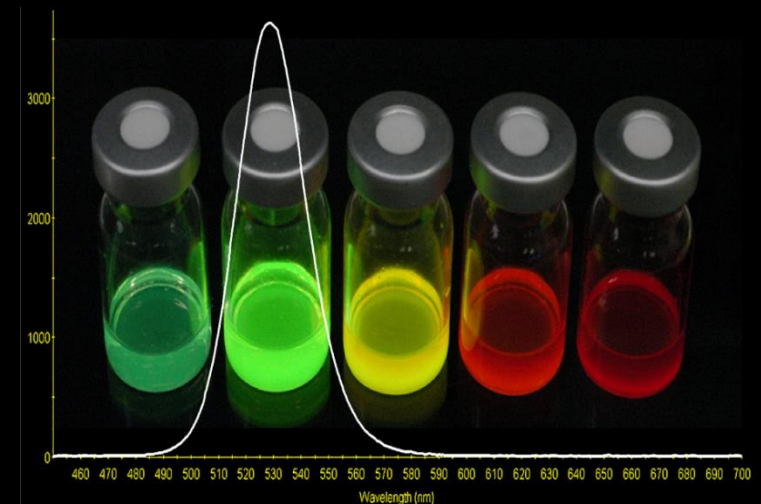
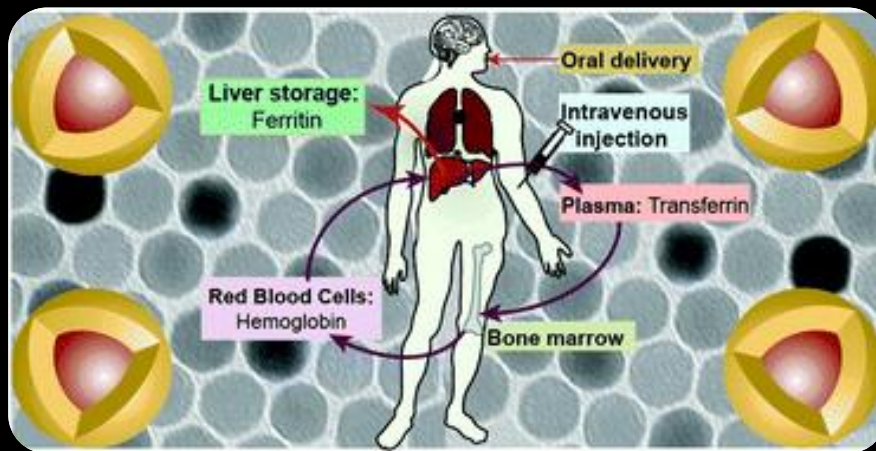


# ICP-MS-based analytical method for engineered nanoparticles



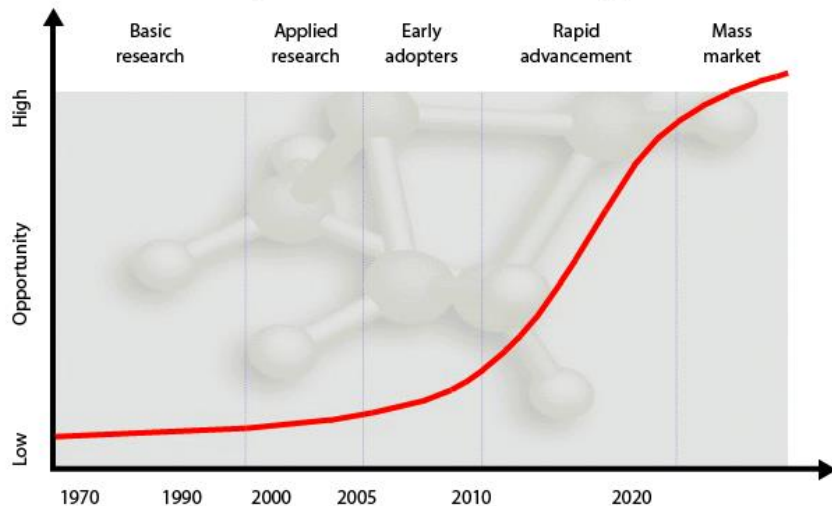
# A decade of uncertainty

Ten years after the publication of an influential report on the uncertainties in nanoscale science and engineering, **Andrew D. Maynard** asks, are we in danger of creating a new metaphorical grey goo?

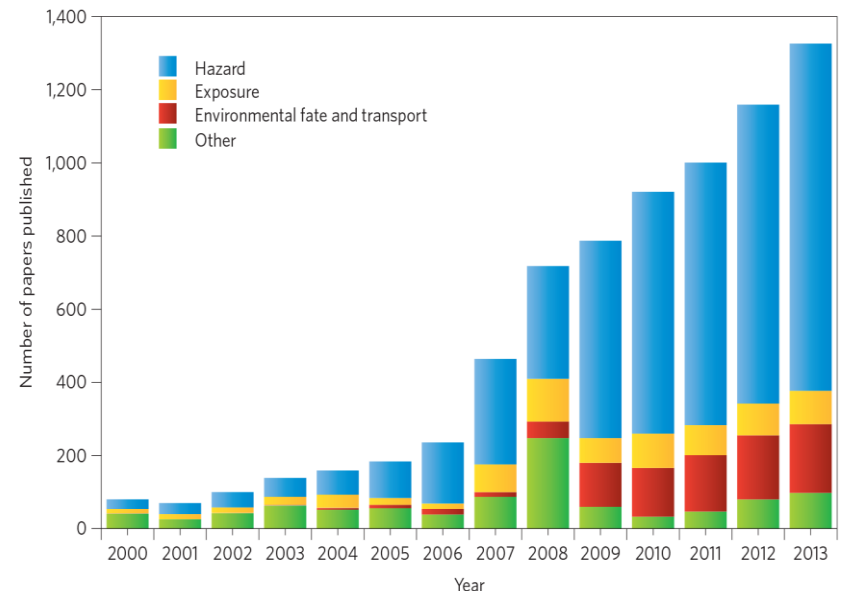


whatever you might think about the economic and societal benefits of this new suite of technologies, extensive further investment into possible applications would be foolish without direct investment in research and action on potential implications.

The growth of nanotechnology



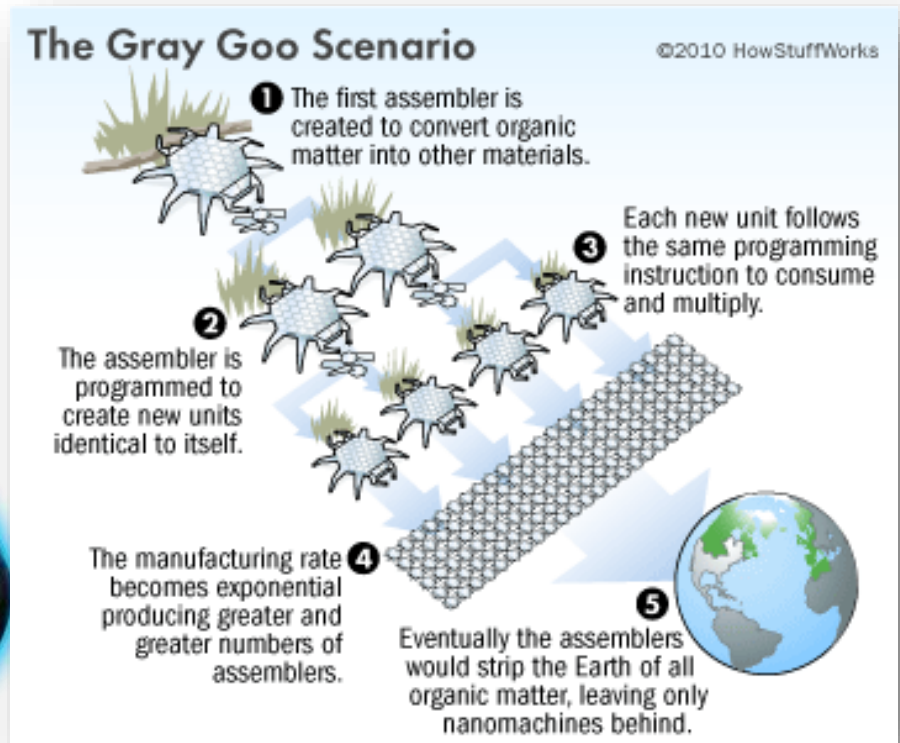
US Department of Energy



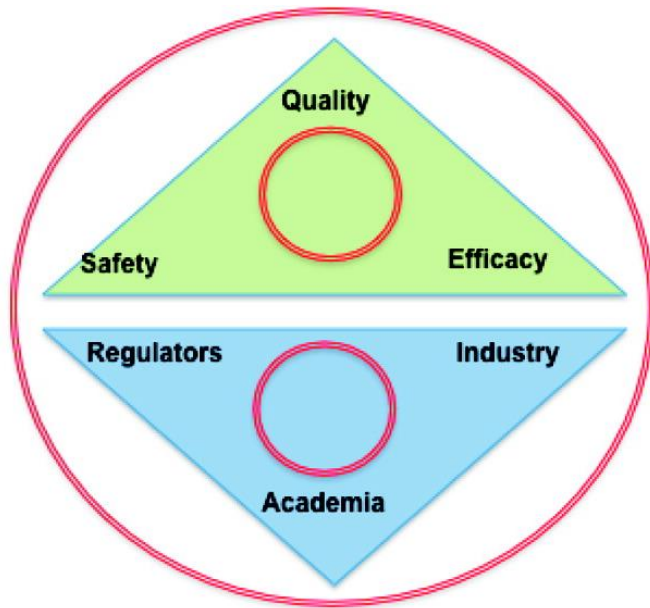
*Nature Nanotechnology 9, 159–160 (2014)*

# What is the gray goo nightmare?

Grey goo is a hypothetical end-of-the-world scenario involving molecular nanotechnology in which out-of-control self-replicating robots consume all matter on Earth while building more of themselves, a scenario that has been called ecophagy ("eating the environment").

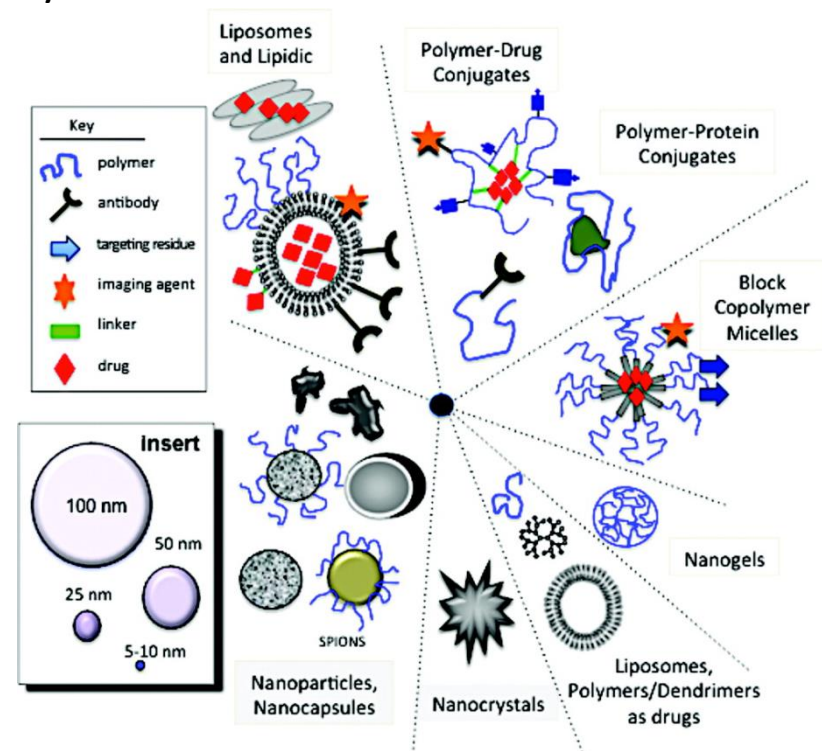


# A realistic look at the promises and perils of nanomedicine



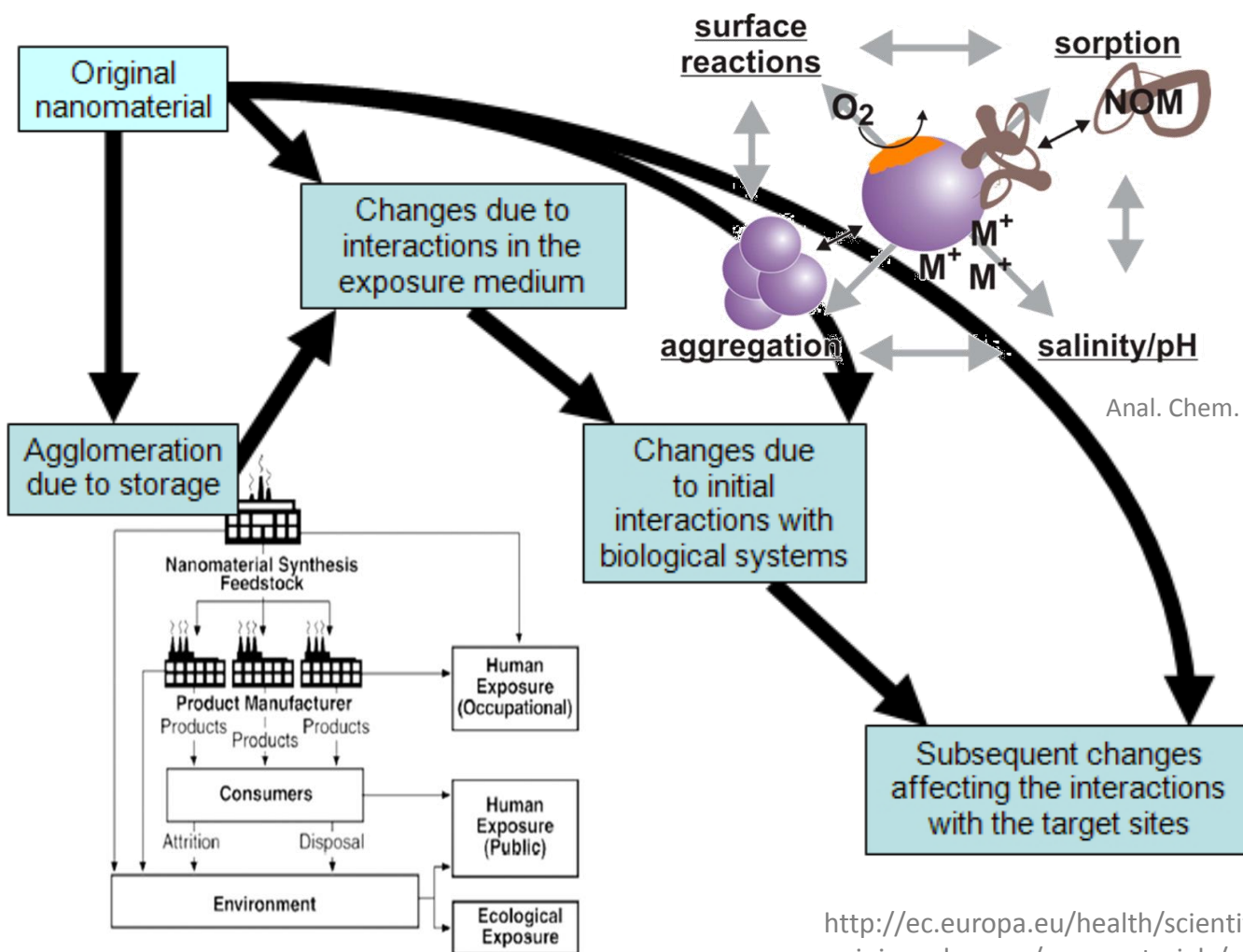
Is the emerging field of nanomedicine a breathtaking technological revolution that promises remarkable new ways of diagnosing and treating diseases? Or does it portend the release of dangerous nanoparticles, nanorobots or nanoelectronic devices that will wreak havoc in the body?

About **40** nano health care products actually are in use and nano-sized drugs, drug delivery devices, imaging agents, and other products are on the horizon.

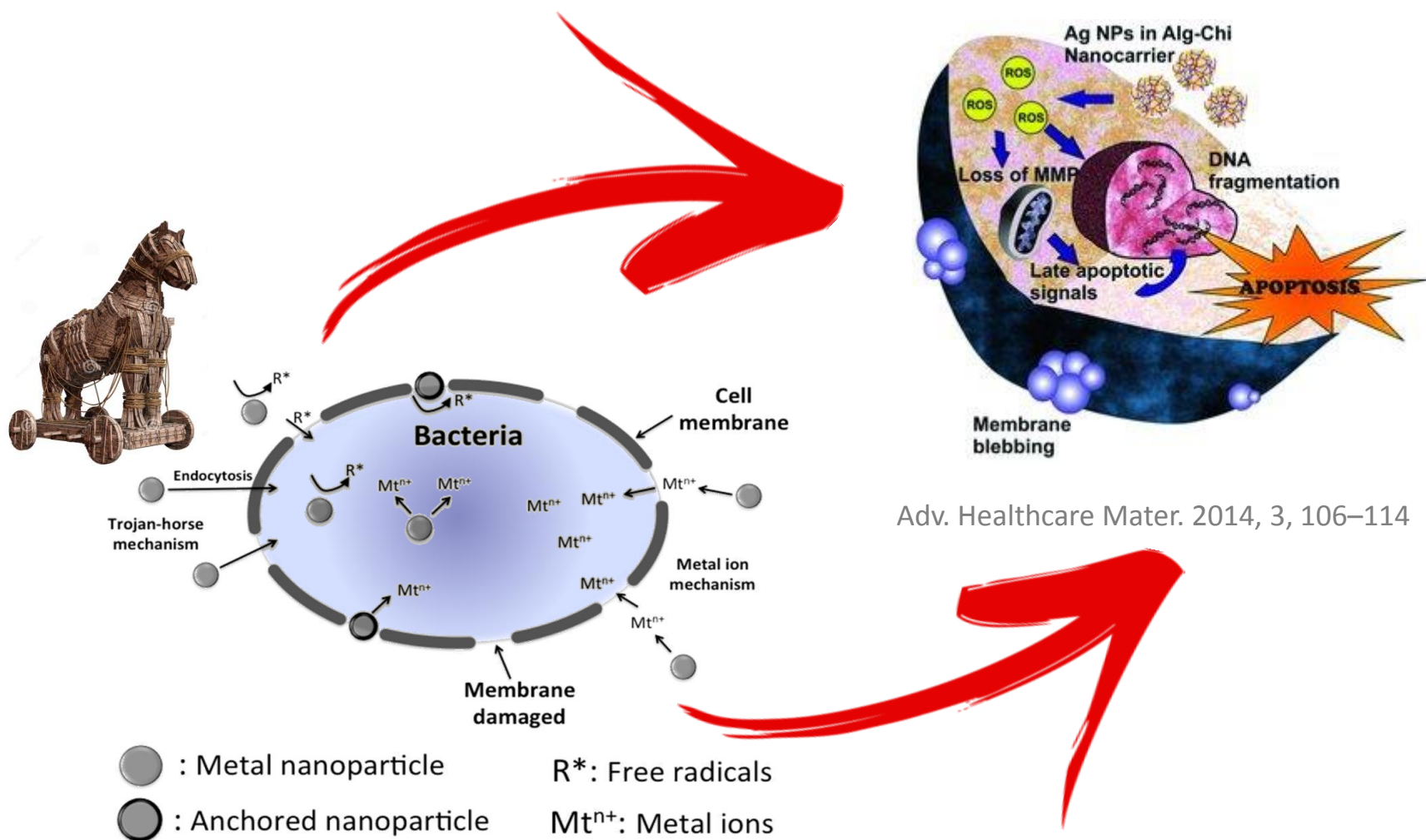




# Dynamic transformations nanoparticles undergo in the body or the environment and the interplay between these transformations

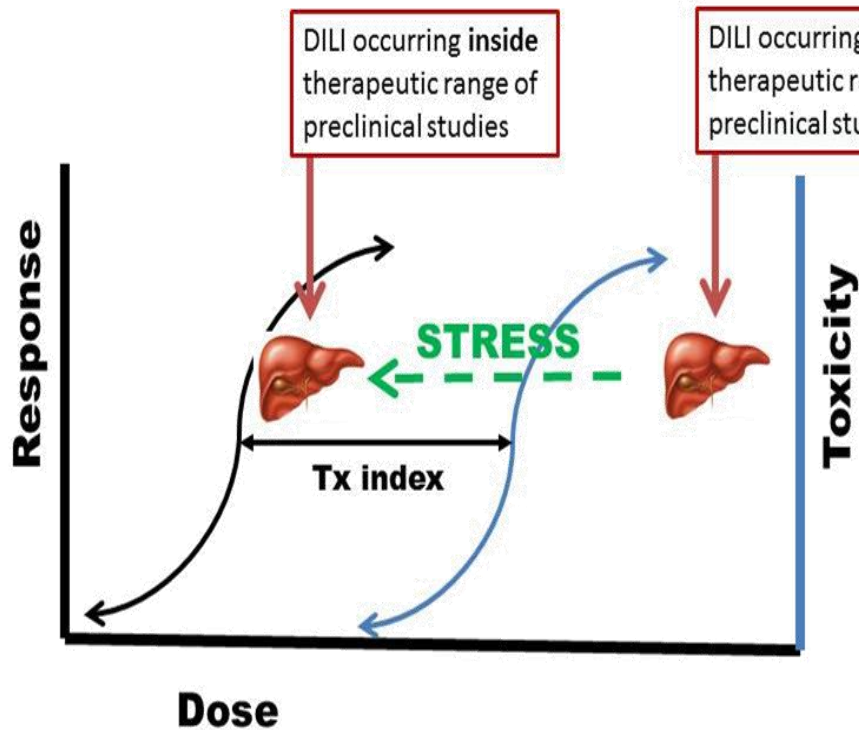


# Antimicrobial behaviour of metal nanoparticles

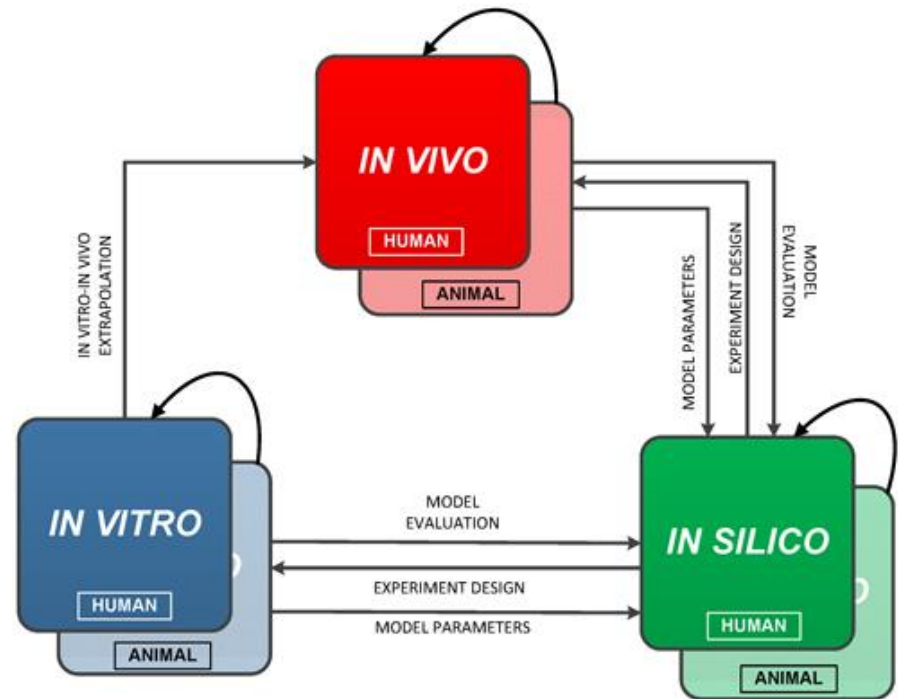


Adv. Healthcare Mater. 2014, 3, 106–114

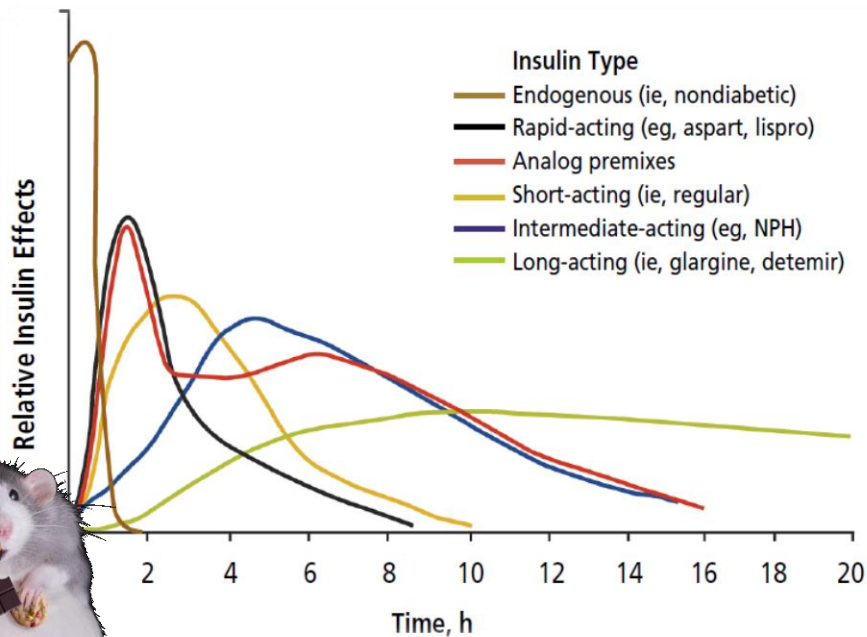
# Toxico-/Pharmacodynamics : Dose-Response Effect



<http://pharmaceuticalintelligence.com/tag/anti-cancer-therapy/>



# Pharmacokinetics of human insulins compared with insulin analogs and endogenous insulin



JAOA • Vol 109 • No 1 • January 2009

## Factors Affecting the Clearance and Biodistribution of NPs

- Size
- Surface Charge
- Surface modifications
- Physiological Defects
- Active Targeting

Mol. Pharmaceutics, 2008, 5 (4), pp 505–515



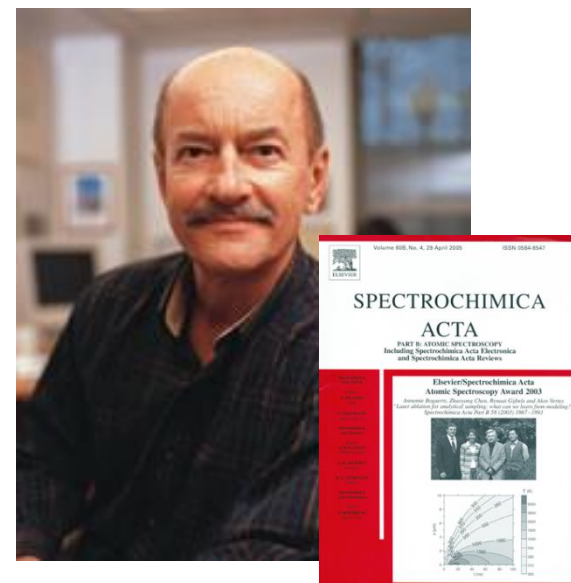


# Current focal areas

In order to fully understand how these **metallo drugs** **behave in vivo**, it is necessary to identify the products of their biotransformation and degradation. Such an analysis includes identification and characterization of chemically transformed species, as well as complexes of the drug with other species present in the biological system and with its target. In many cases, it has been found that the therapeutically active species is not the administered drug but rather a metabolite. Such discoveries can potentially **help in the development of more effective or alternative drug products**.

Furthermore, many metallo drugs are known to have severe side-effects, and the margin between beneficial and toxic doses can be narrow, making it necessary to **understand mechanisms of toxicity as well as therapeutic action**, and to identify the toxicologically active species.

Gary M. Hieftje



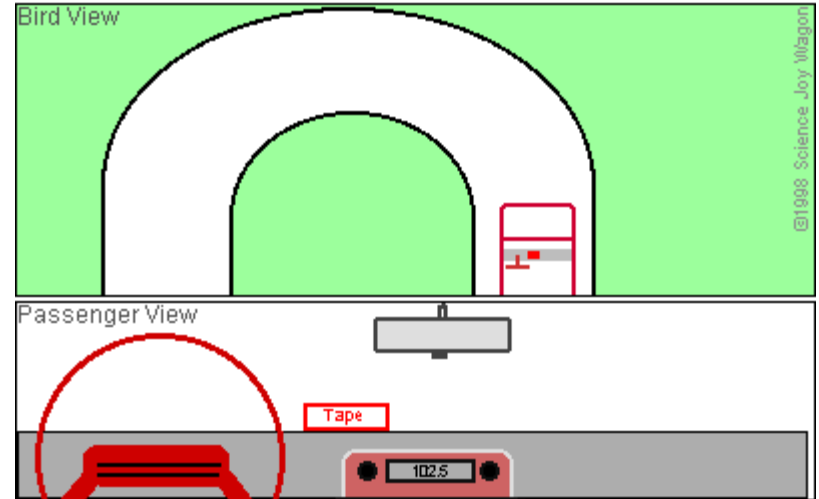
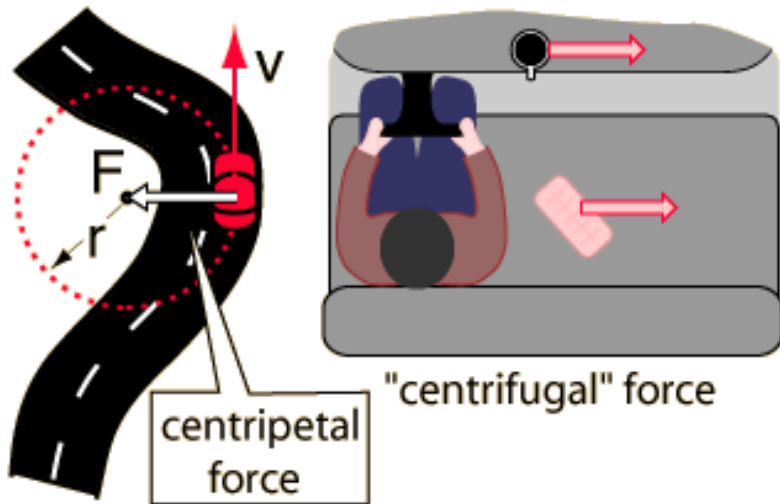
Department of Chemistry,  
Indiana University

Spectrochimica Acta Part B 59 (2004)  
135–146

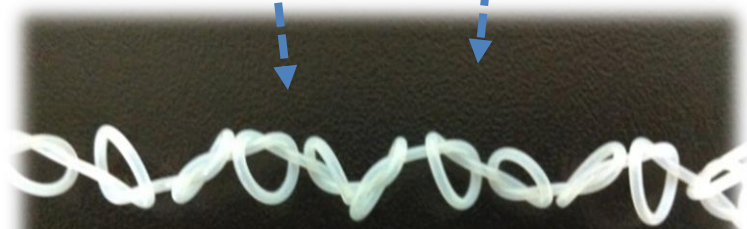
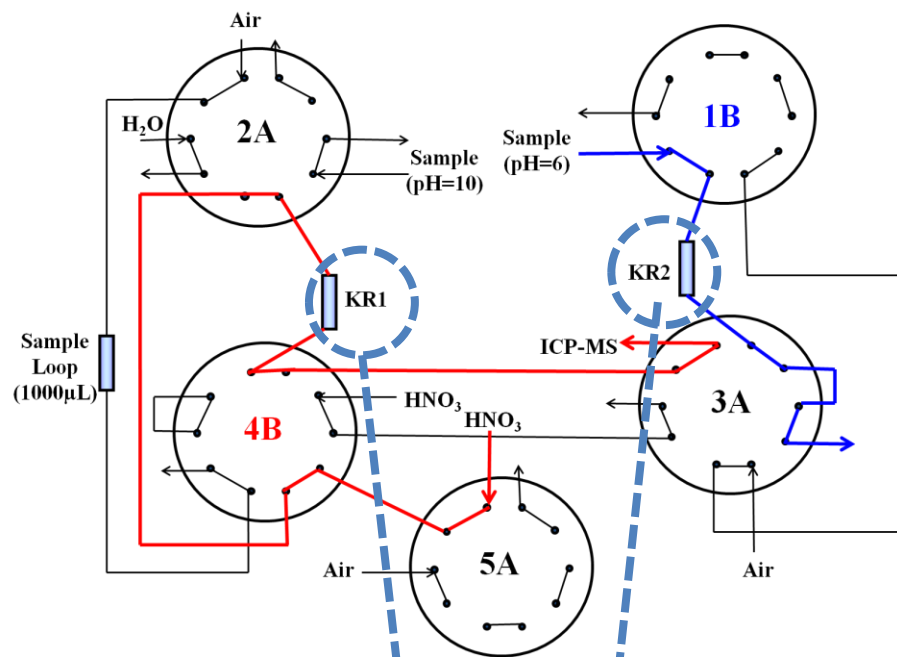
# Online Centrifugal Separation Technique

$$F = \frac{mv^2}{R}$$

When you move along a curved path, unattached objects tend to move toward the outside of the curve.

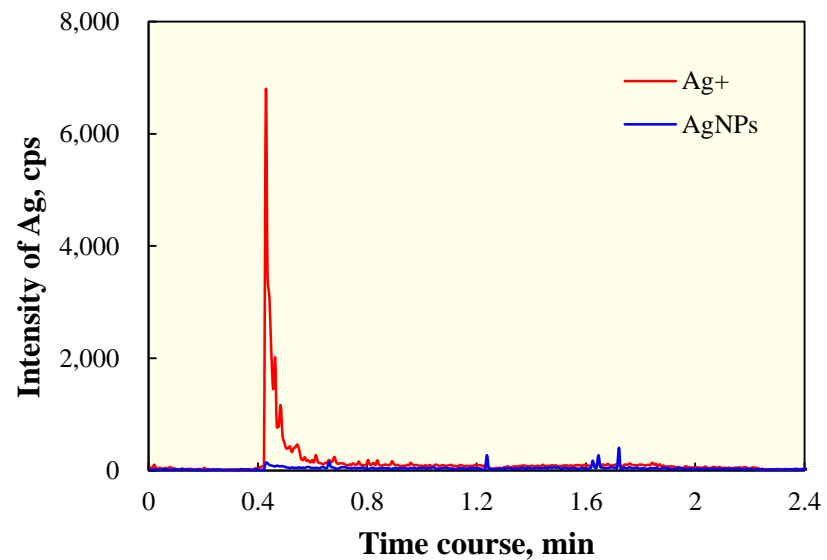
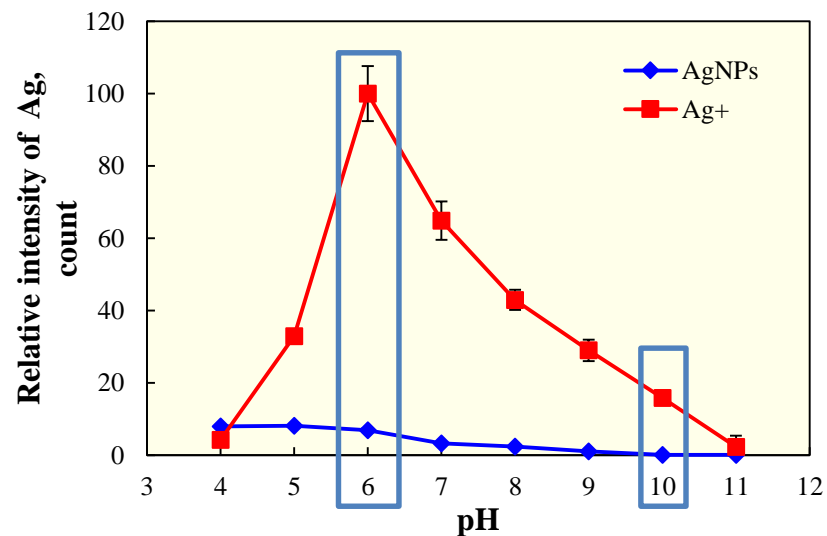


# Differentiation of $\text{Ag}^+$ / $\text{AgNPs}$ by Dual-KR-SPE-ICP-MS System

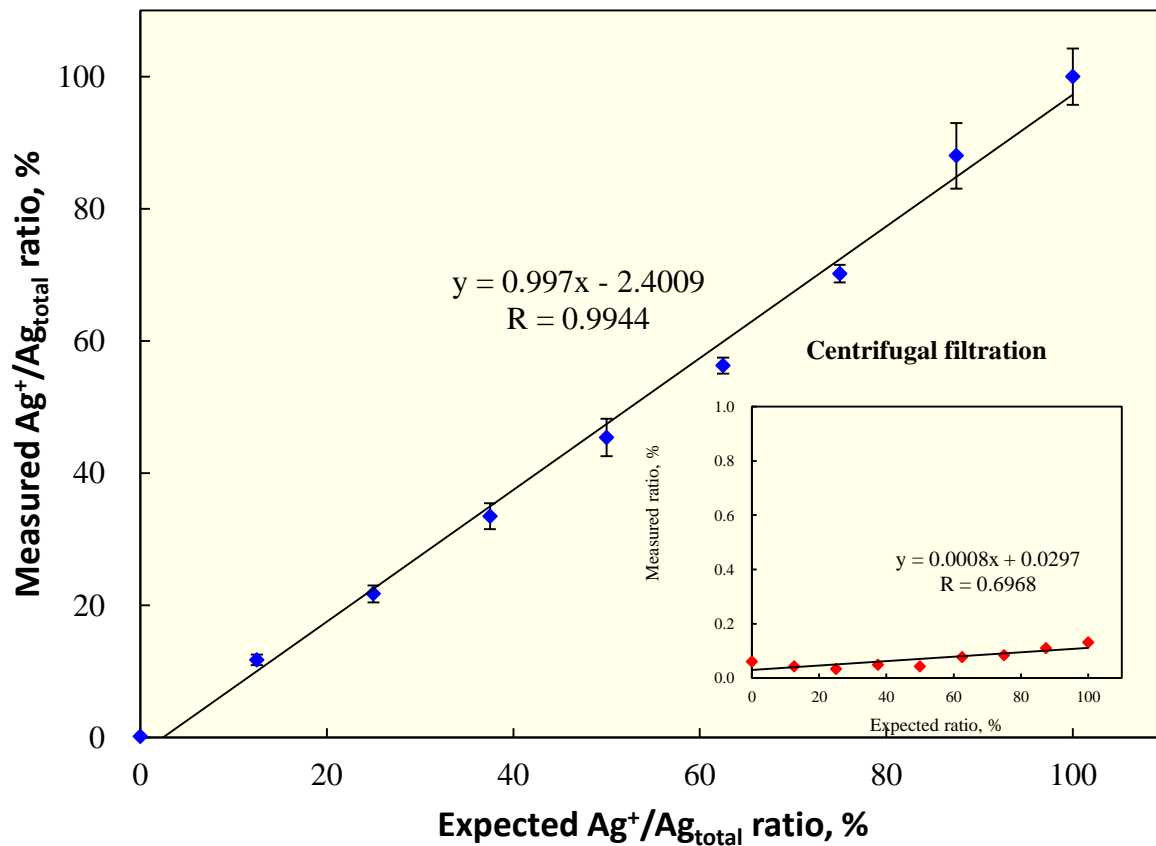


25 knots/100 cm PTFE tubing (0.03 inch i.d.)

**Knotted Reactor**



# Analytical Performance



**Knotted Reactor**



**V.S**

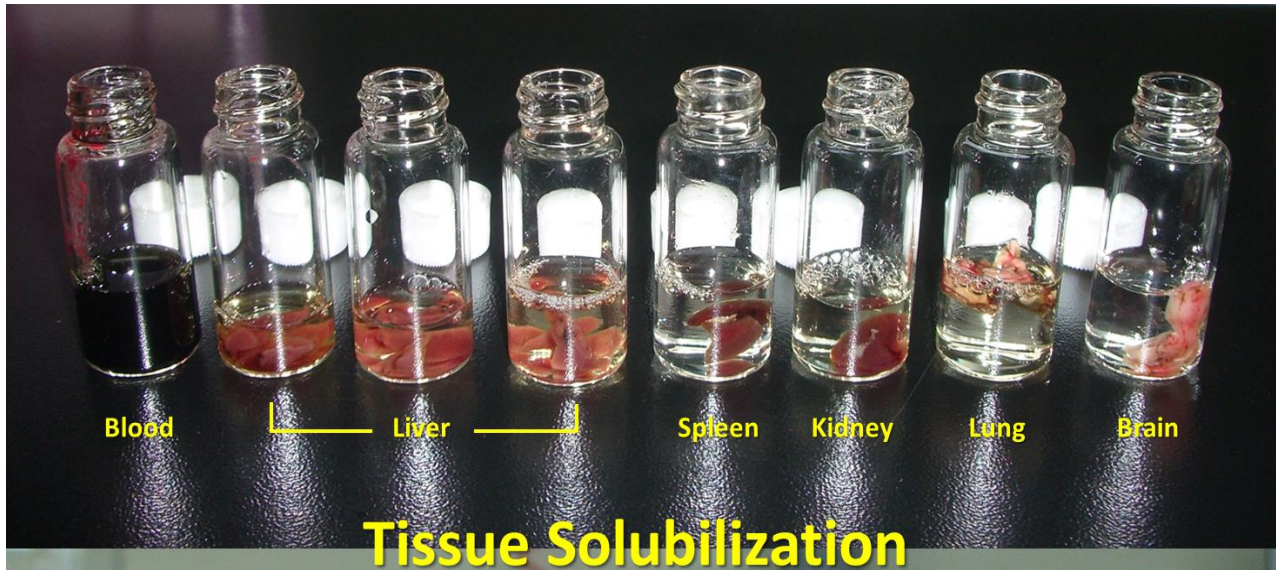


**Centrifugal Filter**

	working range, $\mu\text{g L}^{-1}$	R	MDL, $\mu\text{g L}^{-1}$	spike recovery, %
AgNPs (pH = 6)	0.1 – 10	0.9998	0.006	83 – 111
$\text{Ag}^+$ (pH = 6)	0.1 – 10	0.9989	0.006	89 – 113
$\text{Ag}^+$ (pH = 10)	0.1 – 10	0.9995	0.234	88 – 107



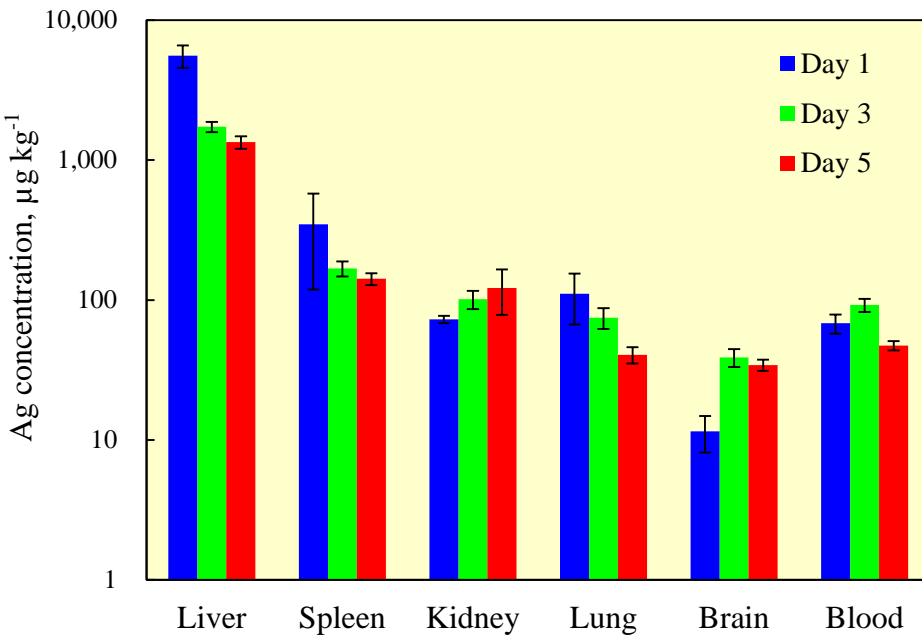
**SOLVABLE™** is an aqueous based solubilizer that has an excellent capacity for the solubilization of wet tissue .



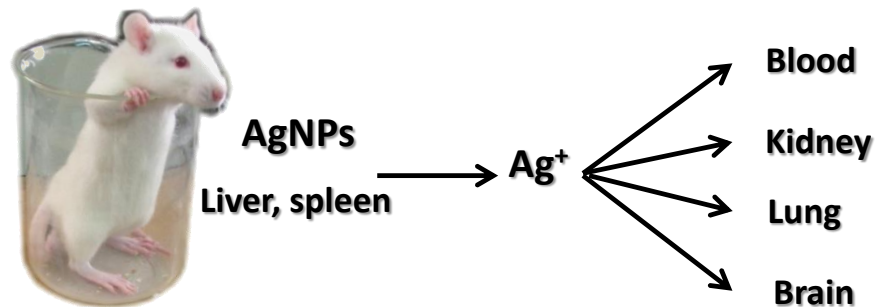
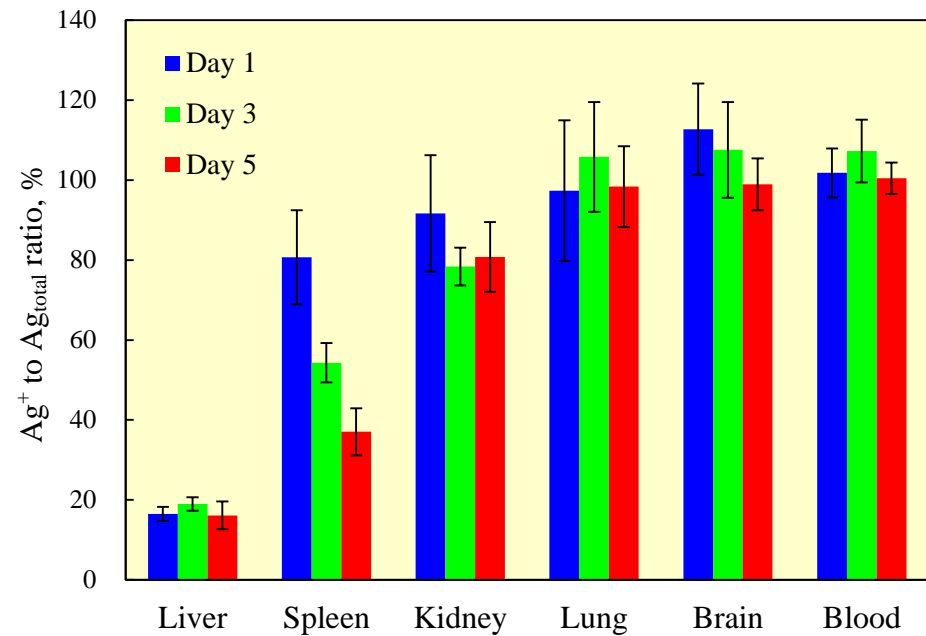
**SOLVABLE™** is a basic mixture.

# Biodistribution and Dissolution of AgNPs *in Vivo*

## AgNP Biodistribution (500 $\mu\text{g kg}^{-1}$ )




## $\text{Ag}^+/\text{Ag}_{\text{total}} \rightarrow \text{AgNP Dissolution}$

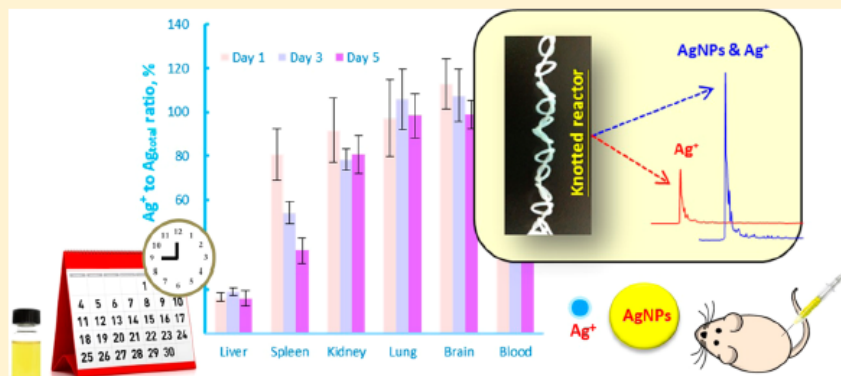


# Quantitatively Profiling the Dissolution and Redistribution of Silver Nanoparticles in Living Rats Using a Knotted Reactor-Based Differentiation Scheme

Cheng-Kuan Su, Hsin-Tung Liu, Sheng-Chieh Hsia, and Yuh-Chang Sun\*

Department of Biomedical Engineering and Environmental Sciences, National Tsing-Hua University, Hsinchu, 30013, Taiwan

 Supporting Information

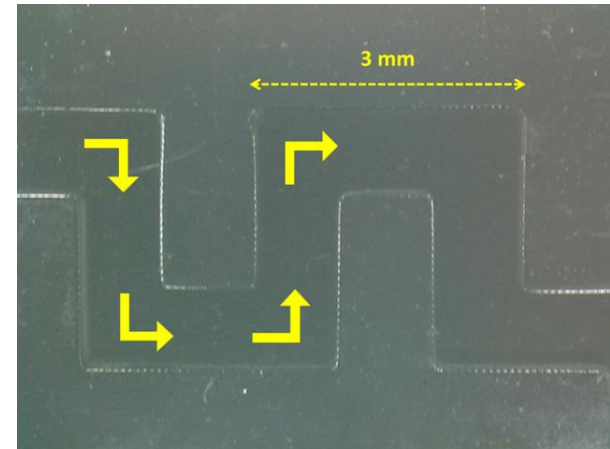
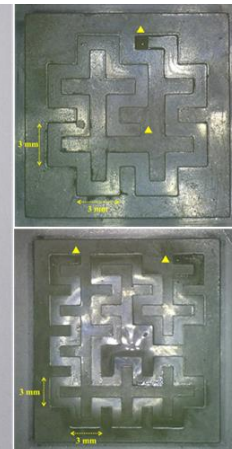
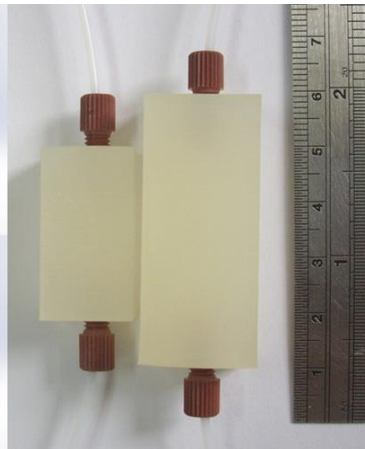
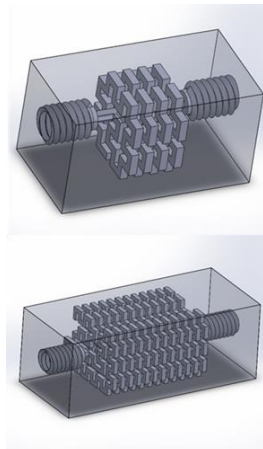
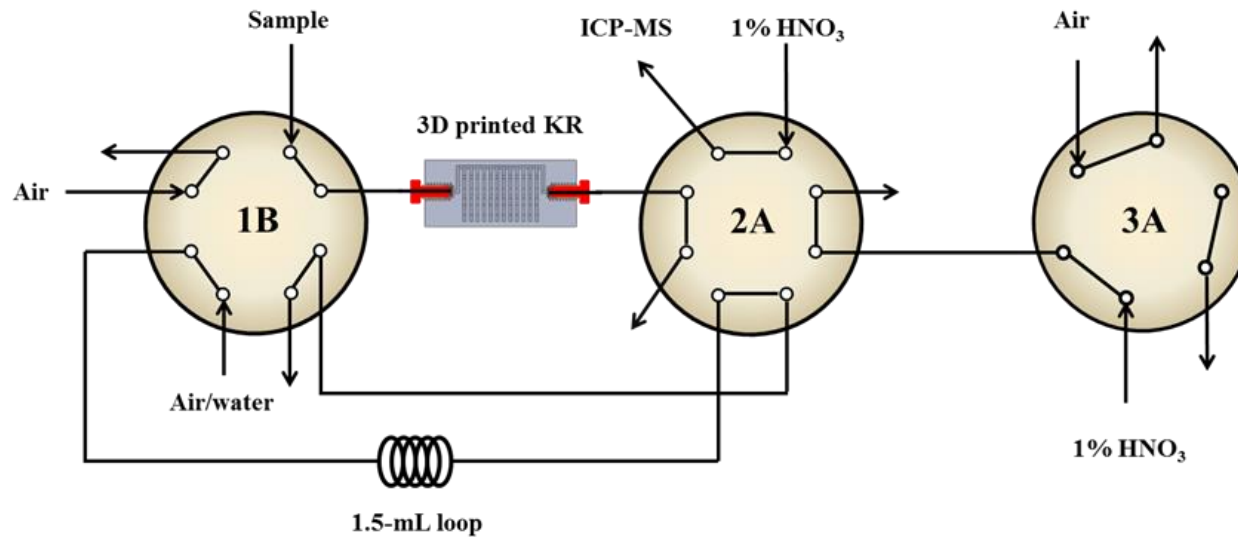


**ABSTRACT:** Whether silver nanoparticles (AgNPs) degrade and release silver ions (Ag<sup>+</sup>) *in vivo* has remained an unresolved issue. To evaluate the biodistribution and dissolution behavior of intravenously administered AgNPs in living rats, we employed a knotted reactor (KR) device to construct a differentiation scheme for quantitative assessment of residual AgNPs and their released Ag<sup>+</sup> ions in complicated animal tissues; to do so, we adjusted the operating parameters of the KR, namely, the presence/absence of a rinse solution and the sample acidity. After optimization, our proposed differentiation system was confirmed to be tolerant to rat tissue and organ matrix and provide superior reliability of differentiating AgNPs/Ag<sup>+</sup> than the conventional centrifugal filtration method. We then applied this differentiation strategy to investigate the biodistribution and dissolution of AgNPs in rats 1, 3, and 5 days postadministration, and it was found that the administered AgNPs accumulated predominantly in the liver and spleen, then dissolved and released Ag<sup>+</sup> ions that were gradually excreted, resulting in almost all of the Ag<sup>+</sup> ions becoming deposited in the kidney, lung, and brain. Histopathological data also indicated that toxic responses were specifically located in the AgNP-rich liver, not in the Ag<sup>+</sup>-dominated tissues and organs. Thus, the full-scale chemical fate of AgNPs *in vivo* should be integrated into future assessments of the environmental health effects and utilization of AgNP-containing products.



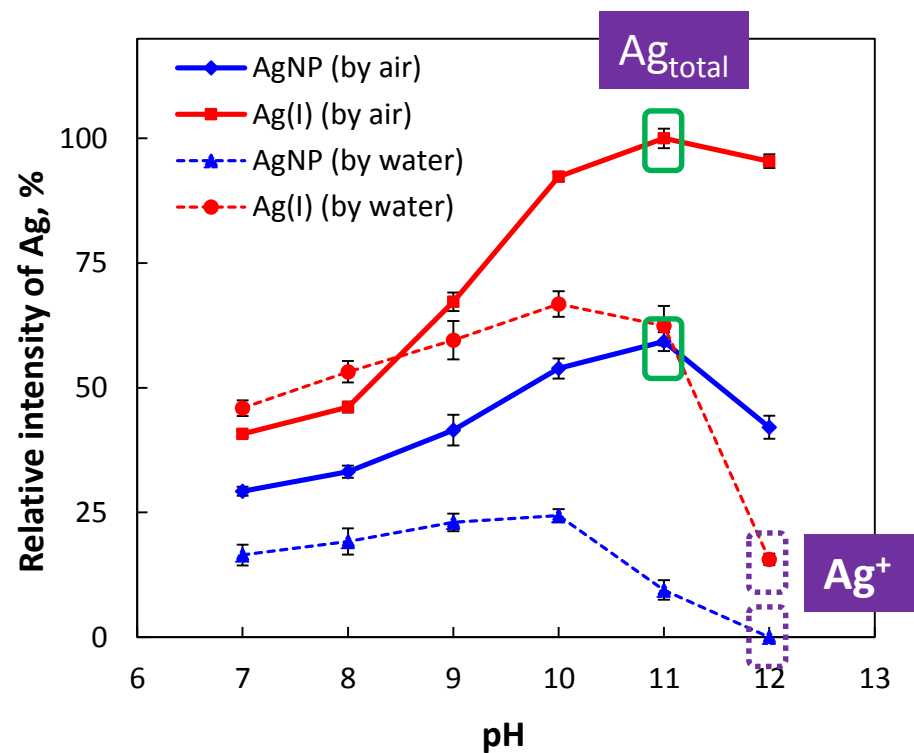
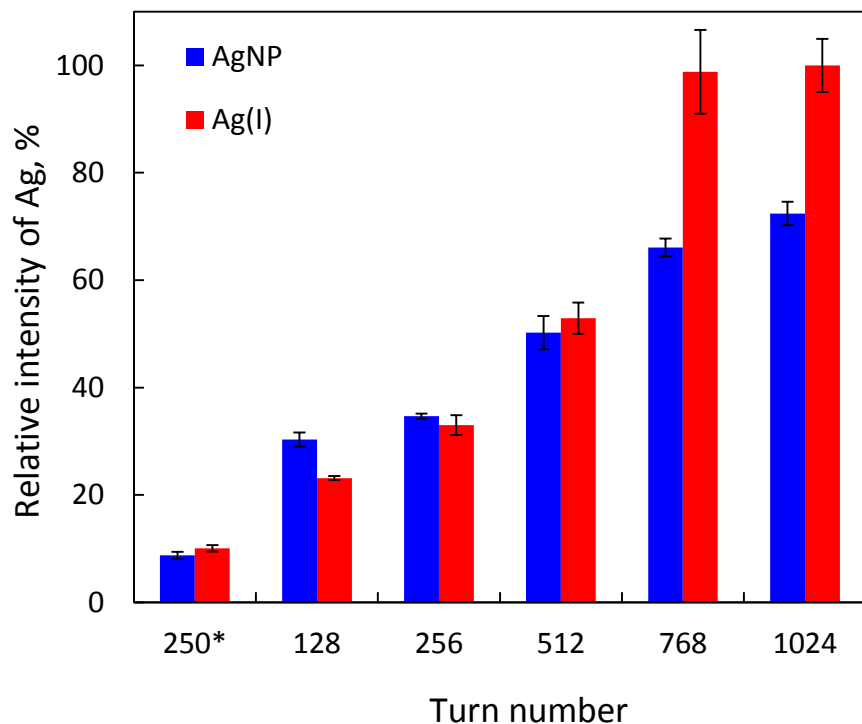


# 3D Printed Centrifugal Separation Technique





# Differentiation of $\text{Ag}^+$ / $\text{AgNPs}$



## Analytical performance of the proposed differentiation scheme

	Working range, ng L <sup>-1</sup>	<i>R</i>	Detection limit, ng L <sup>-1</sup>	Spike recovery*, %
Ag <sup>+</sup>	5–500	0.9947	0.86	96 ± 5
AgNPs	5–500	0.9978	0.51	89 ± 5

\*: Performed in wastewater sampled from a WWTP influent (50 ng L<sup>-1</sup>)