ARTICLES
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Glomerular barrier behaves as an atomically precise bandpass filter in a sub-nanometre regime

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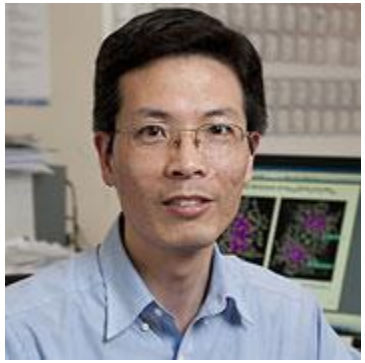
Fundamental structure-property relationships of noble metals on the nano scale and applying new functional nanoparticles in biomedical imaging



Rongchao Jin
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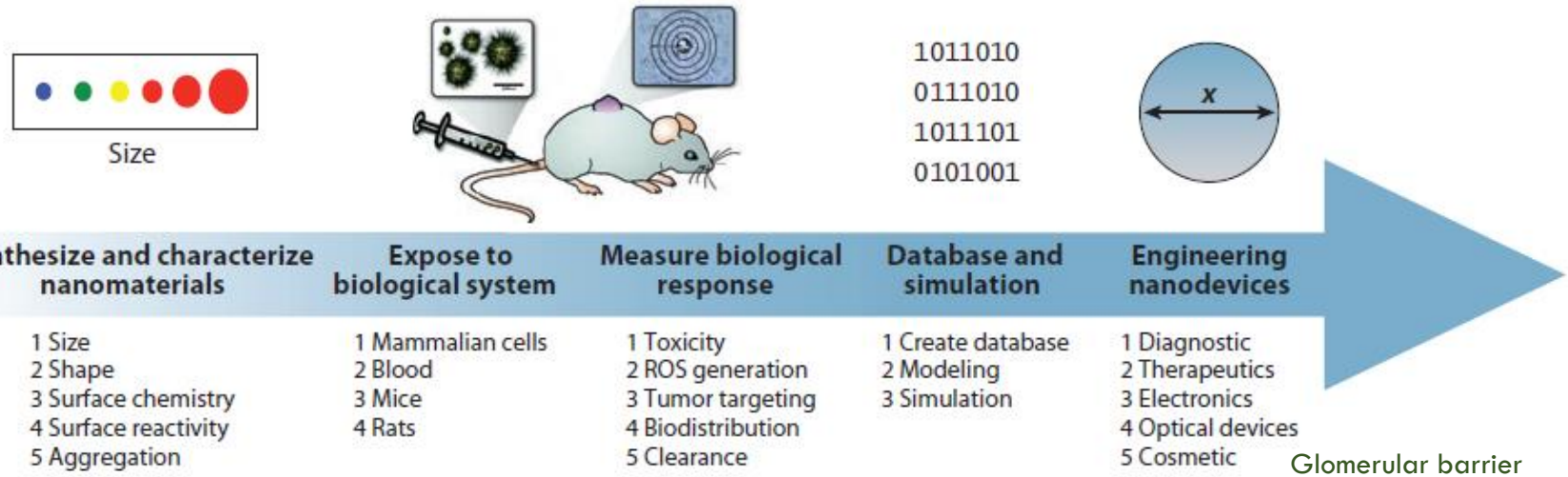
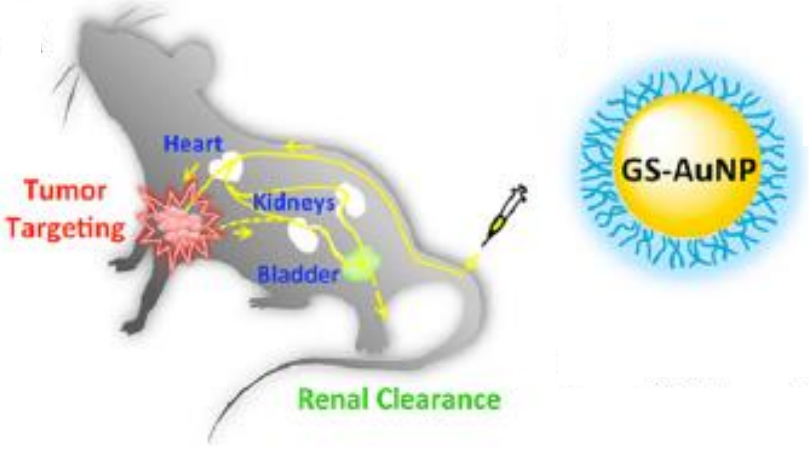
Nanoscience, nanoparticles, synthesis, catalysis, optics

Debasmita Ghosh
03.02.2018

Nano-bio interaction



Albanese et al., *Annu. Rev. Biomed. Eng.*, 2012, 16, 1



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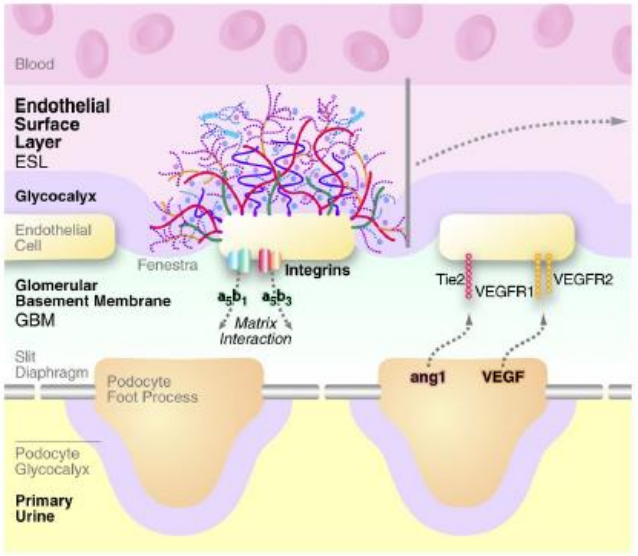
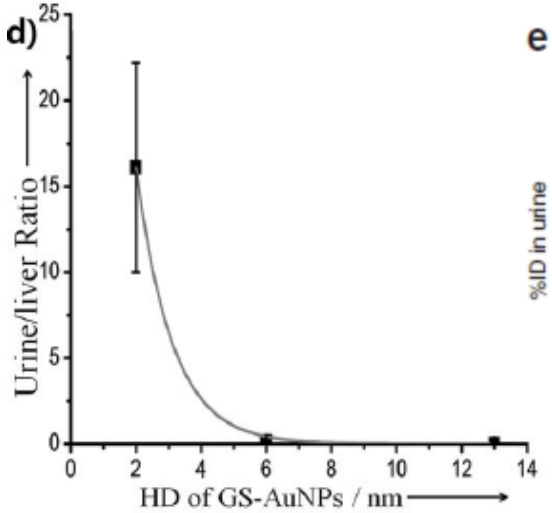
Glomerular barrier



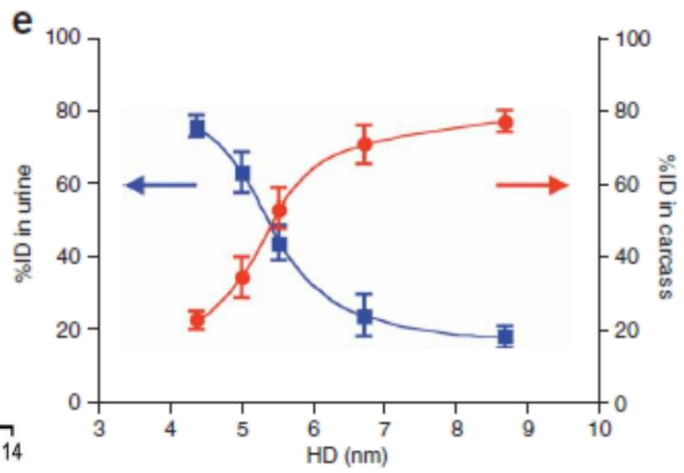
Haraldsson et al., *Physiol Rev.*, 2008, 88, 451

Renal clearance of atomically precise clusters

Importance

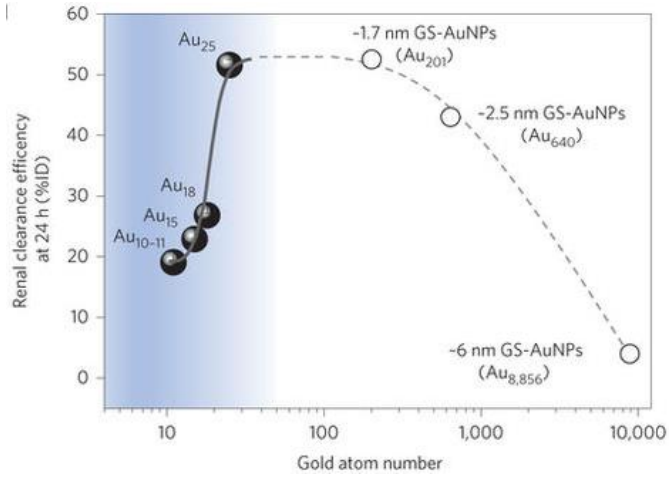


Zhou et al., *Angew. Chem. Int. Ed.*, 2011, 123, 3226



Choi et al., *NATURE BIOTECHNOLOGY*, 2007, 25, 1165

Glomerulas was a "size-cutoff" slit

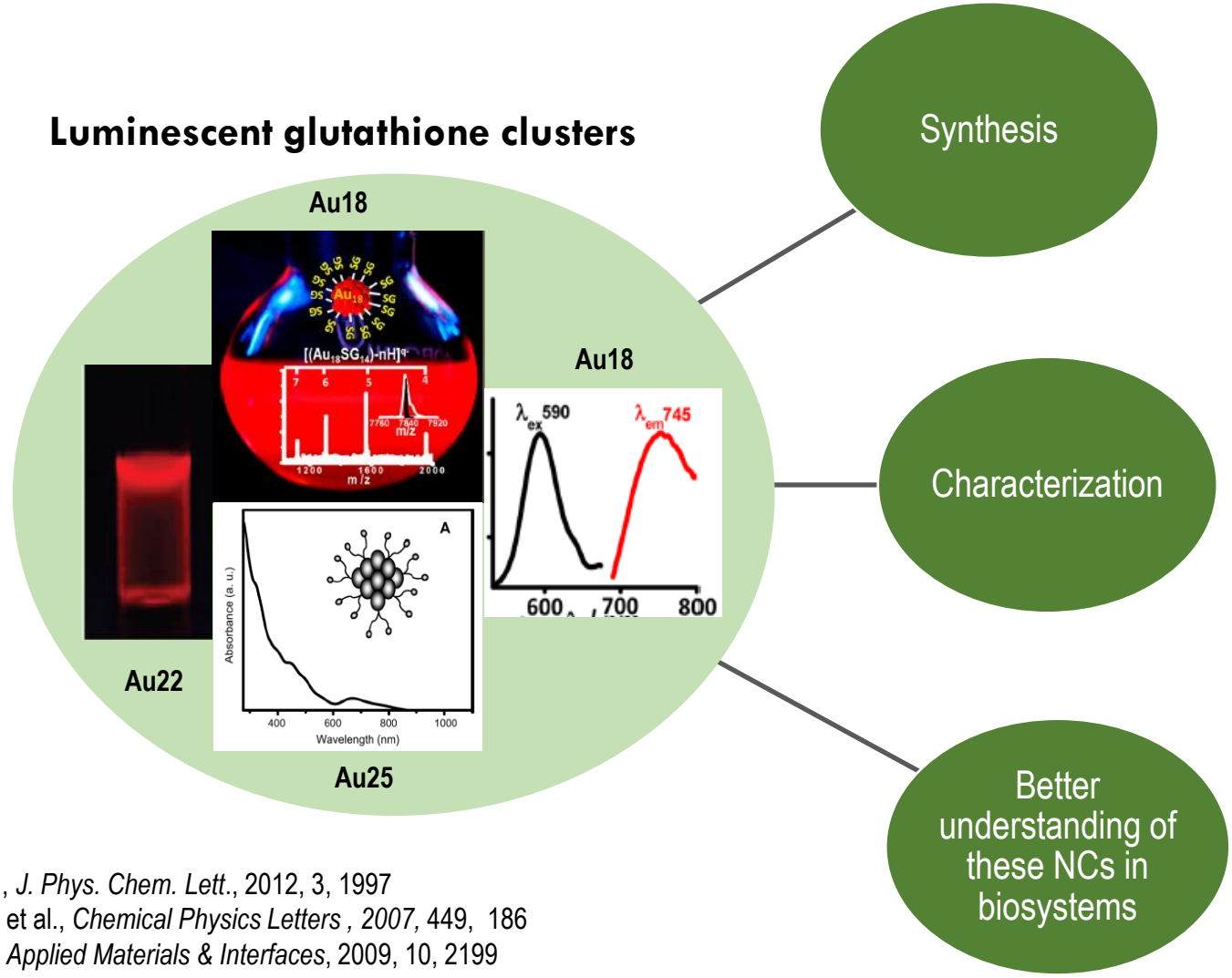


Du et al., *NATURE NANOTECHNOLOGY* , 2017, 12, 1096

Glomerulas becomes an atomically precise "bandpass" barrier of ultrasmall Au NPs

Designing clinically translatable precised nanomedicine for strokes, hypertension, atherosclerosis, chronic renal failure

Relevance



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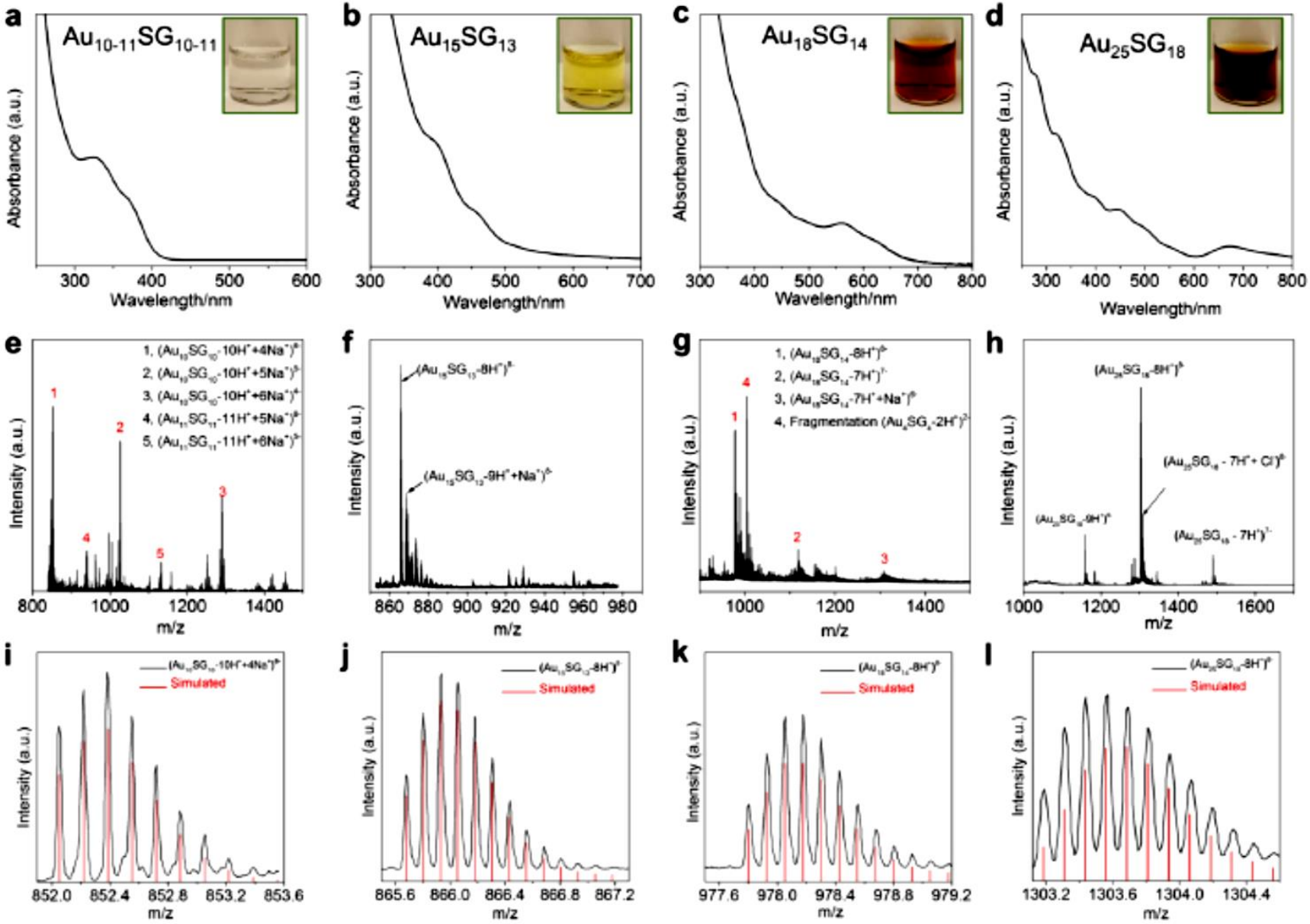
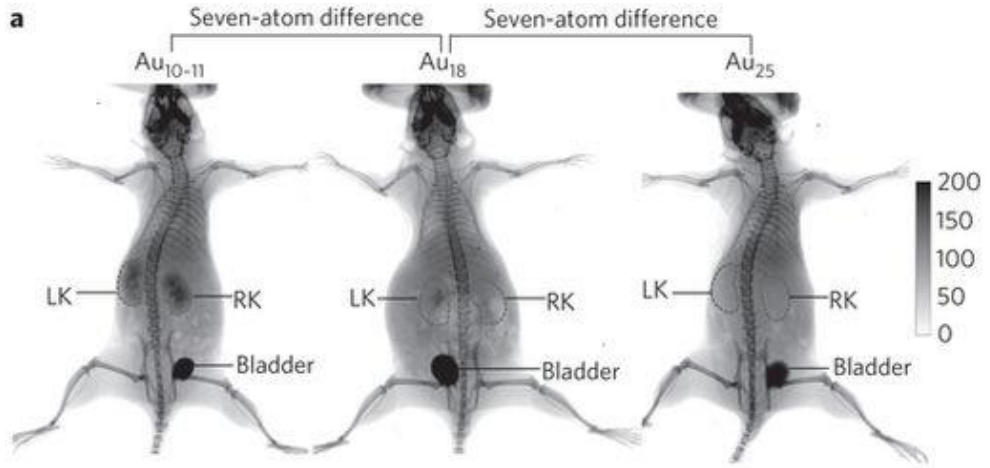
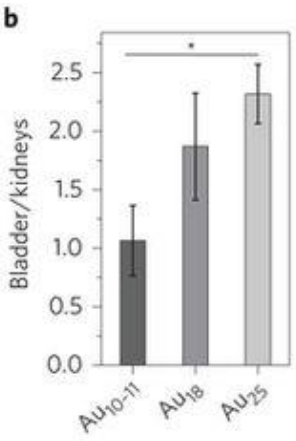
Muhammed et al., *Chemical Physics Letters , 2007,* 449, 186
Shibu et al., *Applied Materials & Interfaces*, 2009, 10, 2199

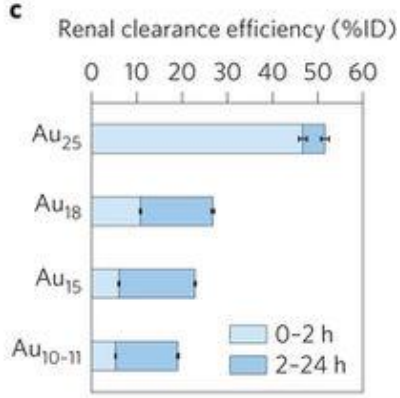
Characterization of NCs

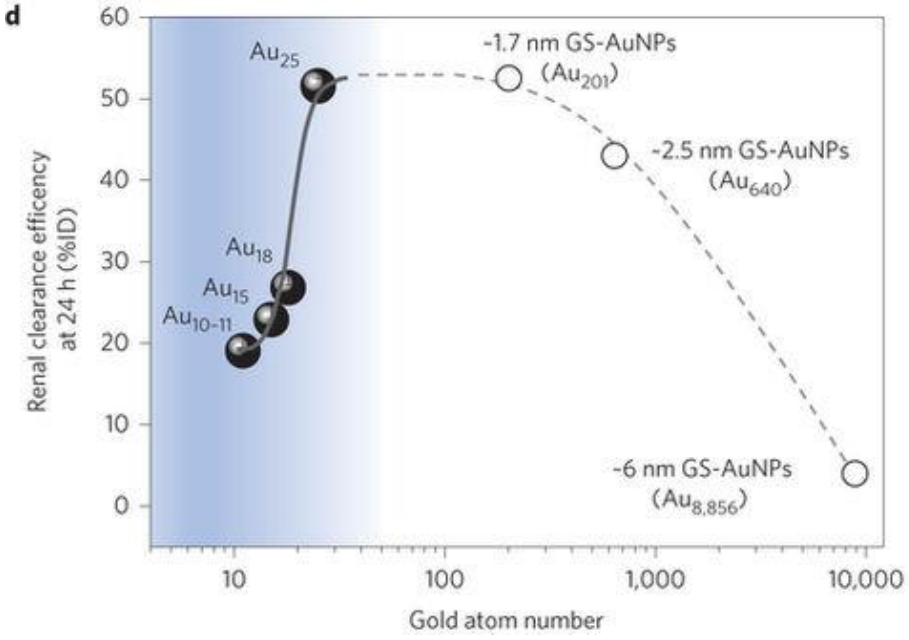


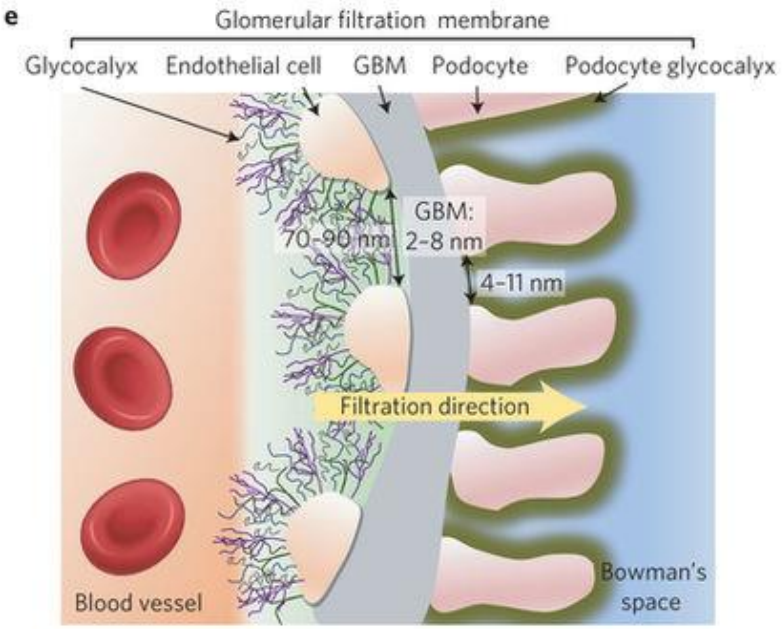
Renal clearance of different sized AuNCs



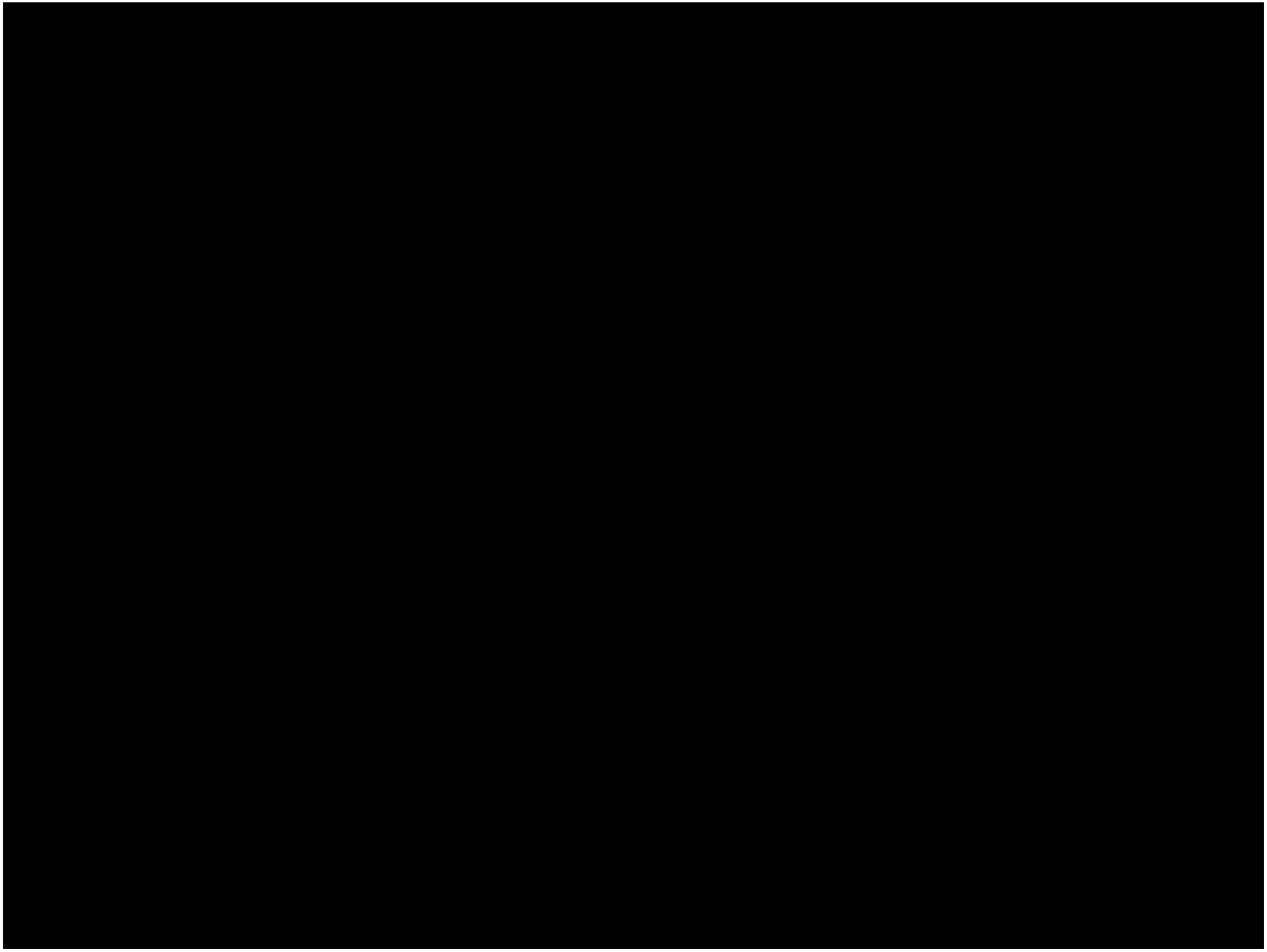




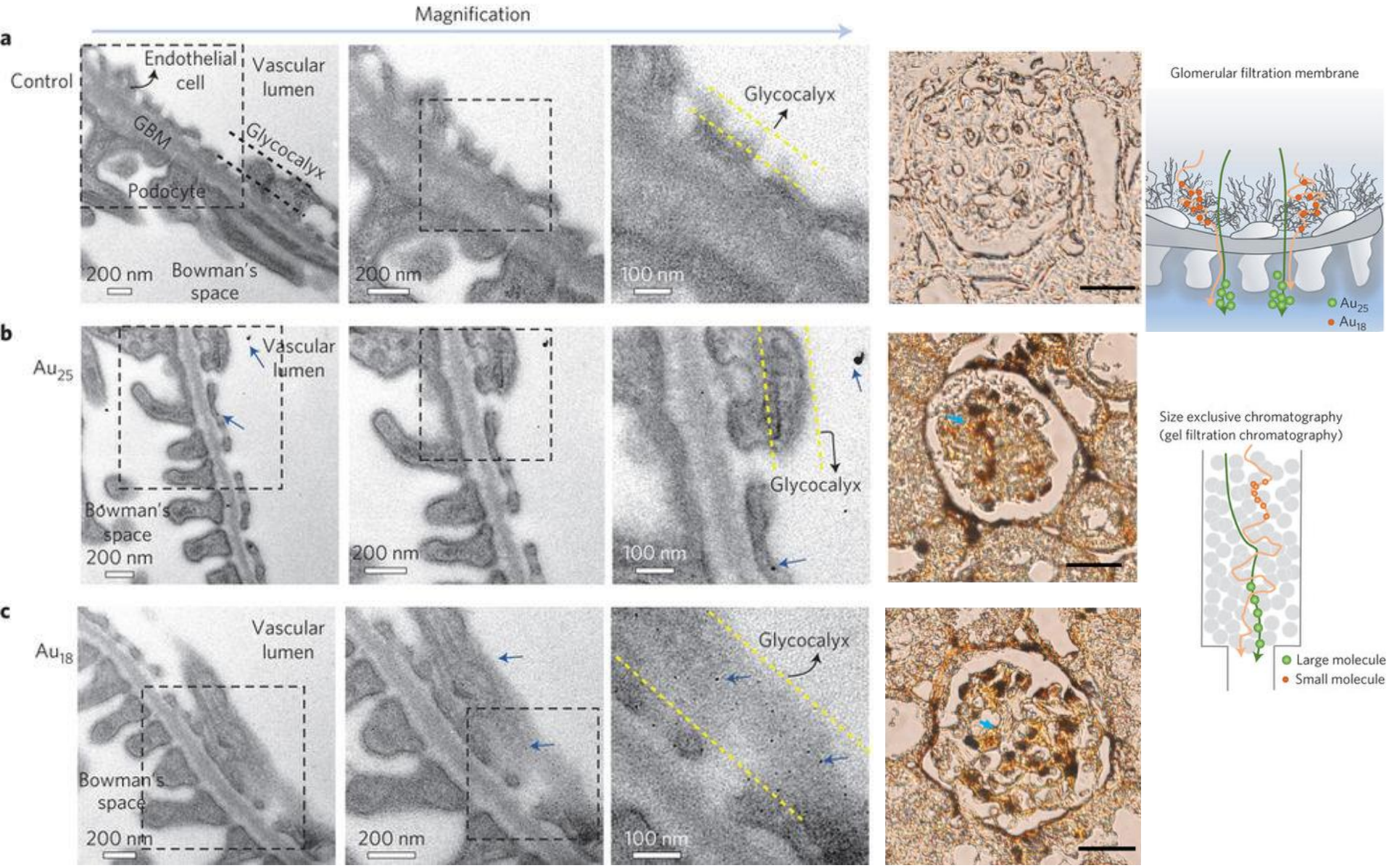




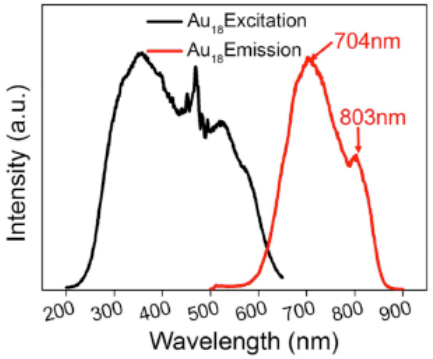
Renal clearance of different sized AuNCs

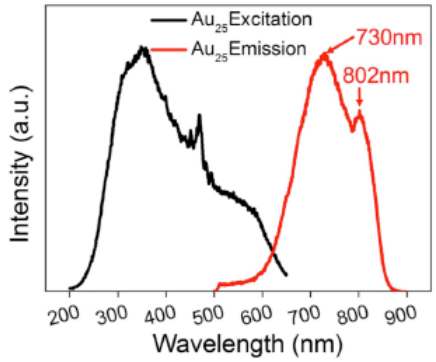


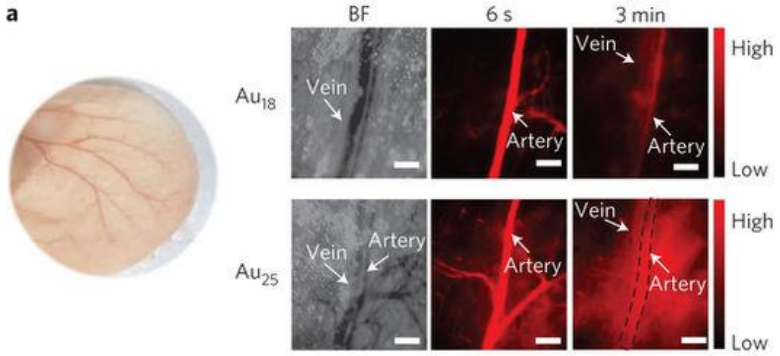
Glomerular filtration of Au_{18} and Au_{25}

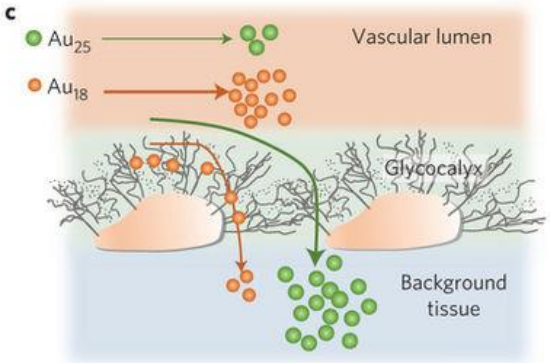


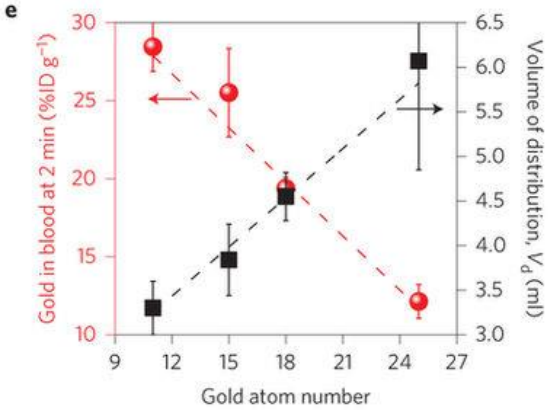
Normal vessel extravasation and pharmacokinetics

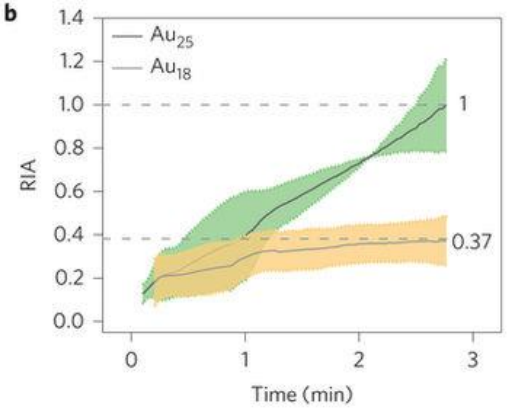


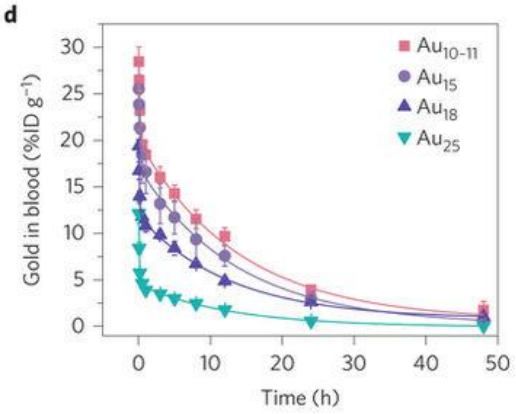


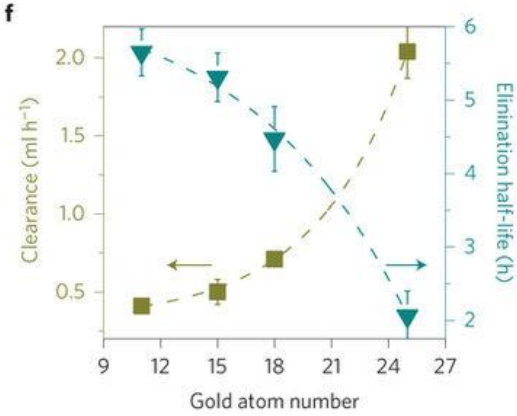




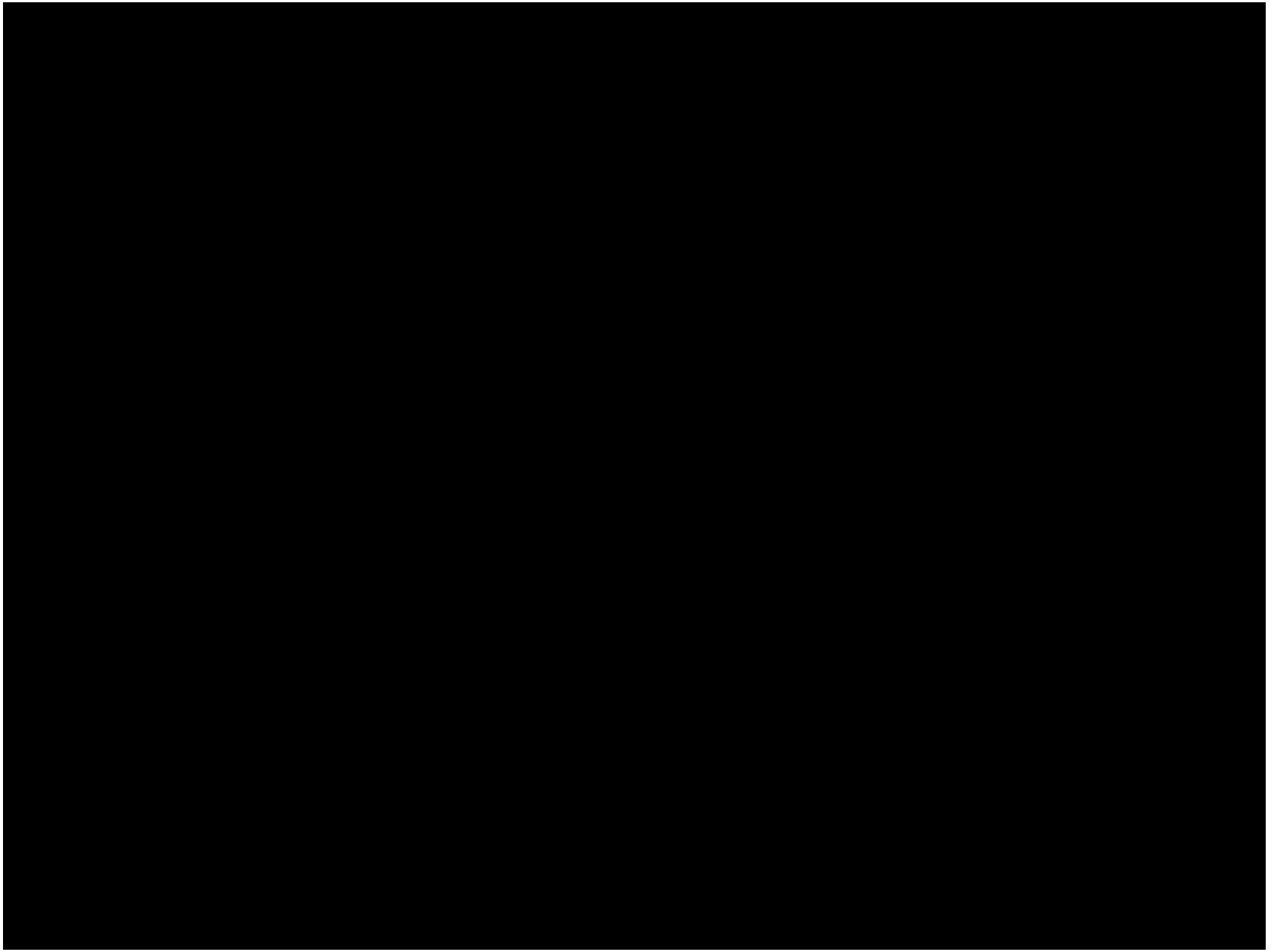




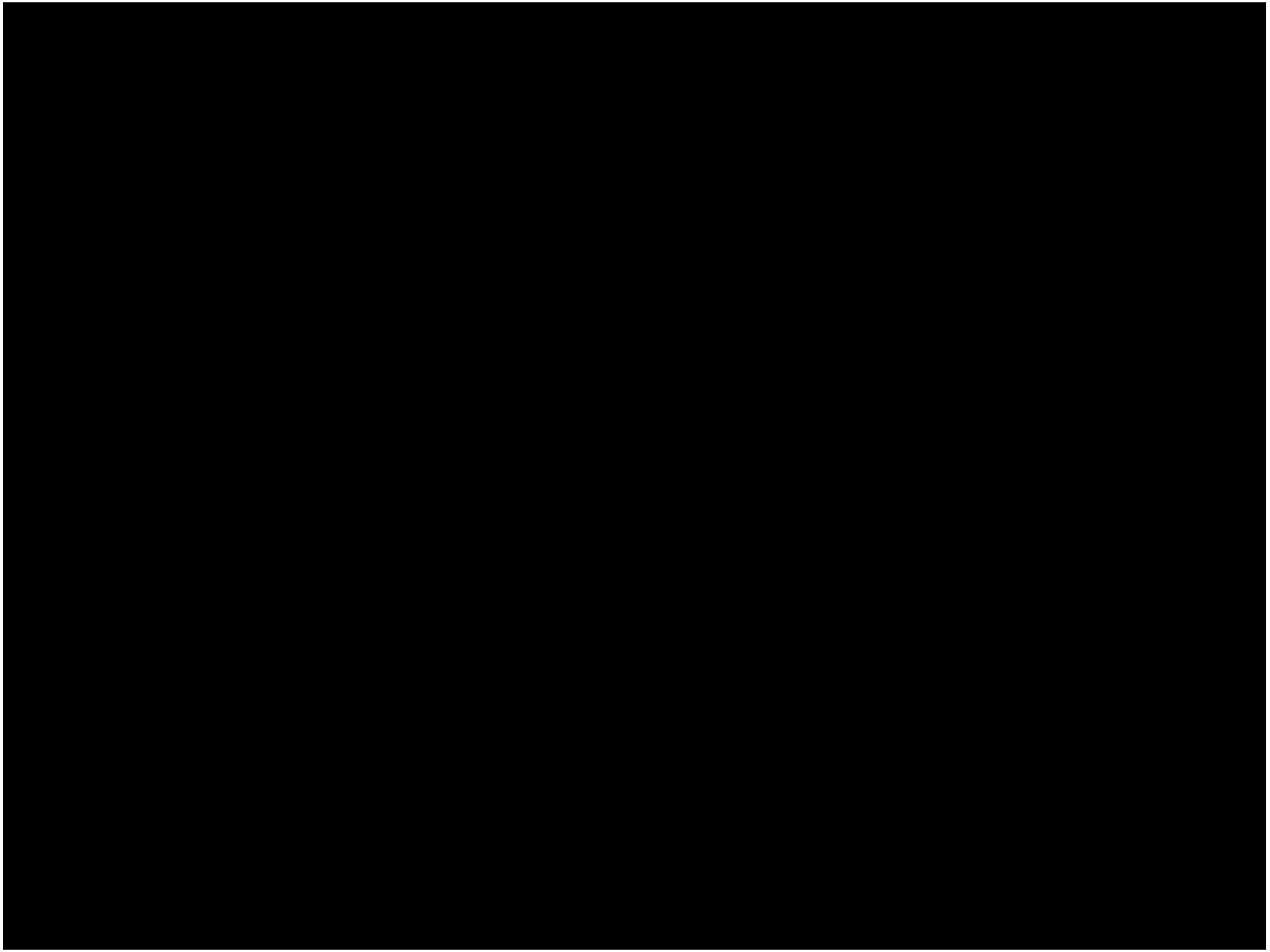




Normal vessel extravasation and pharmacokinetics



Normal vessel extravasation and pharmacokinetics

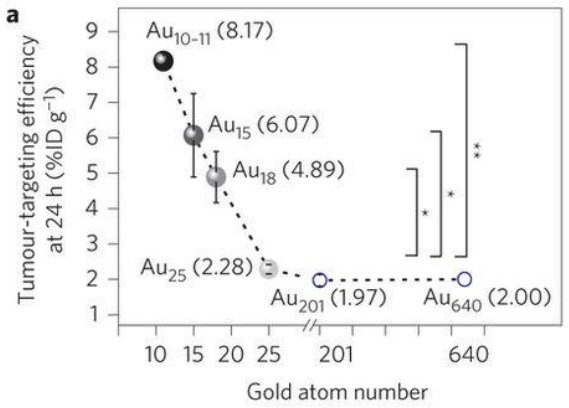


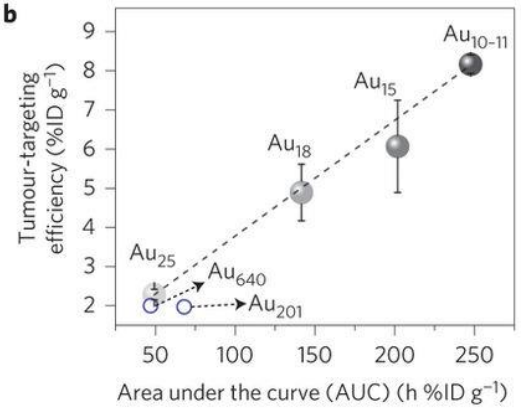
Passive tumor targeting

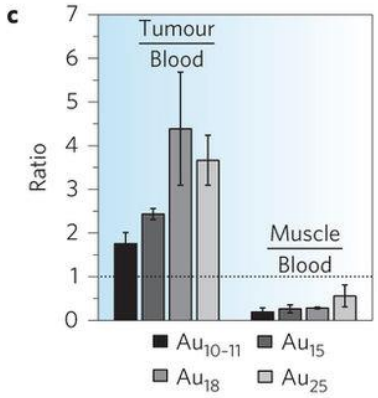
- ✓ Size-dependent properties, multimodality, high physiological stability
- ✓ **Strong Enhanced permeability and retention (EPR) effect**
- ✓ Prolonged elimination half-life
- ✓ **Efficient renal clearance**
- ✓ Low accumulation in RES (Reticuloendothelial system) organs

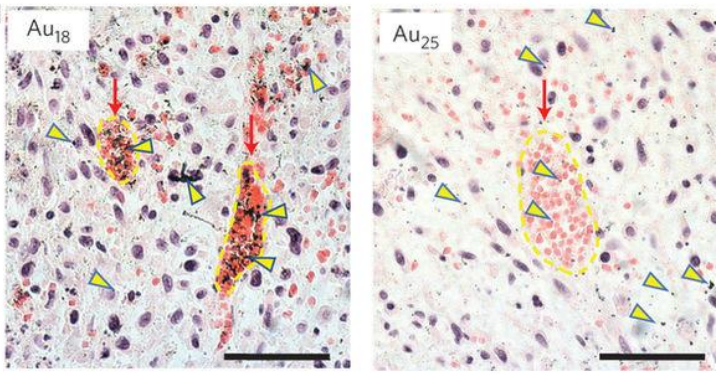
Small molecular probes	less EPR effect	more renal clearance
Conventional nanoprobes	more EPR effect	less renal clearence
Molecular nanoprobes	**more EPR effect**	**more renal clearance**

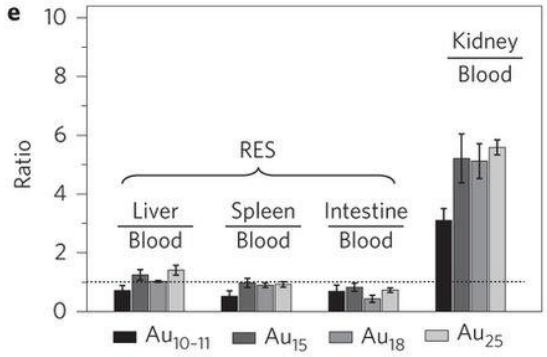
Passive tumor targeting of Au NCs

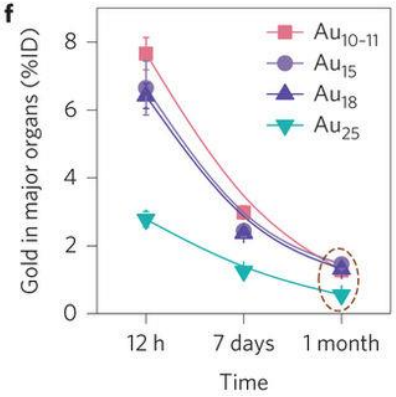


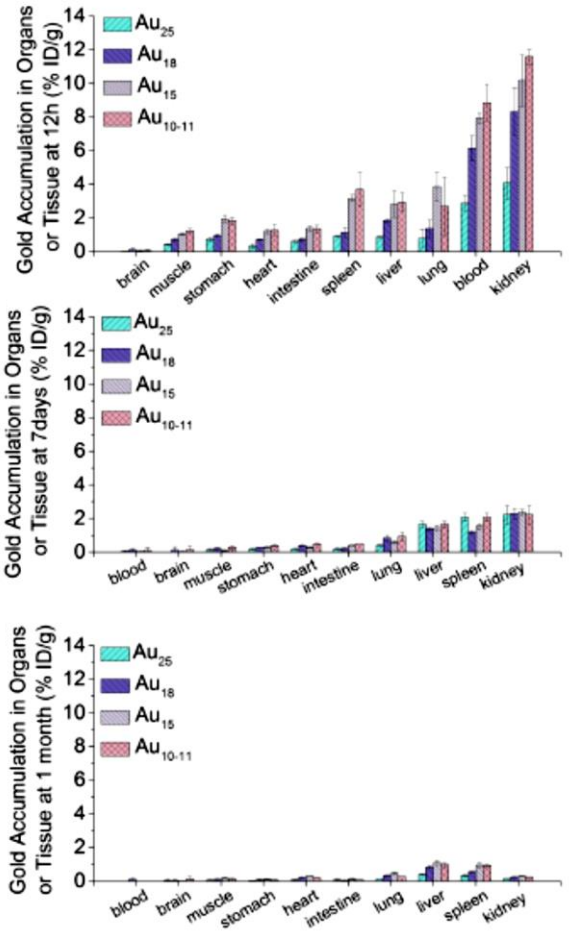












Conclusion

- The glomeruli can serve as an atomically precise barrier to slow down the renal clearance of clusters with size below 1 nm.
- A few-atom decrease in cluster size results in a nearly one order reduction in renal clearance.
- The retention of the smaller NCs by the glycocalyx of glomeruli can be explained by the separation principle used in the size-exclusion chromatography.
- This phenomenon significantly impacts their accumulation in cancerous tissues through the EPR effect.
- This discovery highlights how precisely the glomerulus and the body could response to ultrasmall AuNPs, which might be generalized to many other renal-clearable nanosystems.