Modelling NP
Toxicity at the Molecular Level

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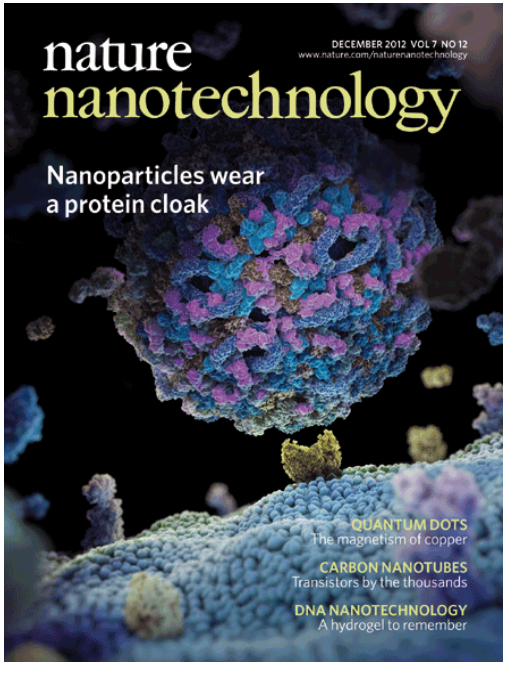
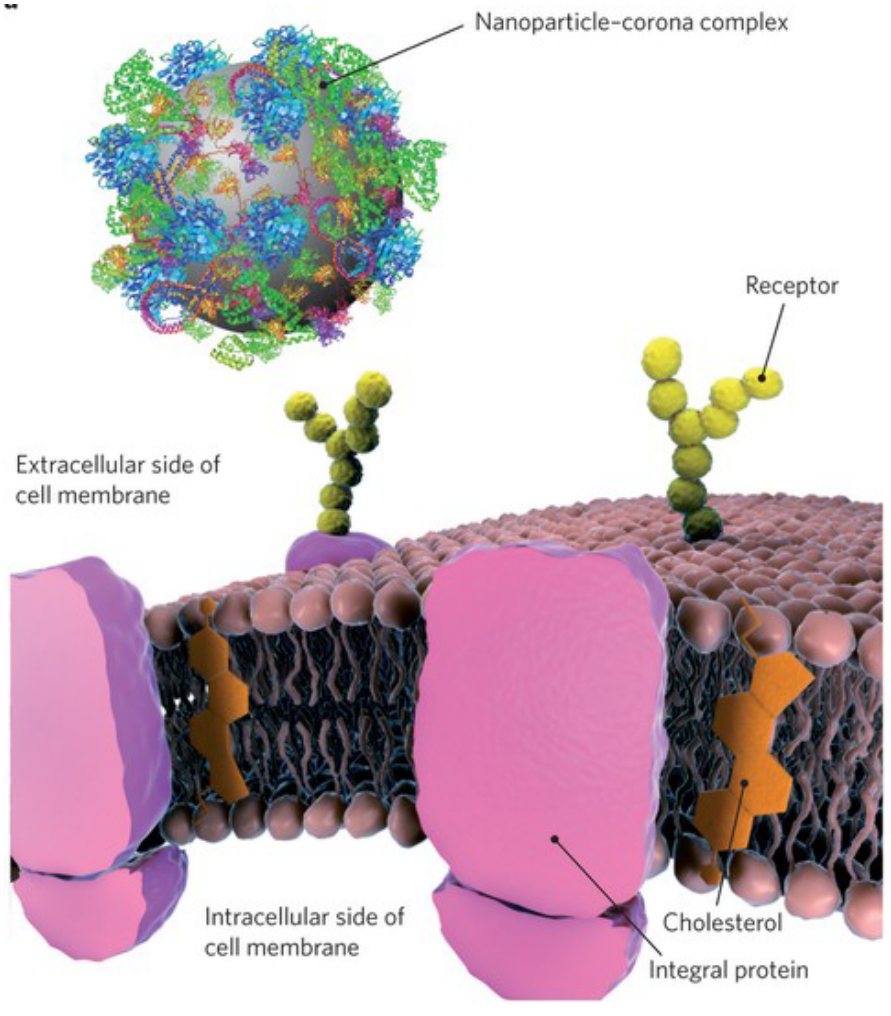
Nanoparticle Identity

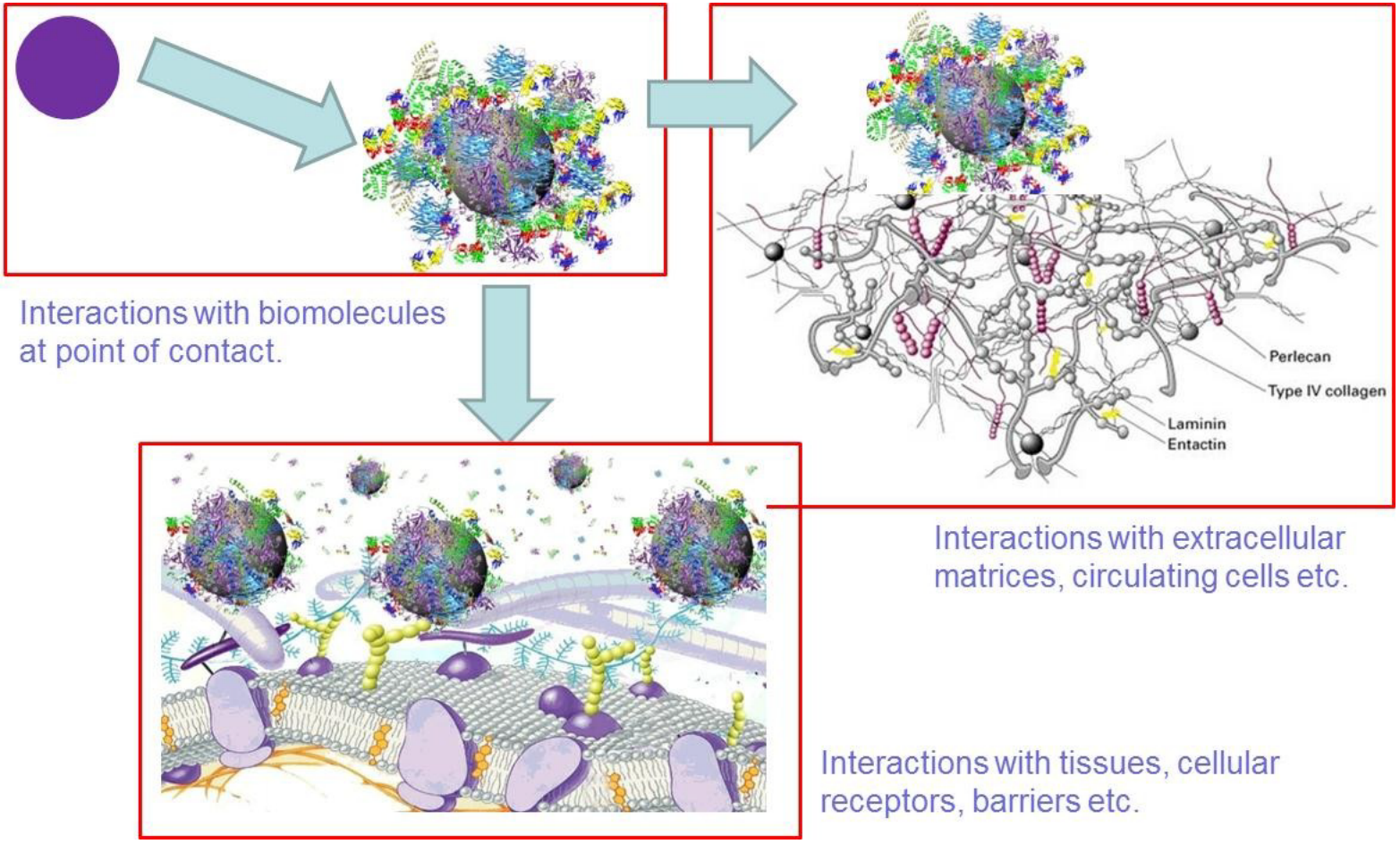
In the body, nanoparticle associates with biomolecules



M. P. Monopoli *et al. Nature Nanotechnology* **7,** 779-786 (2012)



Nanoparticle Identity



M. P. Monopoli *et al. Nature Nanotechnology* **7,** 779-786 (2012)

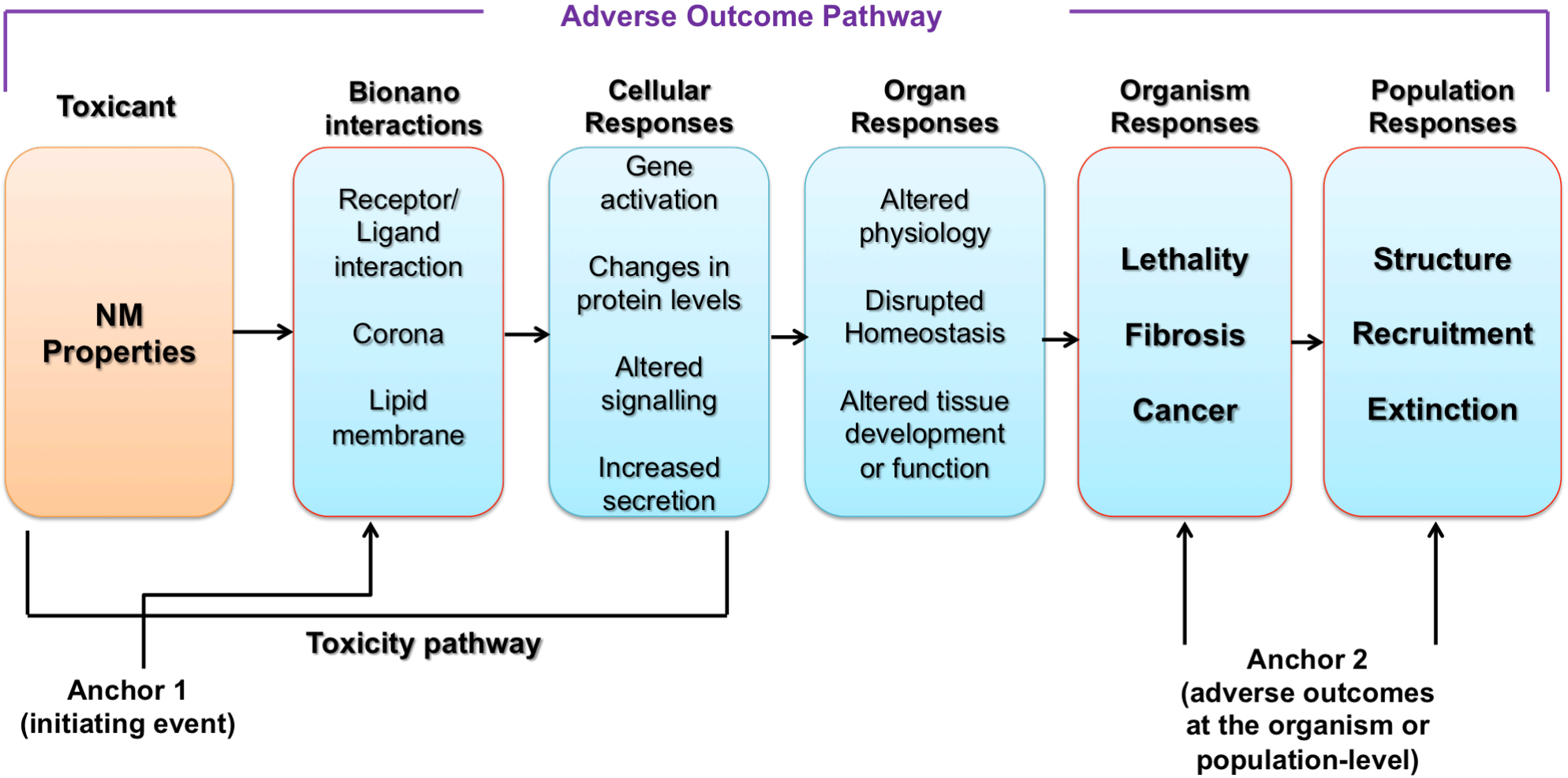
Where we are

- We have limited capacity to model the NP-caused hazards at the molecular level except for local damage
- Systemic responses not known
- Bionano interface is poorly understood
  - more work needed to build predictive models
  - more work needed to obtain relevant descriptors from experiment/simulation

We need more work to estimate real dosage/NP state after uptake

Many of in vitro toxicity endpoints are irrelevant

Mechanistic Understanding of Toxicity



T. E. H. Allen et al., Defining Molecular Initiating Events in the Adverse Outcome Pathway Framework for Risk Assessment. *Chem. Res. Toxicol.* 2014, **27**, 2100−2112

Outlook

New focus:

Pathway-based modelling / assessment:

Understanding of bionano interactions is needed to address MIEs

Mechanistic understanding of nanotoxicity

Another level of complexity:

- Knowing the nanomaterial chemistry is not enough: coating, size, shape, adsorbed materials can be equally important
- Nanoparticles use specific ways of systemic distribution, which are unavailable for individual molecules
- Toxicity and adverse outcomes might be related to molecular perturbation of cell structures

Next steps

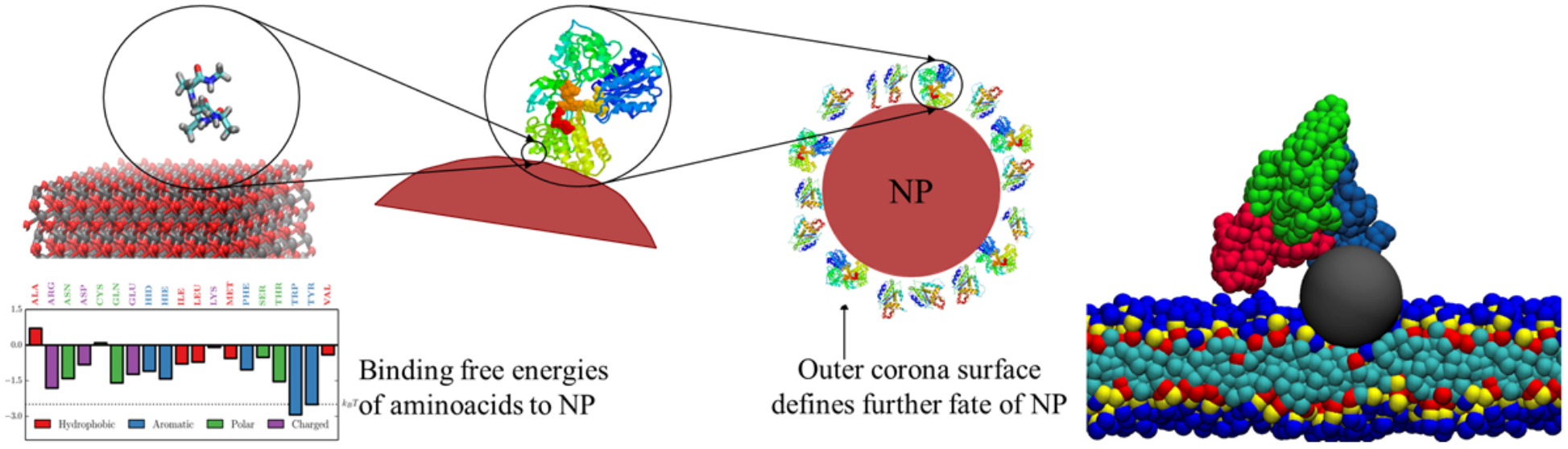
Work with collected databases (MODENA)

Add more advanced / more suitable descriptors:

- Band gap
- Ionisation potential
- Dissolution rate
- Hydration energy
- Surface energy
- Protein binding affinity

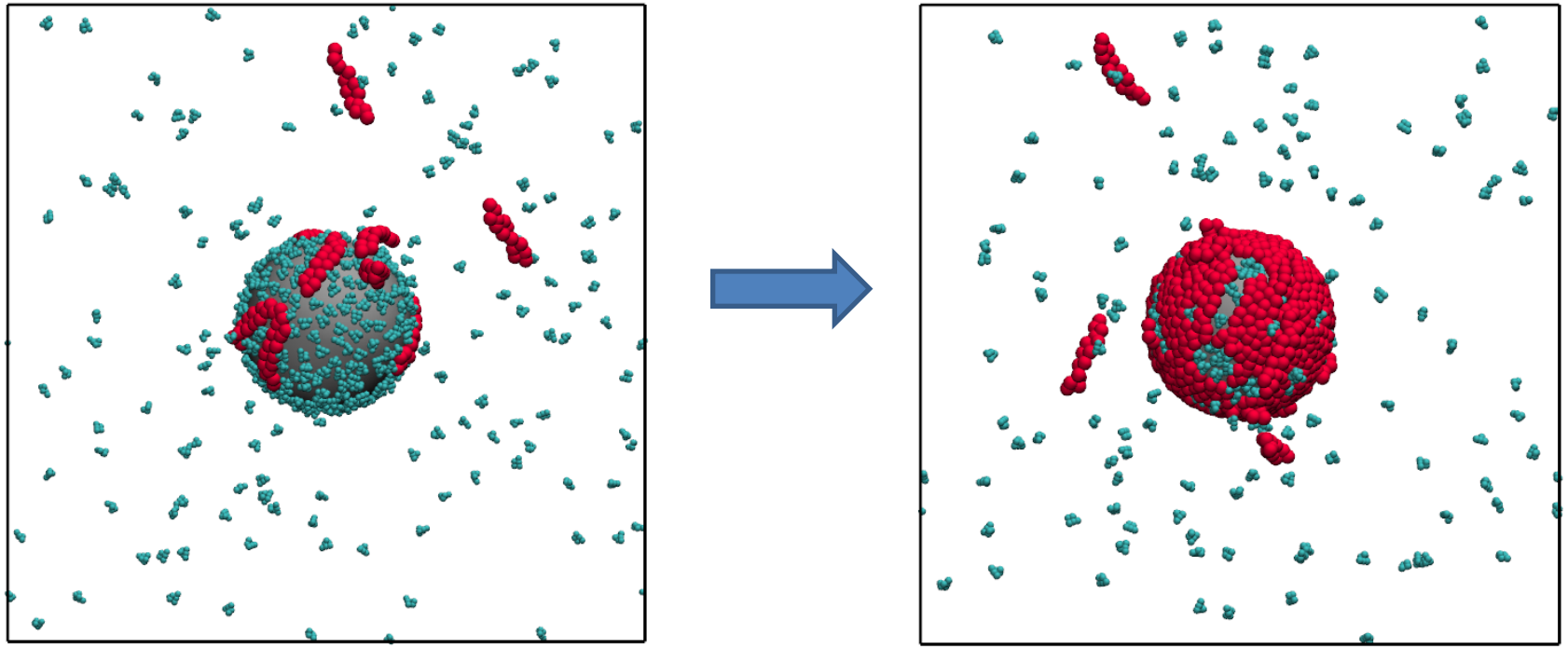
Reanalyse

Multiscale Modelling Approach



FP7 MembraneNanoPart (2013-15)
H2020 SmartNanoTox (2016-20)

Time-resolved Interface Structure



Vroman effect: HSA →Fib

L. Vroman, Nature **196**, 476–477 (1962)

SmartNanoTox