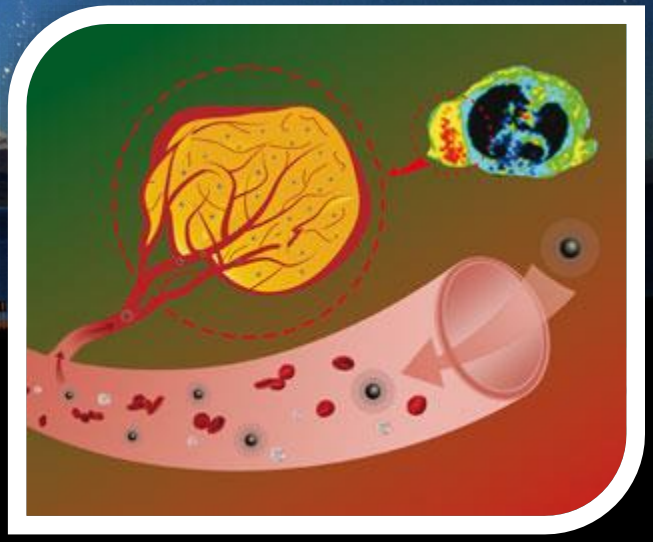
ICP-MS-based *in vivo* analytical method for engineered nanoparticles



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The kinetics of the tissue distribution of silver nanoparticles of different sizes

D.P.K. Lankveld [a], A.G. Oomen [b], P. Krystek [c], A. Neigh [d], A. Troost – de Jong [c], C.W. Noorlander [b], J.C.H. Van Eijkeren [f], R.E. Geertsma [e], W.H. De Jong [a,*]

To date,almost all toxicological experiments dealing with nanoparticles describe the total inhaled, ingested, injected, or dermally applied dose of nanoparticles and do not investigate absorption or internal exposure. The internal exposure is that part of the external dose of nanoparticles that enters the systemic circulation and thus potentially reaches all organs and tissues.

Potential target organs for toxicity can be identified, by studying the distribution of nanoparticles over various organ systems preferably following intravenous administration.

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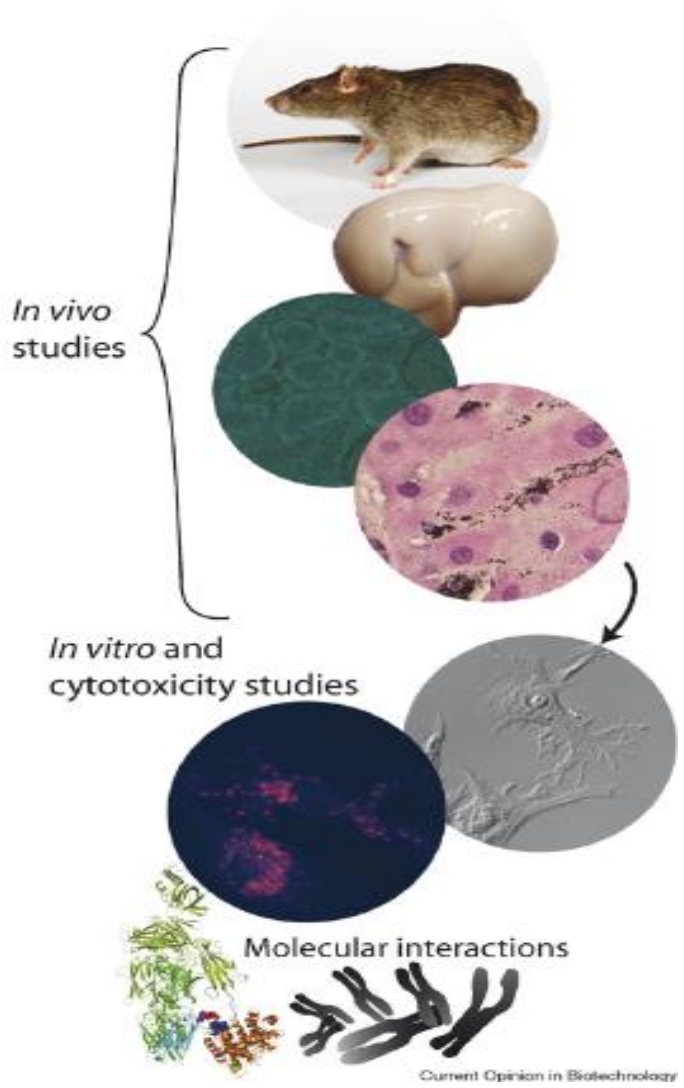
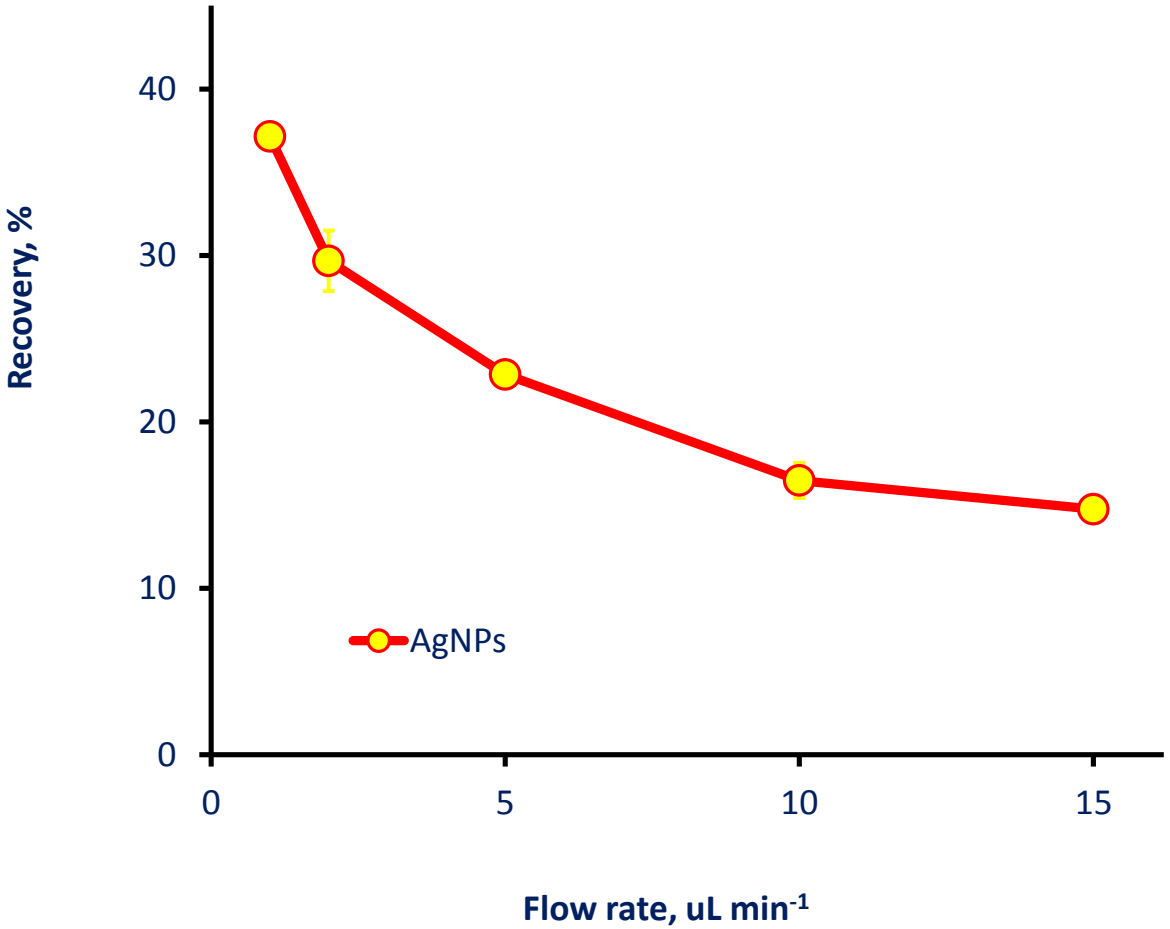
Nanotoxicity: the growing need for *in vivo* study

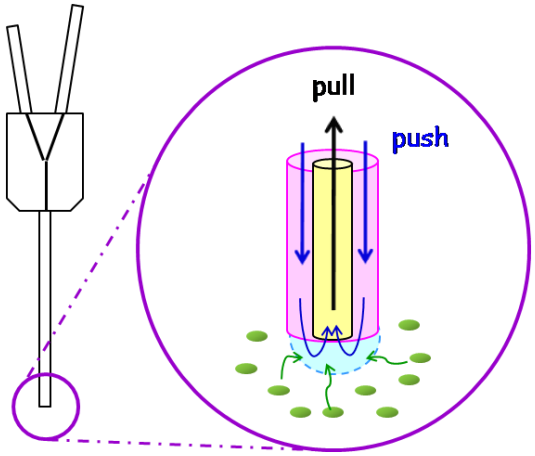
Hans C Fischer[1,2] and Warren CW Chan[1,2]

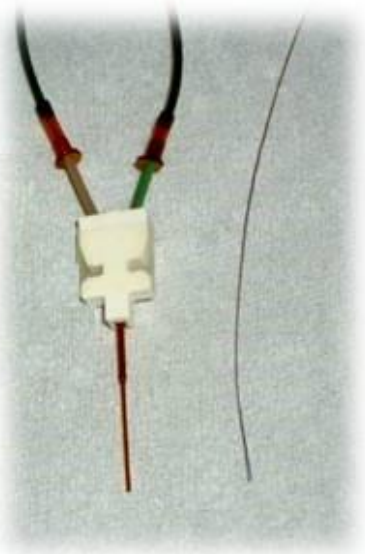
Nanotoxicology is emerging as an important subdiscipline of nanotechnology. Nanotoxicology refers to the study of the interactions of nanostructures with biological systems with an emphasis on elucidating the relationship between the physical and chemical properties (e.g. size, shape, surface chemistry, composition, and aggregation) of nanostructures with induction of toxic biological responses. In the past five years, a majority of nanotoxicity research has focused on cell culture systems; however, the data from these studies could be misleading and will require verification from animal experiments. *In vivo* systems are extremely complicated and the interactions of the nanostructures with biological components, such as proteins and cells, could lead to unique biodistribution, clearance, immune response, and metabolism. An understanding of the relationship between the physical and chemical properties of the nanostructure and their *in vivo* behavior would provide a basis for assessing toxic response and more importantly could lead to predictive models for assessing toxicity. In this review article, we describe the assumptions and challenges in the nanotoxicity field and provide a rationale for *in vivo* animal studies to assess nanotoxicity.



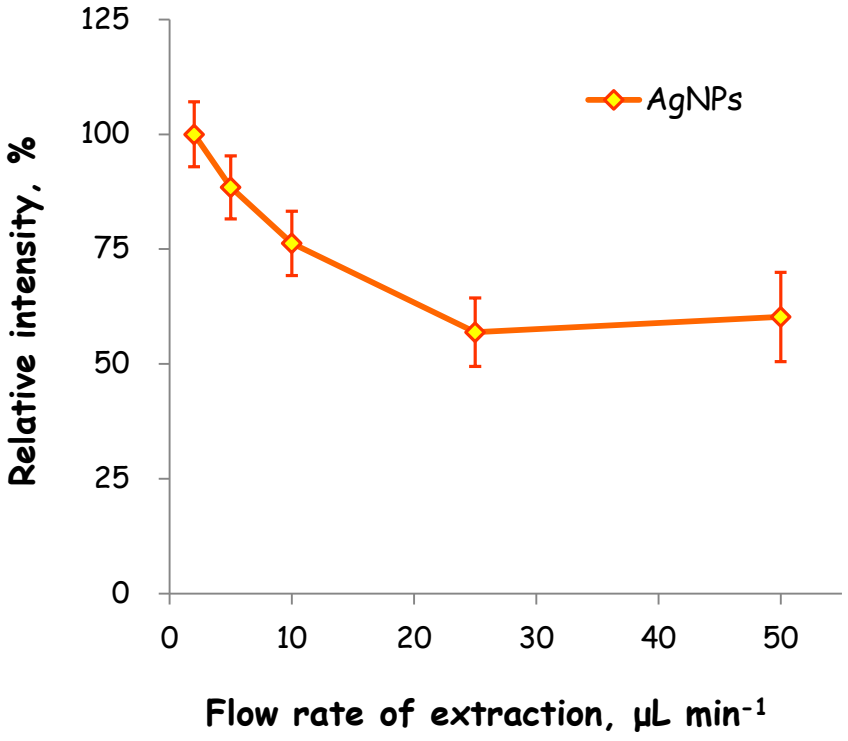
Push-pull Perfusion Sampling for AgNPs

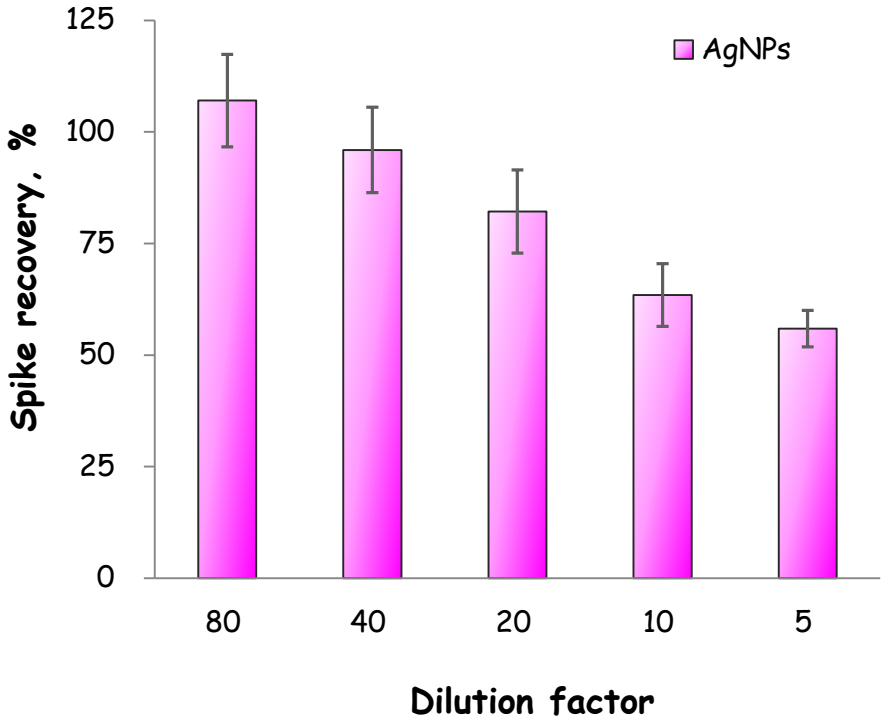


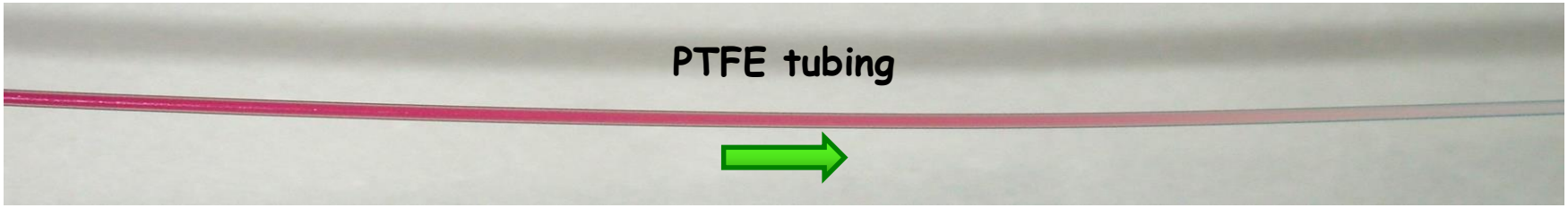




Effect of Extraction Flow Rate and Blood Matrix on Extraction Efficiency







Optimized operational conditions

Solid Phase Extraction

Length of PTFE Tubing	200 cm
Inner diameter	0.007 inch
Capacity	0.46 fmole cm^{-2}

Elution

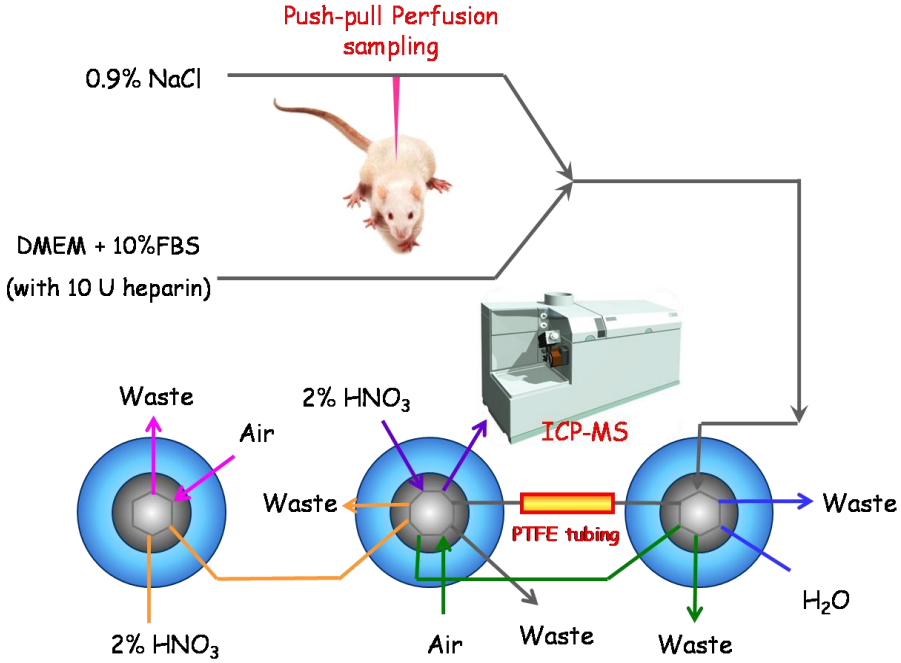
Eluent	2% HNO_3
Flow rate	400 µL min^{-1}

Sample Loading

Flow rate	50 µL min^{-1}
pH value	7.4
Mixing buffer	DMEM+10% FBS

Push-pull Perfusion

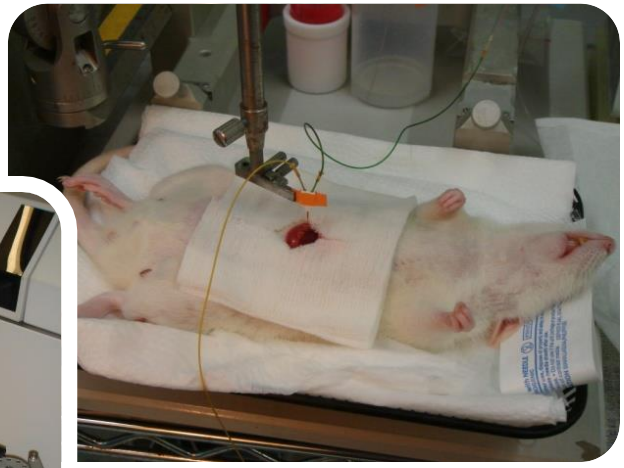
Flow rate	5 µL min^{-1}
Dilution factor	10
Sampling frequency	6 h^{-1}

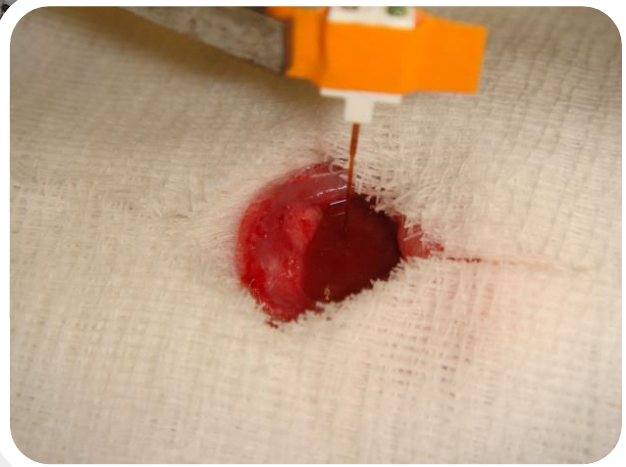


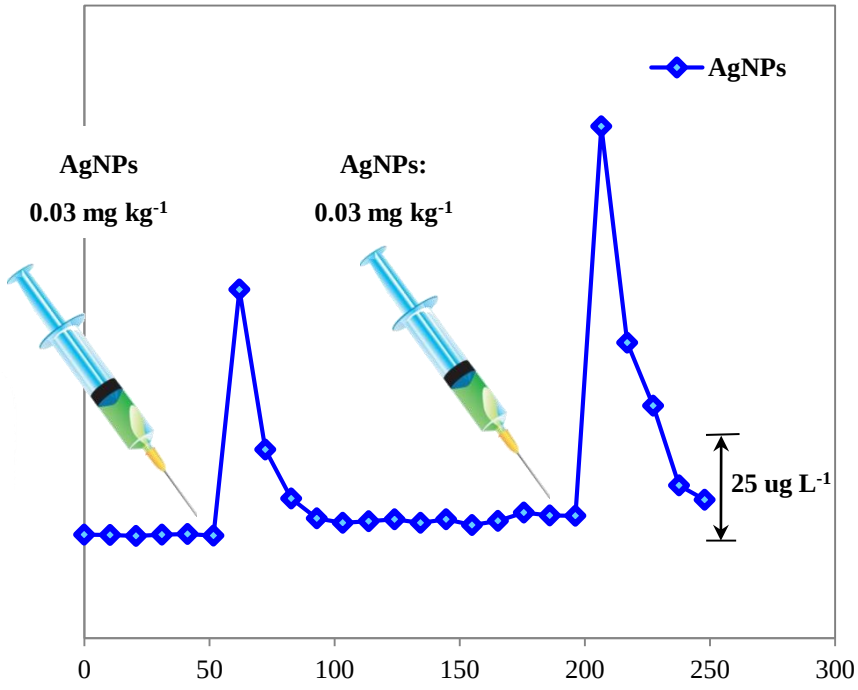
Analytical performance

	m/z 107	m/z 109
Calibration curve (µg L^{-1})	1-100	1-100
Correlation coefficient	0.996	0.997
Detection limit (µg L^{-1})	0.74	0.64
Spike recovery (%)	101	103

In vivo Monitoring of AgNPs in Rat Liver







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In vivo measurement of extravasation of silver nanoparticles into liver extracellular space by push–pull-based continuous monitoring system

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HIGHLIGHTS

- An analytical system composed of PPP sampling, in-tube SPE, and ICP-MS was developed.
- The system's detection limit and temporal resolution were 0.64 μg L^{-1} and 10 min.
- The transport kinetics of extracellular AgNPs in rat liver was investigated *in vivo*.
- Our results revealed the clearance of AgNPs may be blocked by a prior administration.

GRAPHICAL ABSTRACT