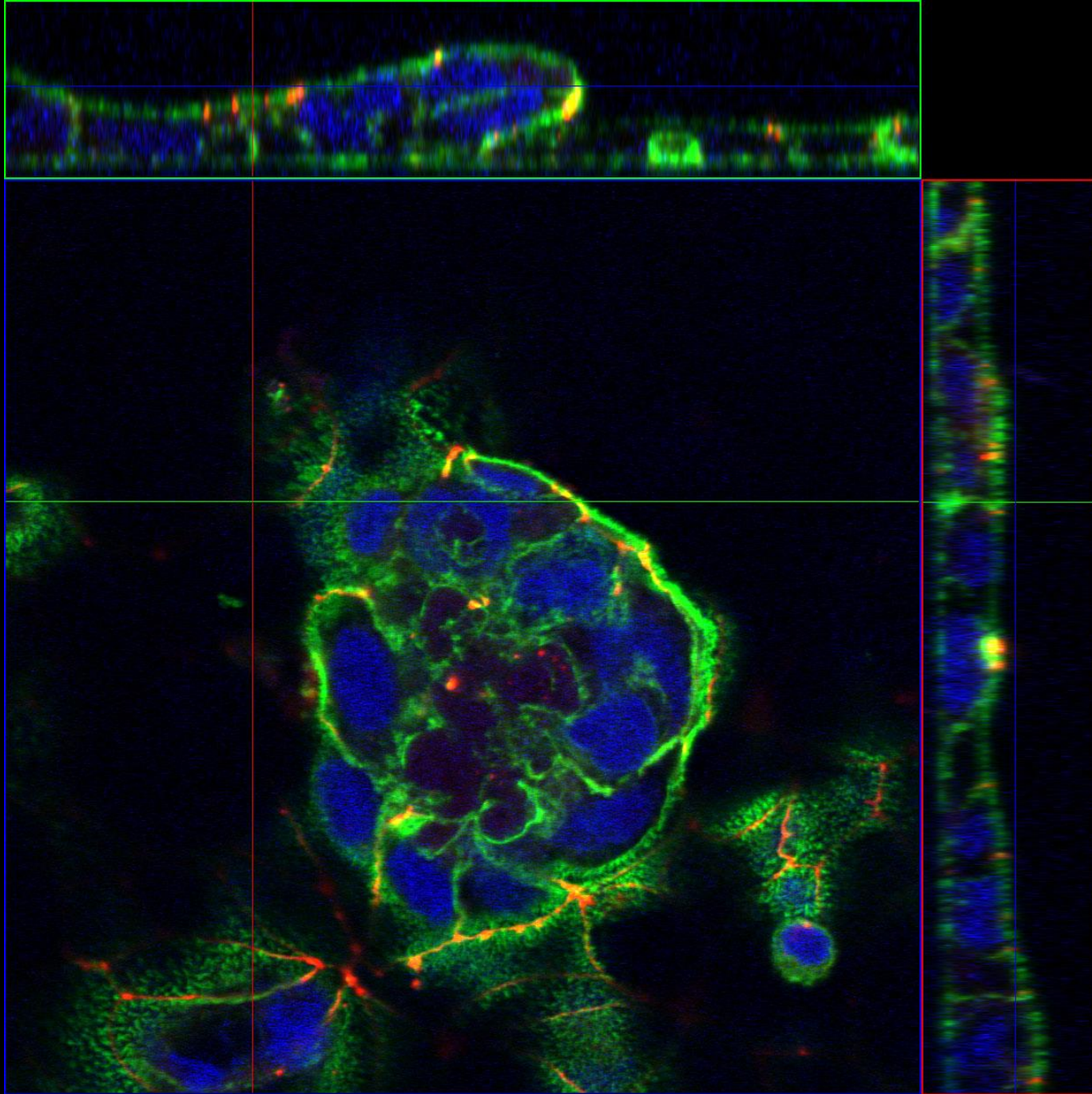
Caco-2 in CHIP

Day 7

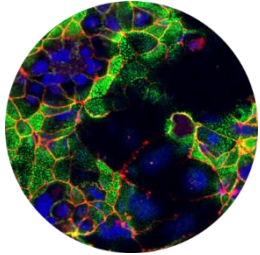
Day 6





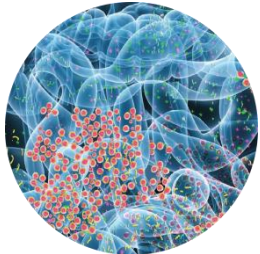


# Gut-on-a-chip



Personalized  
(stem) cell biology

- iPSCs, organoids
- human biopts



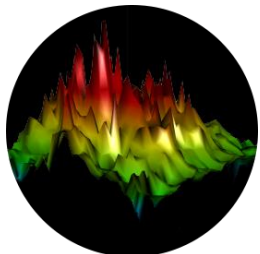
Microbiome

- host-microbe interactions
- drug/food conversion



On chip,  
on line testing

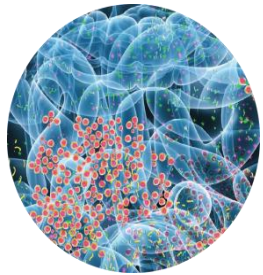
Chip sensor technology



Analytical detection

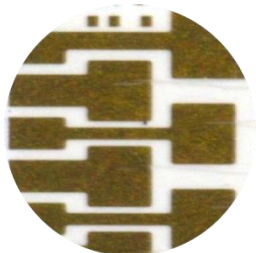
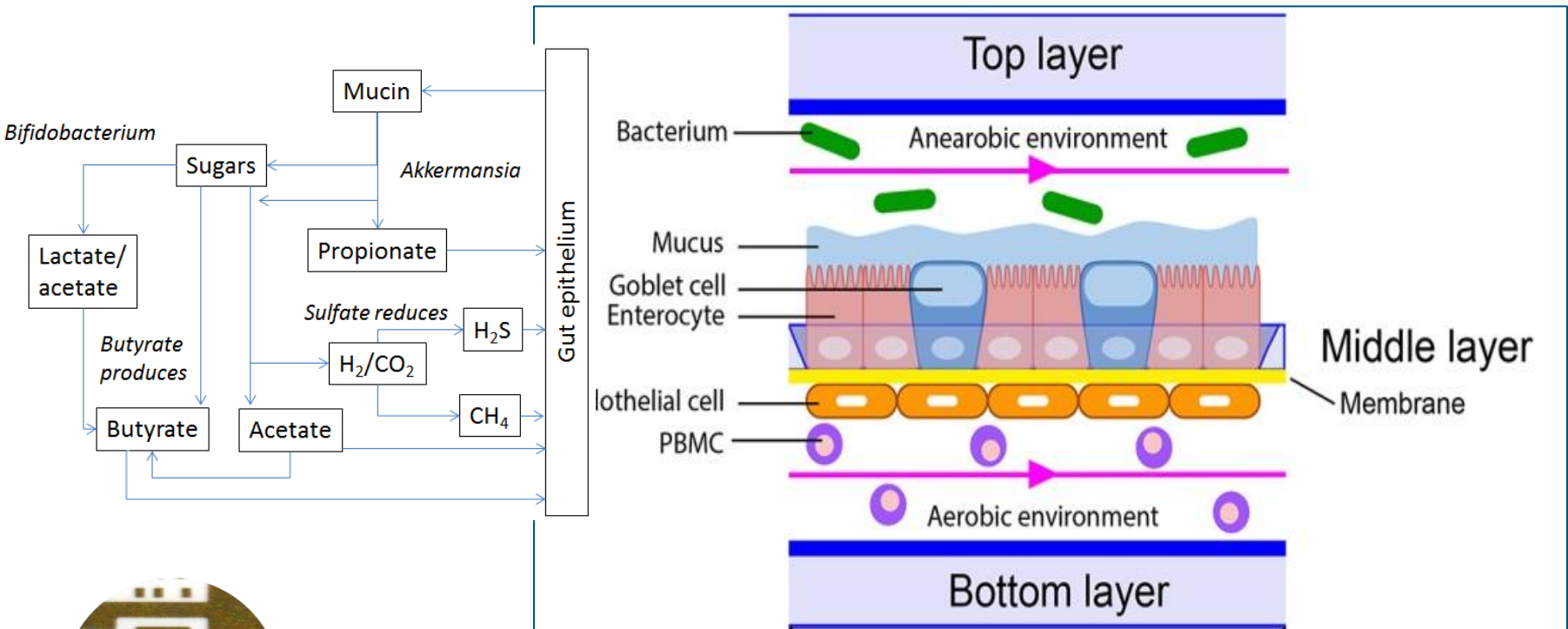
On-line sample preparation and  
detection





Microbiome

- host-microbe interactions
- drug/food conversion



Chip sensor technology



# Acknowledgements

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**Kornphimol Kulthong**



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**Prof. dr. ir. Ivonne Rietjens**

## University of Groningen – Pharmaceutical Analysis



**Prof. dr. Sabeth Verpoorte**



**Pim de Haan**

# Thank you for your attention



Sustainable Nanotechnologies Project



The European  
Chemical Industry Council



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