Protein stability and drug delivery

Morphology and protein-protein interactions
Rheology: subcutaneous injection

Advanced Functional Nanomaterials (metals and metal oxides/polymers)

Control morphology/crystallinity via nucleation and growth in sol’n
Colloidal stability (ligands and polymers on the surface)
Optical, magnetic and electrocatalytic properties $= f$ (morphology)
Biodegradable photonic Au nanoclusters for cancer imaging

Nanoparticle Interact. with Liq. and Solid Interfaces

Oil/water and gas/water interfaces (emulsions and foams)
Solid surfaces (adsorption and transport in porous media)
Subcutaneous injection (SC) of concentrated monoclonal antibodies at 300 mg/ml is a major drug delivery challenge

- >20% of all biopharmaceuticals in clinical trials are mAbs
- Treat cancer, autoimmune diseases, allergies and more
- At high conc. spacings are small – specific short-ranged attraction cause association and high viscosity
  - Hydrogen bonds, anisotropic elect. attraction
  - Hydrophobic interactions

### mAb drugs converted from IV to SC

<table>
<thead>
<tr>
<th>Name</th>
<th>Indication</th>
<th>Company</th>
<th>Conc.</th>
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<tr>
<td>AETEMRA</td>
<td>RA, juvenile arthritis</td>
<td>Genetech</td>
<td>180 mg/mL</td>
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<td>Herceptin</td>
<td>Breast and gastric cancer</td>
<td>Roche</td>
<td>120 mg/mL</td>
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Use co-solutes to mitigate attractive interactions to lower viscosity up to 10 x

- Local anisotropic electrostatic attraction
- Hydrophobic interactions
- Depletion attraction

![Chemical structures](image)

<table>
<thead>
<tr>
<th>Co-solute</th>
<th>mAb concentration (mg/mL)</th>
<th>Viscosity (cP)</th>
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<tr>
<td>15:40 His(HCl):Mannitol</td>
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<tr>
<td>40:50:17 Tre:His:CitrA</td>
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<td>50:50:12 Tre:His:PhosA</td>
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Reduce viscosity and incr. protein stability with cosolutes and relate to mAb association

- Co-solutes, ex. (Arg), can be used to reduce self-association and therefore viscosity
- Techniques to measure mAb association
  - Light scattering (DLS, SLS, SAXS)
  - Viscosity vs. shear rate

Reversible Gold Nanoclusters for Imaging/Therapy

- Tune colloidal interactions to form nanoclusters
  - Colloidal assembly based on free energy model
  - Close spacing of gold particles produces intense NIR extinction

- Design reversibility and lack of protein adsorption for clearance

Johnston, Sokolov, Truskett, Stover: ACS Nano (13), JACS (13), JPChem (14), Langmuir(16)
Zwitterionic Polymer/Magnetite Hybrids with High Magnetic Susceptibility and Mobility at High T and Salinity

[3-(Methacryloylamino)propyl]dimethyl(3-sulfopropyl) ammonium hydroxide inner salt (MPDSA)

Foster, Xue, KPJ et al., ACS Macro Letters (14)
Wormlike Micelles Impart Viscoelasticity for Ultra Dry Foams

\[ \mu_{\text{app,capillary}} = \frac{\pi \cdot \Delta P \cdot R^4}{8 \cdot q \cdot L} \]

- 208 trillion m$^3$ of CH$_4$ in shale (world)
- 2~5 million gallons of water/well for disposal

Cationic micelles:
Jamming: slow drainage maintains thick lamellae
Fameau et al., Ang. Chem. (11)
Nanostructured Perovskite Oxides for Electrocatalysis
batteries, supercapacitors, water splitting

Oxygen Evolution Reaction (OER)
\[ 4\text{OH}^- \rightarrow 2\text{H}_2\text{O} + 4\text{e}^- + \text{O}_2 \]

High Surface Area Means High Rate

Mass Activity @ 1.63V

Precursors Incorporation

Mesoporous Template (e.g. KIT-6)
Composite
Mesoporous replica

M.M. Nair et al. C. R. Chimie 17 (2014) 641–655

Cao, Kruk. RSC Adv. 2014

Metal 3d and Oxygen 2p density of states should overlap!


Mefford, Hardin, Johnston, K.P. et al.; LaMnO\textsubscript{3} Pseudocapacitor, Nature Mater. 2014
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NSF Inspire Program
DOE CFSES, DOE NETL
Advanced Energy Consortium, AbbVie, Pfizer, Merck

Welch Foundation
Abu Dhabi Nat. Oil. Co.
GOMRI, NSF CBET, NIH
## Destination of PhD Students

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<tr>
<th>Name</th>
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