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Scientific Project

# SCALE

(SCiences AnaLytiques et nanostructurEs)



CS IPHC, March 31, 2021

# SCALE (SCiences AnaLytiques et nanostructurEs)

Integration of a new team in the Department of Analytical Sciences  
(DSA, Head: Éric Marchioni)



## Multidisciplinary team

Analytical Sciences / Nanochemistry / Microbiology

## Single theme team

**Development of innovative analytical and diagnostic strategies**

Separative supports and original detection modes



# The SCALE Project

Highlights

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## 1. Scientific Innovation: Nanotechnologies + Separative Sciences + Diagnostics

There is no similar thematic in UL, Unistra and Grand Est  
(no national or international equivalent either)

## 2. Complementarity of skills with the scientific objective

Analytical Chemistry, Physico-chemistry, Nanochemistry, Microbiology

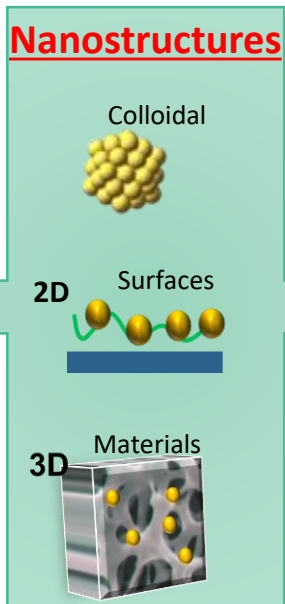


# SCALE

Innovation / Context / Findings

## For Separation

- **Not widely used but :**
- ⇒ Very high surface / volume ratio
- ⇒ Platforms for surface functionalisation
- ⇒ Efficiency
- ⇒ Interesting for selective extraction



## For Detection

- **Widely used for their spectroscopic properties (gold, silver in particular)**
- ⇒ Specificity
- ⇒ Platforms for surface functionalisation
- ⇒ High Sensitivity
- ⇒ SERS
- ⇒ Innovations in coupling with separative methods



# SCALE

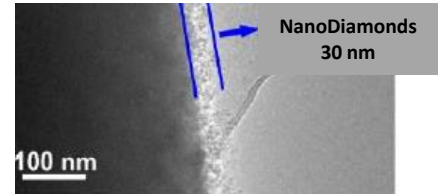
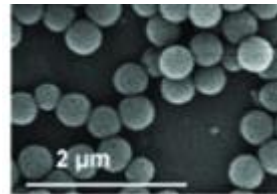
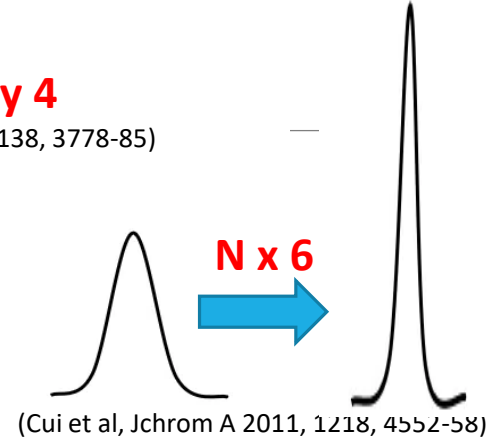
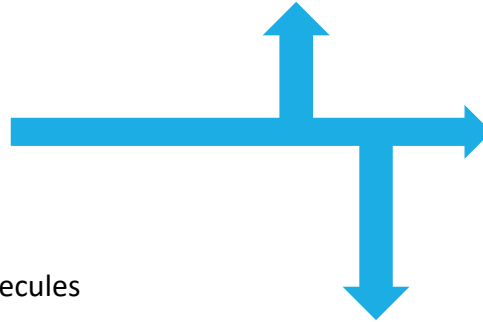
Innovation / Context / Findings

## For Separation

- ⇒ All partition modes (Normal ou reversed Phase, HILIC...)
  - ⇒ Dual retention mode
  - ⇒ Chiral separation
  - ⇒ Affinity chromatography
  - ⇒ All support types (capillary, column, plate, gel...)
- + robust (temperature, pressure) for small or large molecules (proteins) + Sample treatment (SPME, SPE, complex matrices)

**Retention time divided by 4**

(with equal Rs, Speltini et al, Analyst 2013, 138, 3778-85)



**Specific Surface x 50**

(SI-RSH-AgNP, Sandron et al, Curr. Chromatogr. 2015, 2, 122-35)

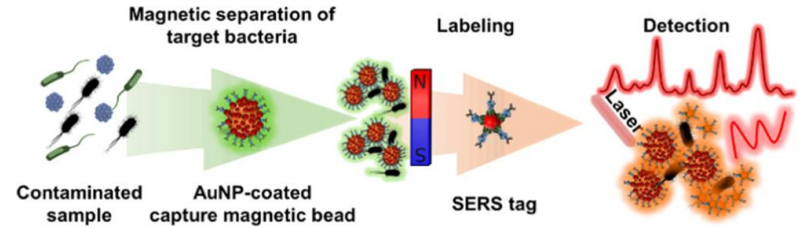
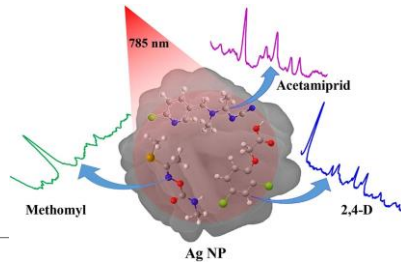
HILIC: Hydrophilic Liquid Interaction Chromatography

SPME: Solid Phase Micro Extraction; SPE: Solid Phase Extraction; N: plates number)



# SCALE

Innovation / Context / Findings

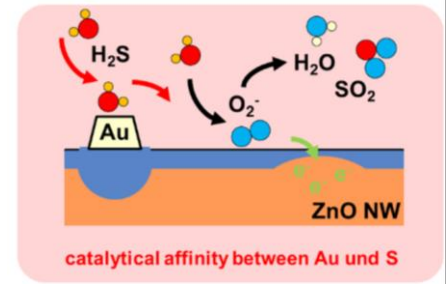
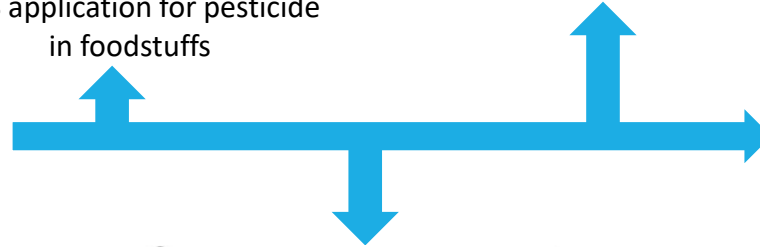


## For Detection

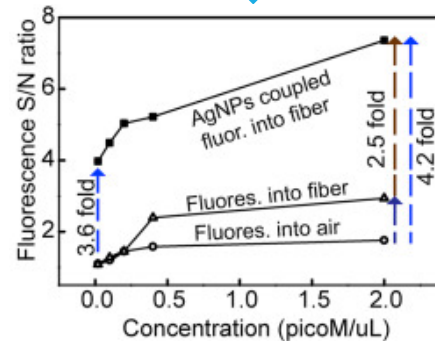
- ⇒ Remarkable properties
- ⇒ Very high specificity
- ⇒ Toward analytical innovations

SERS application for pesticide in foodstuffs

AuNP Magnetic Beads and SERS-Based Detection of E. coli



H<sub>2</sub>S sensing with AuNP ZnO nanowires



Coupling of silver nanoparticle-conjugated fluorescent dyes into optical fiber modes for enhanced signal-to-noise ratio

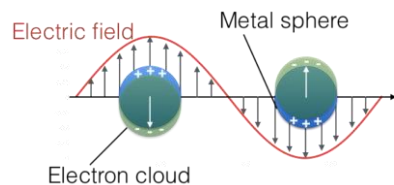
SERS: Surface Enhanced Raman Spectroscopy



# SCALE

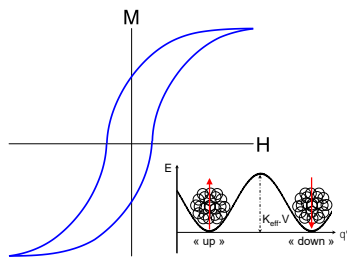
New analytical and diagnostic strategies

## ➤ Nanoparticle synthesis: Physical properties & applications



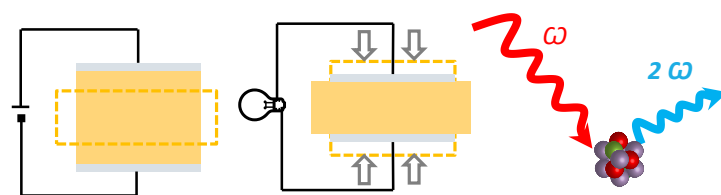
*Localized surface plasmon resonance (LSPR)*

- Sensing (SERS; wavelength shifting),
- Photothermal imaging and therapy,
- Bio-sensor,
- Detection of bacteria, viruses...



*Superparamagnetism*

- Magnetic Resonance Imaging,
- Substrate concentration,
- Molecular detection...



*Piezoelectricity / Second Harmonic Generation*

- Acoustic-wave transducers,
- SHG imaging probe,,
- Optical sensor for chemical/biological analyses...

**... Towards monodisperse multifunctional nano-object synthesis**

SERS: Surface Enhanced Raman Spectroscopy; SHG: Second Harmonic Generation



# SCALE

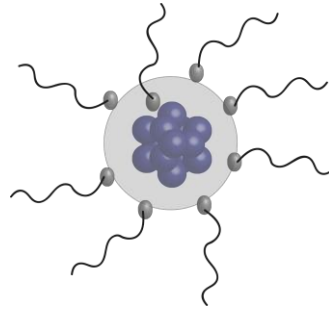
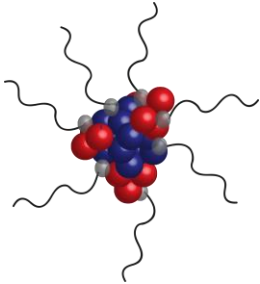
New analytical and diagnostic strategies

## Process development:

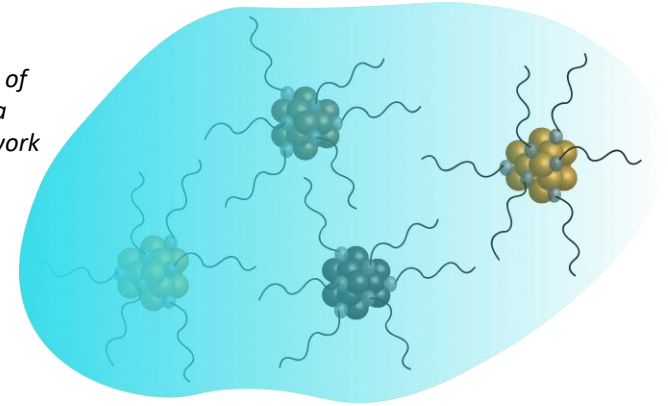
- Size and size distribution
- Morphology
- Dispersion/solvent
- Surface state/stabilization
- Functionalization

## ➤ Nanoparticle synthesis: *multifunctional NPs*

*Heterogeneous/homogeneous nucleation/growth*



*Different kind of NPs within a polymeric network*



**Size distribution, inhomogeneity, ...**

**... Towards core@multishells systems**

Combining different materials exhibiting specific properties.  
(for example, magnetic@plasmonic@ferroelectric NPs)

*& Deep eutectic solvents  
Sustainable chemistry*

**Original and high-quality nano-object synthesis (pharmaceutical grade!)**

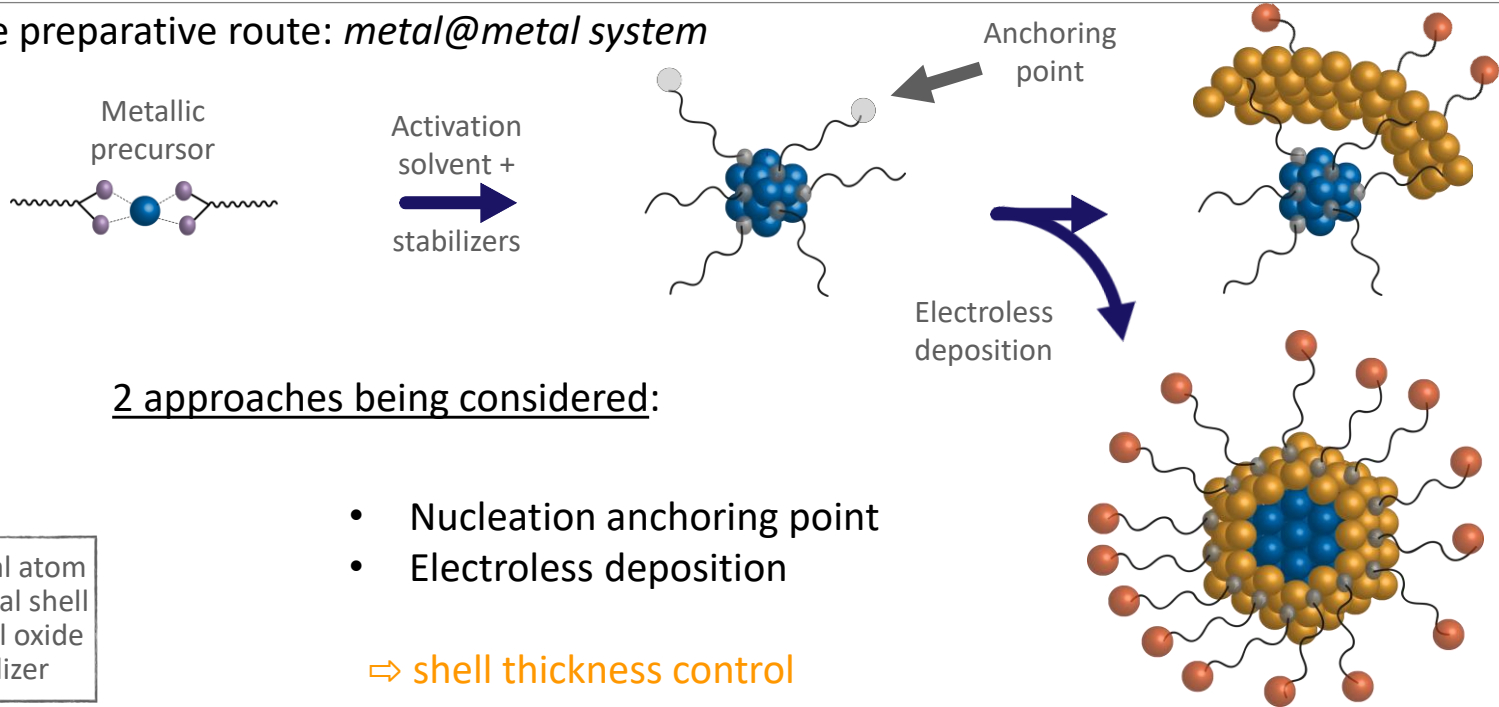




# SCALE

New analytical and diagnostic strategies

## Nanoparticle preparative route: *metal@metal* system

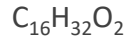
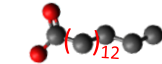
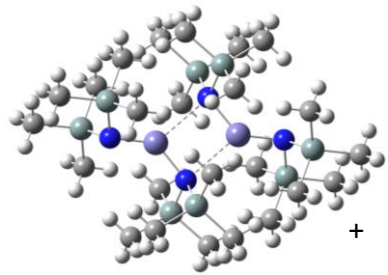




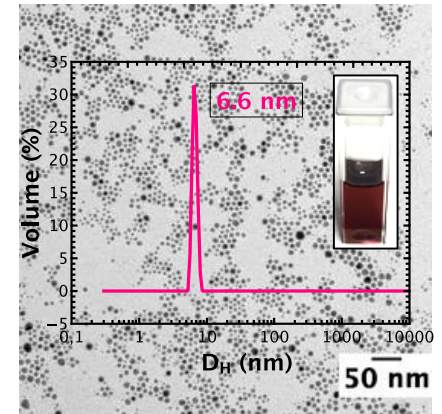
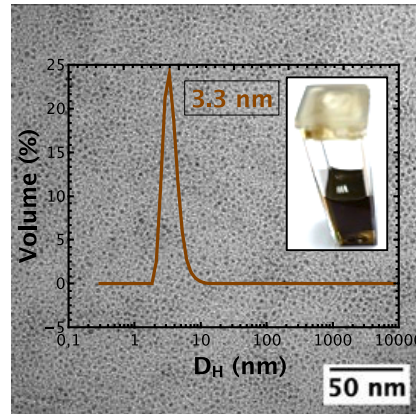
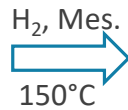
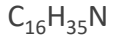
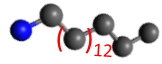
# SCALE

New analytical and diagnostic strategies

## Nanoparticle preparative route: *preliminary results Fe@Au system*



+



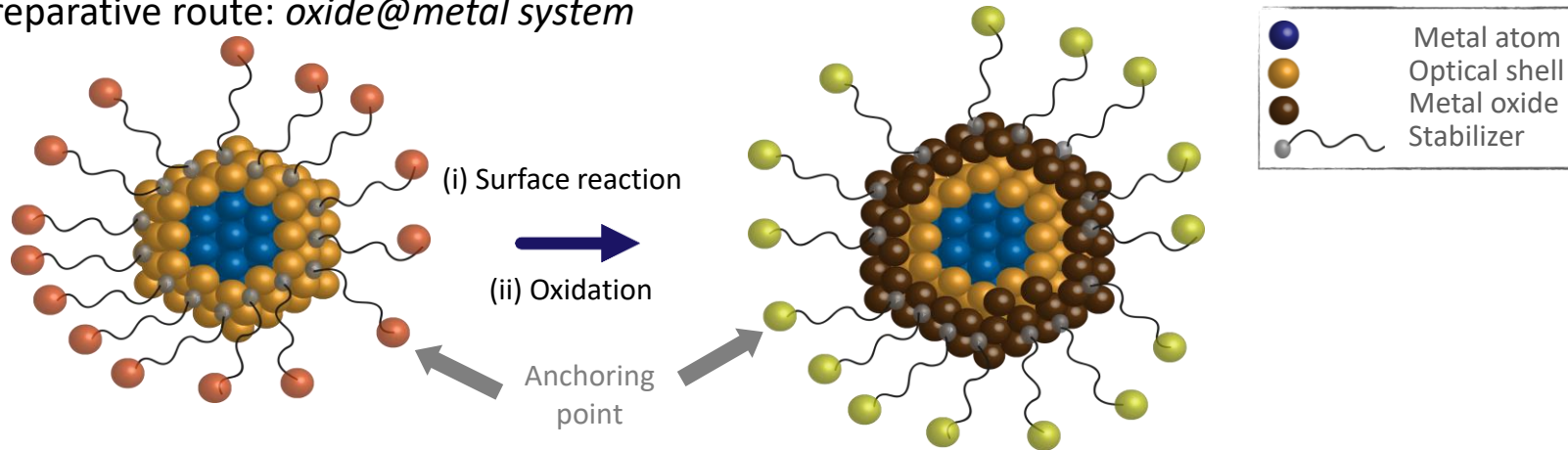
*Properties studies in progress*



# SCALE

New analytical and diagnostic strategies

Nanoparticle preparative route: *oxide@metal* system



2 approaches (two steps) being considered:

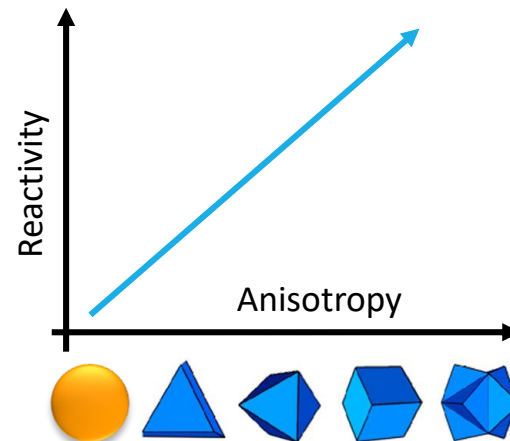
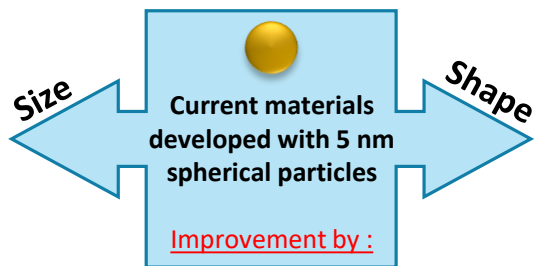
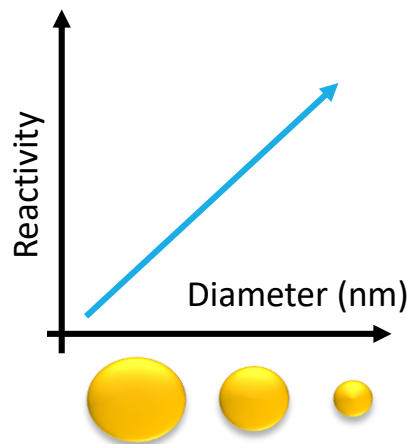
- (i) electroless deposition, (ii) oxydation
- (i) coordination polymer growth, (ii) decomposition\*

⇒ shell thickness control

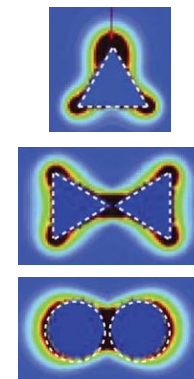


# SCALE

Nanostructured materials: shape and size effect



Hot spots !

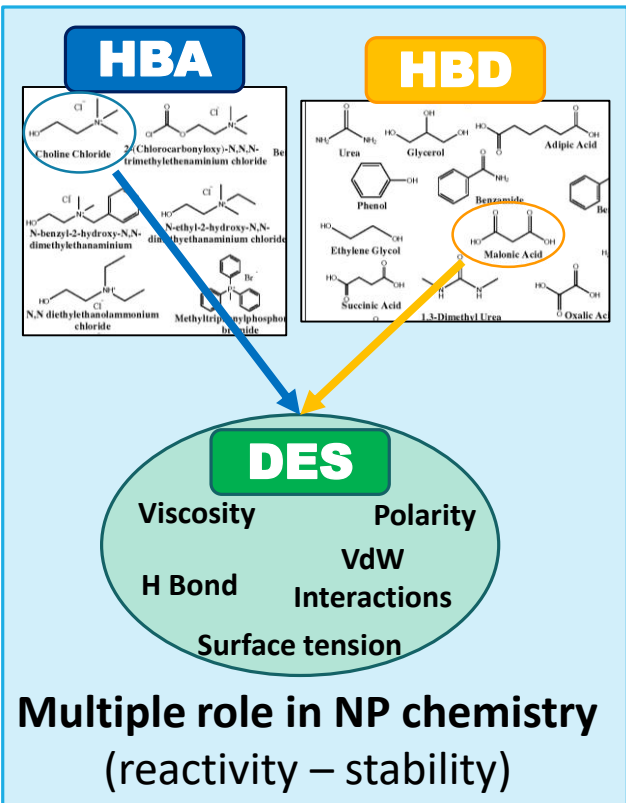


Typical  
electromagnetic  
illustration

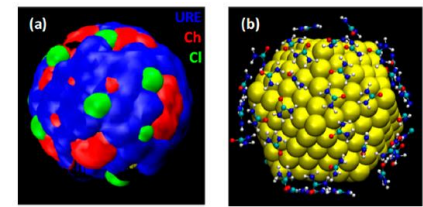
## Towards hyper-reactive nanostructured materials

- Better yields of functionalization by molecules of interest
- Better catalytic reactivity: accelerated kinetics (half-life times, kinetic constants)
- Best reactivity and activity (antioxidant, ...)

**CHALLENGE** : to synthesize well-defined nanocrystals (anisotropy ++)



→ **DES as NP Solvent**



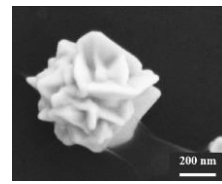
Better NP Solvation by DES

↳ **NP Stabilization**

→ **DES as Shape directing agent**

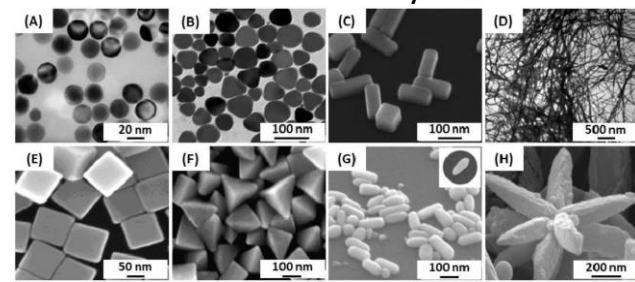
**Example**

Au nanoflower synthesis by electrodeposition

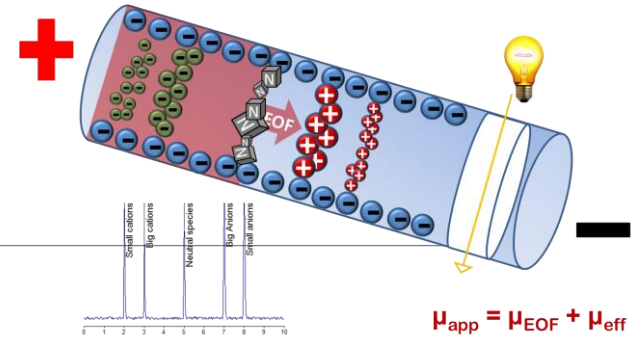


**Hot spots !**

Opportunity for sophisticated nanostructures synthesis

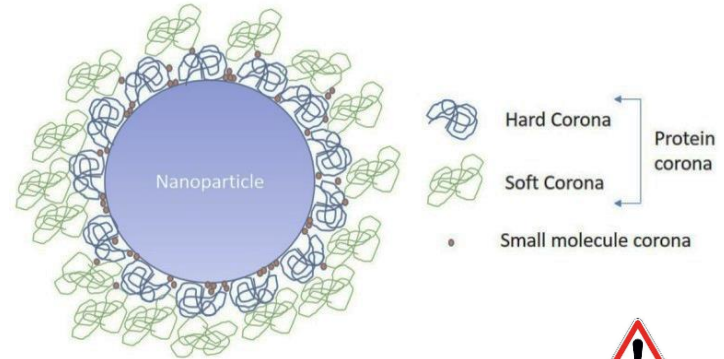
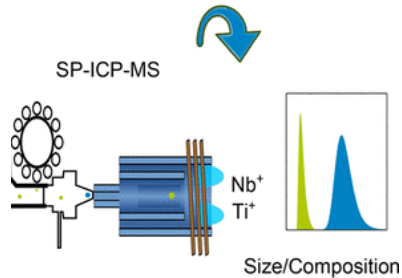


# Control of Nanoparticles



CE/UV for spherical NP polydispersity and impurity profile  
 CE/TDA for NP size } Actual work

CE/MSMS (triple quadrupole for impurity identification) → FRCR NOSE, ANR SNIF...



## NEXT STEPS :

**CE/ICP-MSMS for unknown multielemental description**

**CE/spICP-MS for elemental analysis and corona characterization (biomolecules adsorbed layers!)**

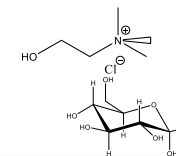


spICP-MS  
 Available at IPHC



# SCALE - Use of DES and NP for extraction

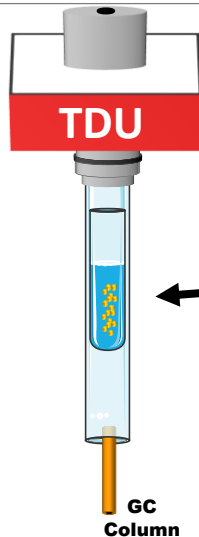
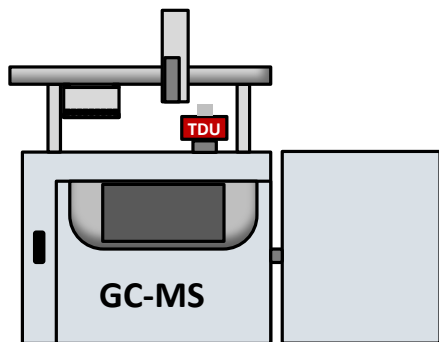
Tailor-made solvent  
Adjustable viscosity  
High solubilization capacity  
NP carrier and stabilizer



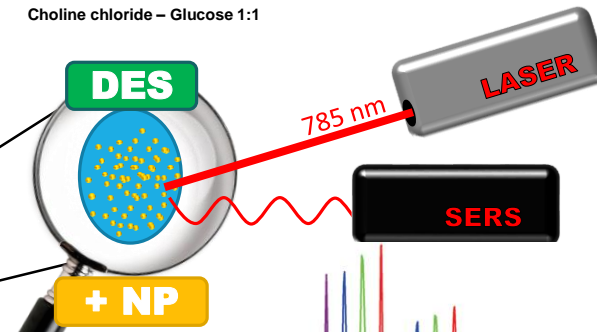
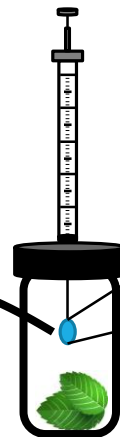
Choline chloride - Glucose 1:1

## CHALLENGE : Extract and analyze bioactive terpenes from plants

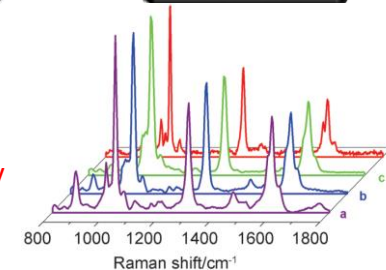
Automated Thermal Desorption Unit (TDU) With liner Exchange ATEX



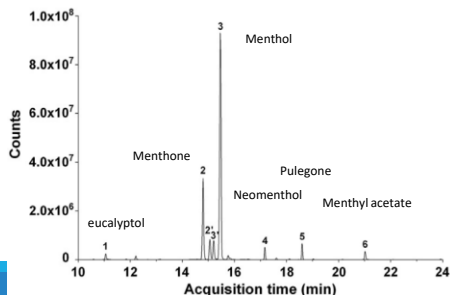
GC Injection in TDU



Higher surface area  
Adjustable selectivity  
Enhanced detection



Raman Shift of volatile monoterpene extract

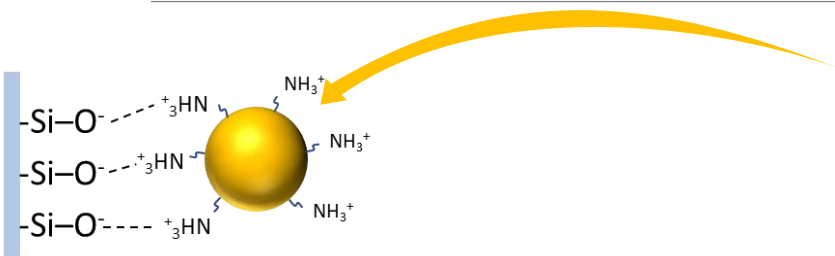


Mint extract Chromatogram

- Increase mass transfer
- Improve extraction efficiency and LOD
- Adjustable Selectivity
- Synergistic effect of DES and NP

GC: Gas Chromatography; LOD: Limit of Detection; MS: Mass Spectrometry

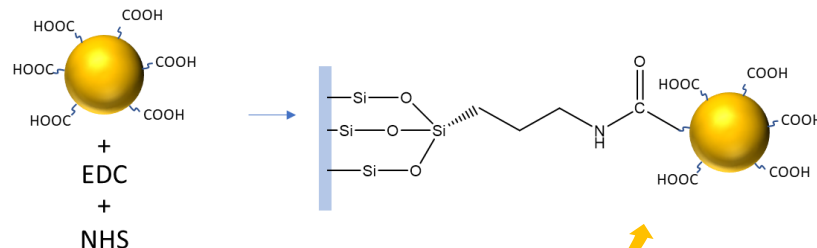
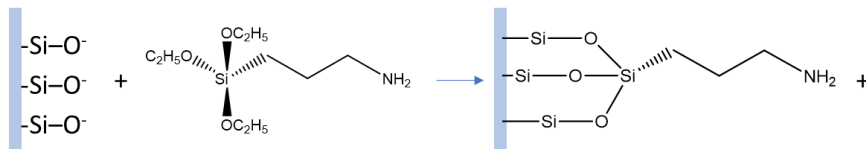
# Nanostructuration



## Direct nanostructuration via electrostatic interactions

Simple surface modification: one layer (« low stability »)

- Capillary electrophoresis → stable cationic grafting
- SPE Cartridge → specific surface ++



## Indirect nanostructuration via covalent bonds

- Higher surface chemistry: possibility of multilayers (« high stability »)
  - HPLC → Specific surface ++, customised functionalisation
  - GPC → Thermal resistance



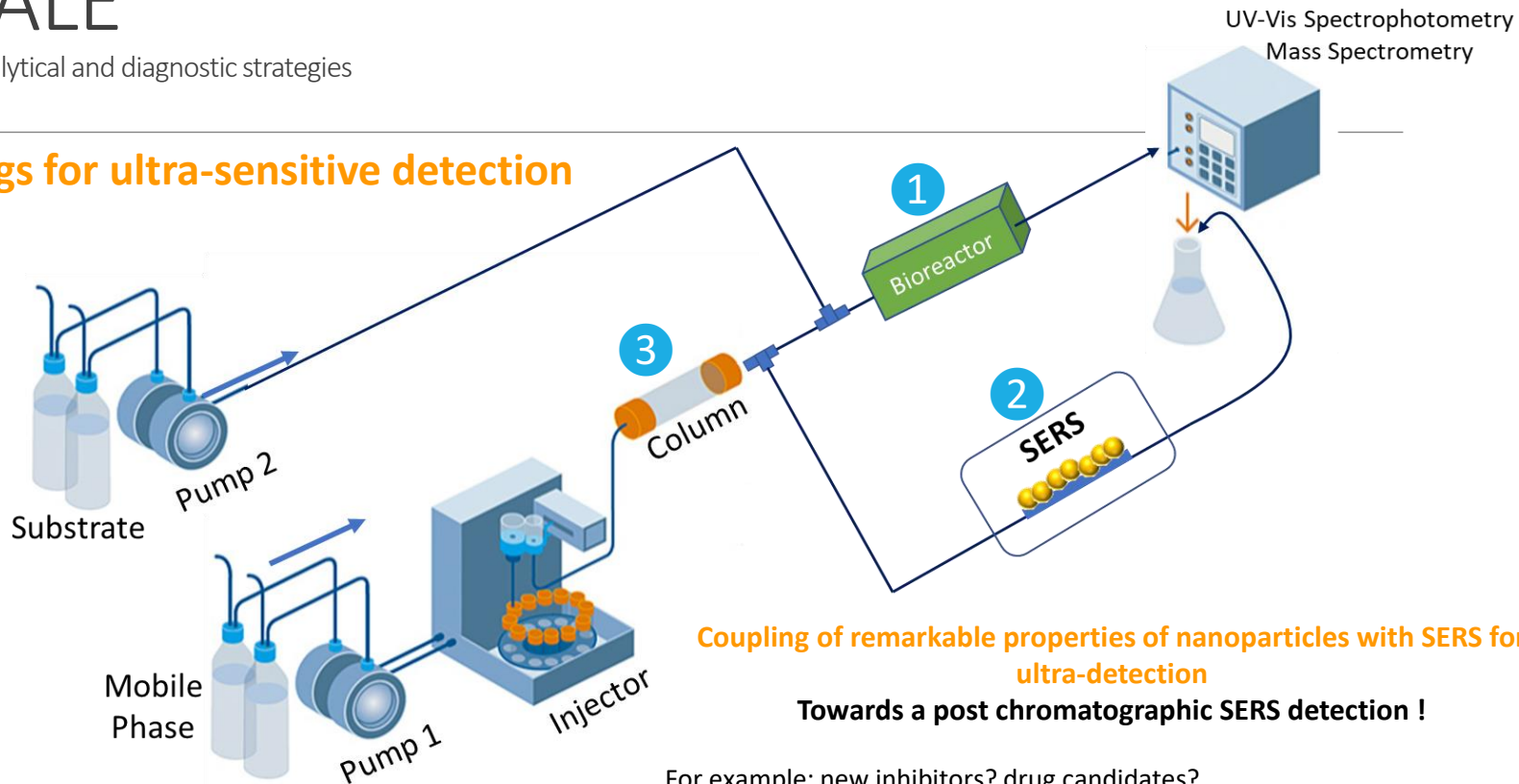


# SCALE

New analytical and diagnostic strategies

## New couplings for ultra-sensitive detection

### HPLC – SERS



**Coupling of remarkable properties of nanoparticles with SERS for ultra-detection**

**Towards a post chromatographic SERS detection !**

For example: new inhibitors? drug candidates?

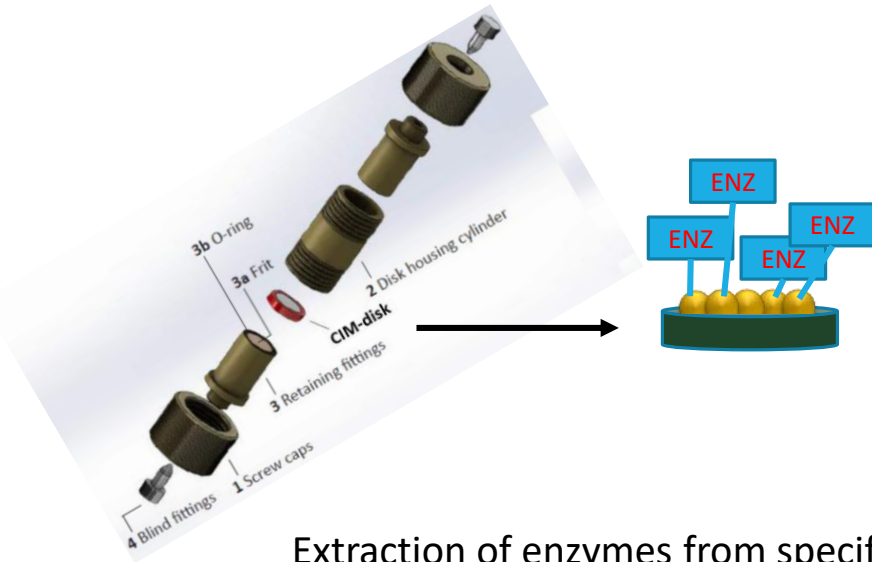


# SCALE

New analytical and diagnostic strategies

1

Bioreactor



Key Enzyme examples:

- Dipeptidylpeptidase 4 (DPP4) *versus* **Diabetes**
- Acetylcholine esterase *versus* **Alzheimer**
- Lipase, *versus* **Obesity**

Extraction of enzymes from specific bacteria and immobilized on nanostructured CIM-disk

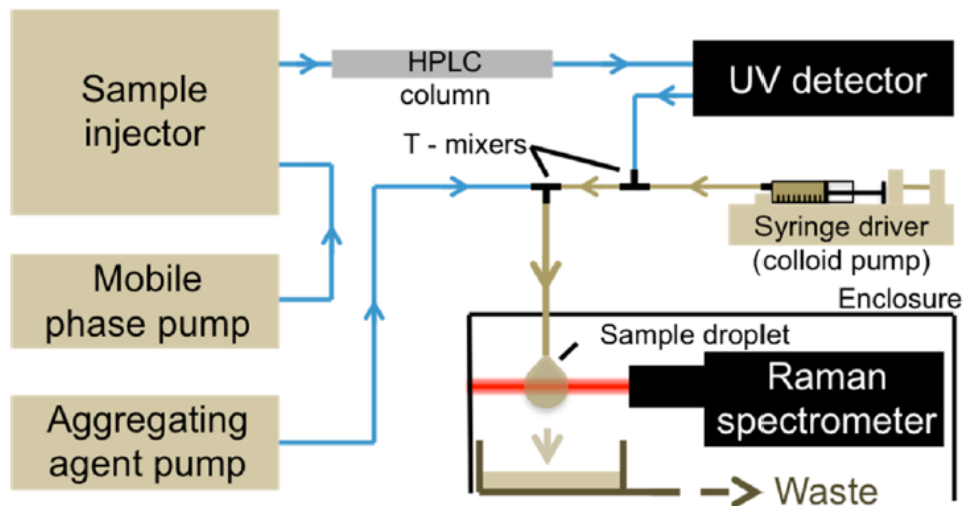
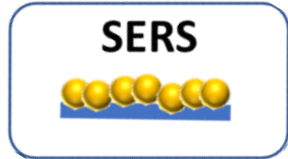
**Towards screening of anti-enzymatic molecules (inhibitors)**



# SCALE

New analytical and diagnostic strategies

2



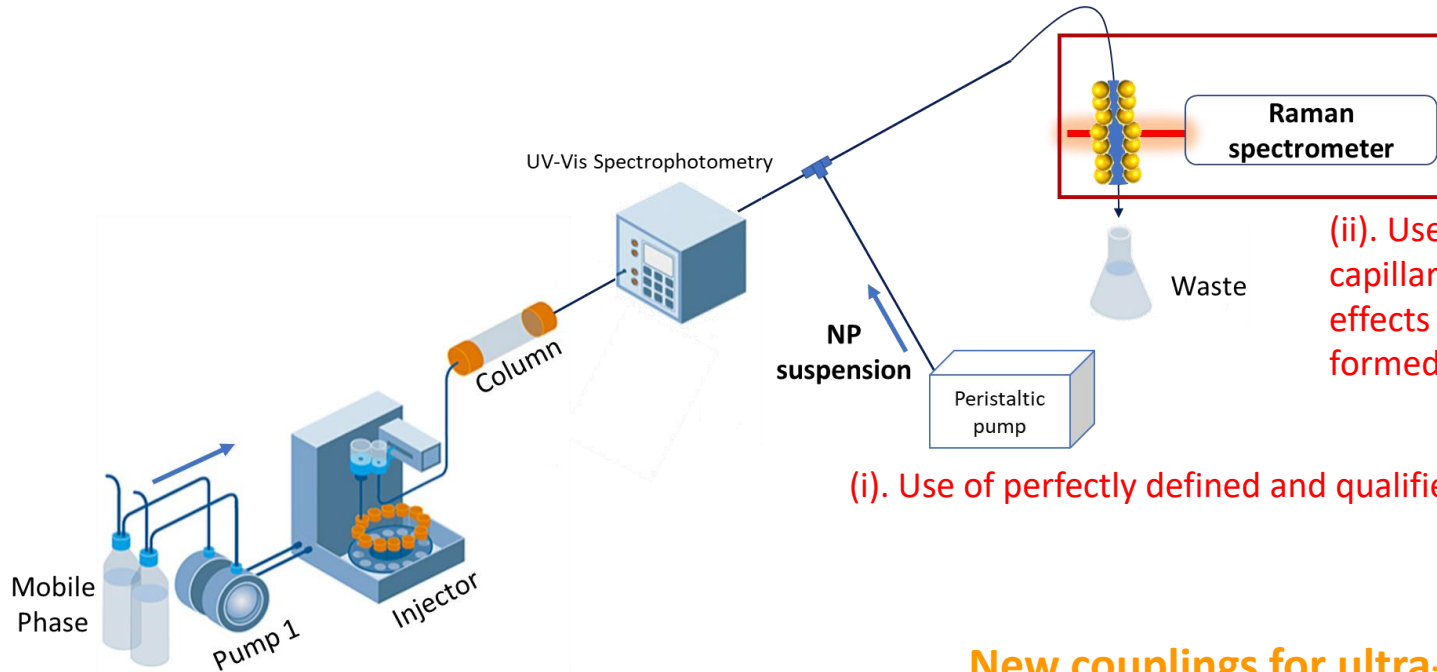
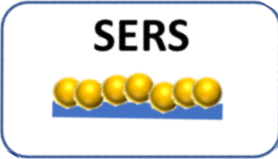
**Compact spectrometer easily integrated to a chromatographic system**



# SCALE

New analytical and diagnostic strategies

2



(ii). Use of a specific fiber or a capillary to avoid geometrical effects due to the shape of the formed drops.

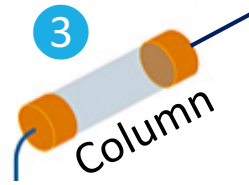
(i). Use of perfectly defined and qualified nanoparticles

**New couplings for ultra-sensitive detection**



# SCALE

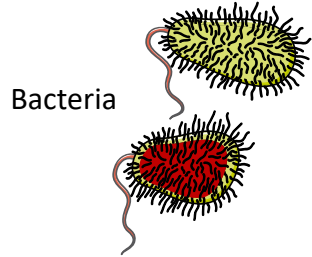
New analytical and diagnostic strategies



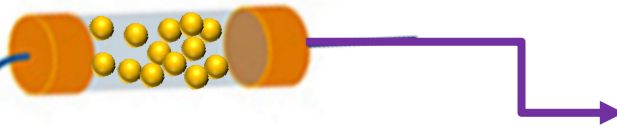
## Specific preconcentration / extraction systems Adapted to complex molecules / microorganisms

### Functionalized nanoparticles:

- Antibodies
- Biomolecules
- Antibiotics
- ...



Bacteria



### Nanostructured devices

Chromatographic columns  
Capillaries

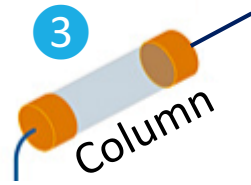
### Towards Screening

- Screening/separation of bacteria by nanostructured surfaces
- Nanostructured surfaces + bacteria for antibacterial screening

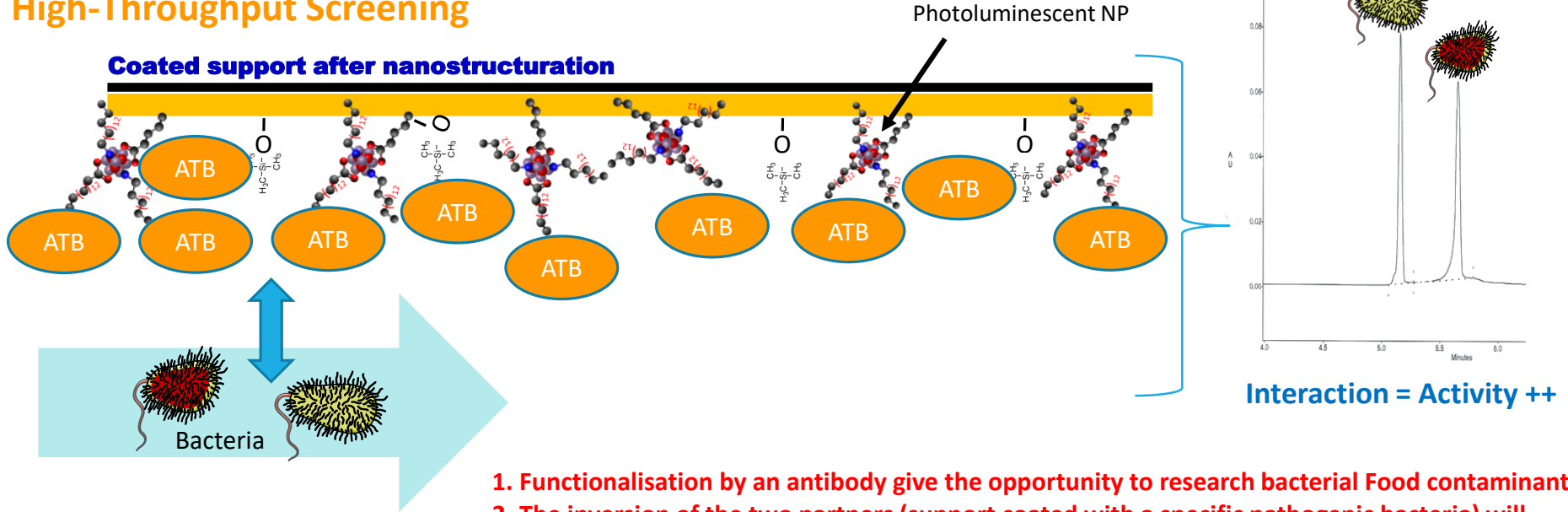


# SCALE

New analytical and diagnostic strategies



## High-Throughput Screening

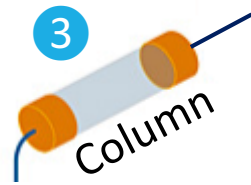


1. Functionalisation by an antibody give the opportunity to research bacterial Food contaminants
2. The inversion of the two partners (support coated with a specific pathogenic bacteria) will allow to screen active substances !



# SCALE

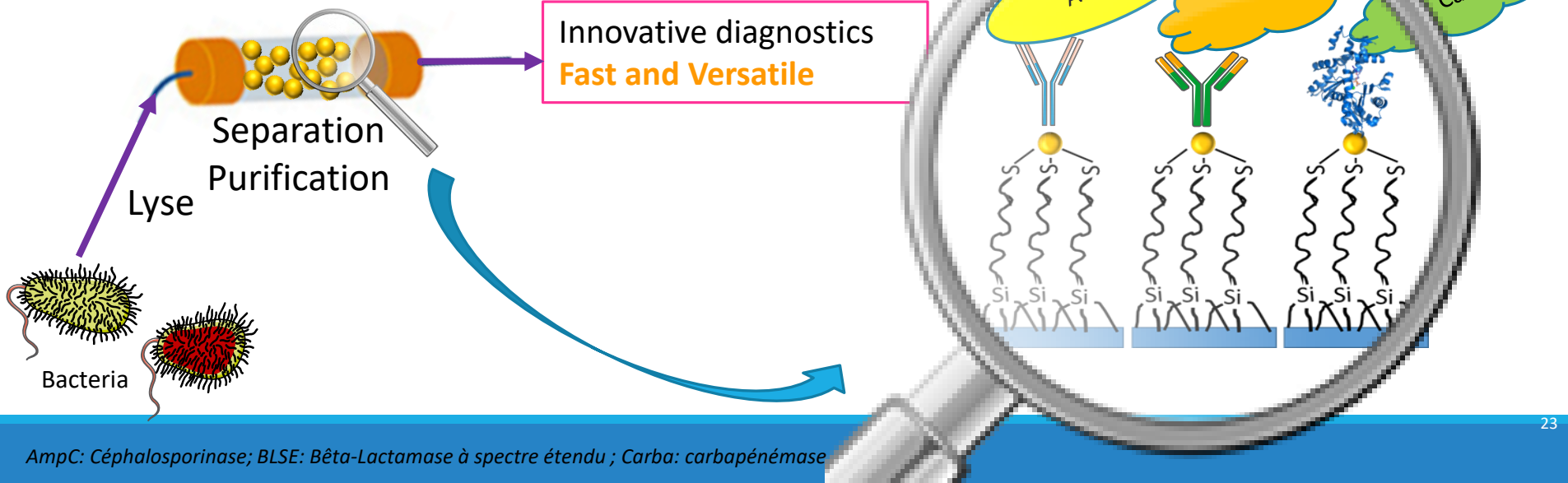
New analytical and diagnostic strategies



## Innovative strategies for the detection of resistance mechanisms

Detection of resistance mechanisms (proteins/enzymes, not genes)

Functionalized nanoparticles (antibody, protein/substrate...)





# SCALE

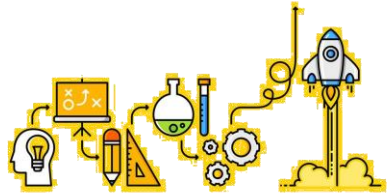
Project progress

Working meeting of SCALE members

04/10/2019, 07/11/2019, 20/12/2019

23/07/2020, 24/08/2020, 03/11/2020, 17/12/2020

04/02/2021, 25/02/2021, 09/03/2021, 16/03/2021, 26/03/2021



Scientific Council



HCERES project



2018

2019

August 2019

March 2020

Nov. 2020

March 2021

Dec. 2021

2024

SCALE

SCALE  
Presentation to  
team managers

SCALE  
Presentation of IPHC  
management  
+  
All DSA

SCALE  
Presentation  
CCOSL UL

UL Scientific pole  
and council

SCALE







Igor CLAROT (Pr.)



Ariane Boudier (Pr.)



Thomas Chaigneau (IE)



Benjamin Creusot (Adj.Tech.)



Raphaël E. Duval (Pr.)



Emmanuel Lamouroux (MCF)



Eric Marchioni (Pr.)



Christophe Marcic (MCF)



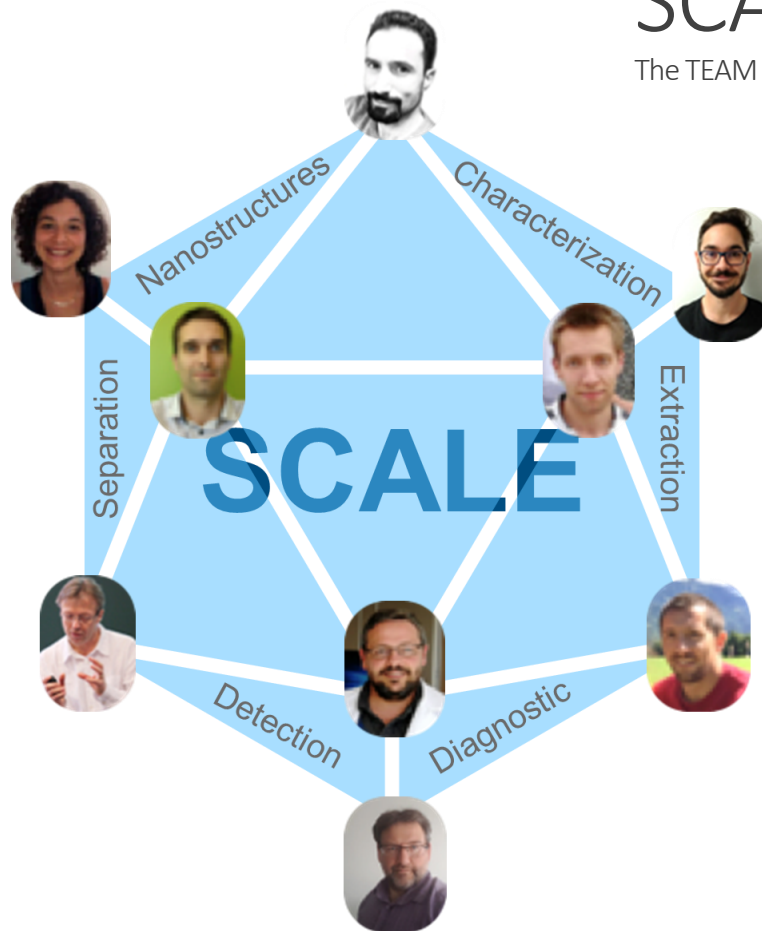
Arnaud Pallotta (MCF)



MCF 2021

# SCALE

The TEAM



**Complementarity of  
skills with the  
scientific objective**



# SCALE

...Under construction




**ELECTROPHORESIS**

Short Communication

Capillary electrophoresis for fast detection of heterogeneous population in colistin-resistant Gram-negative bacteria

Guillaume Sautrey, Raphaël E. Duval, Alicia Chevalley, Stéphane Fontanay, Igor Clarot ✉



Contents lists available at ScienceDirect

Colloids and Surfaces B: Biointerfaces

journal homepage: [www.elsevier.com/locate/colsurfb](http://www.elsevier.com/locate/colsurfb)

Long-lasting and controlled antioxidant property of immobilized gold nanoparticles for intelligent packaging

J. Beurton<sup>a</sup>, I. Clarot<sup>a</sup>, J. Stein<sup>a</sup>, B. Creusot<sup>a</sup>, C. Marcie<sup>b</sup>, E. Marchioni<sup>b</sup>, A. Boudier<sup>a\*</sup>



International Journal of Molecular Sciences

Article

Investigation of Nanoparticle Metallic Core Antibacterial Activity: Gold and Silver Nanoparticles against *Escherichia coli* and *Staphylococcus aureus*

Jimmy Gouyau<sup>1</sup>✉, Raphaël E. Duval<sup>1,2</sup>, Ariane Boudier<sup>3</sup> and Emmanuel Lamouroux<sup>1,\*</sup>




**or-nano**  
GROUPEMENT DE RECHERCHE

**Or-Nano 2019**  
Rennes, 13-15 mars 2019

3<sup>rd</sup> INTERNATIONAL CONFERENCE ON

**Analytical and Bioanalytical Methods**

OCTOBER 18-20, 2021 | BOSTON, MA

« Nanostructured support for thiolated substances evaluation »

*Beurton J, Boudier A, Pallotta A, Marchioni E, Clarot I.*

« Online acetylcholinesterase inhibition evaluation by HPLC-MS hyphenated with an immobilized enzyme reactor »

*Marchioni E, Yuan Y, Clarot I*



## International symposium APA 2022 - Nancy (Advances in Pharmaceutical Analysis)

Organization and Scientific committee :

Clarot I, Boudier A, Duval R.E., Pallotta A., Marchioni E



# SCALE

...Under construction

## Research projects



CopperNic  
Development and in-vivo monitoring of metal nanoclusters as active agents for an orphan pediatric disease



Collab. DRHIM - IPHC

ANR

National

## Funding Calls

Region

FRCR

European

H2020



NOSE (Nanostructured support for thiolated Substances Evaluation)



NOSE (Nanostructured support for thiolated Substances Evaluation)



FUNgredients - 2020 Produce bio-based functional ingredients and additives for high-end markets



Susfun Sustainable and Functional bioactive extracts from underexploited plant and marine sources for food and cosmetic applications

LabCom



Projection : ANR à venir, thèses (covidog, CMI EC)



# SCALE

*Memento*

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- **Innovation**  
Original and innovative theme / Nano and Analytical communities
- **Contributions** of new analytical and diagnostic strategies (separation, detection)
- **Structuration**  
No thematic equivalent  
Complementarity with current IPHC competences
- **Access to platforms (IPHC/UL) and associated skills**
- **Grand Est Region Team** (strategic innovation and visibility)



Some Questions ?