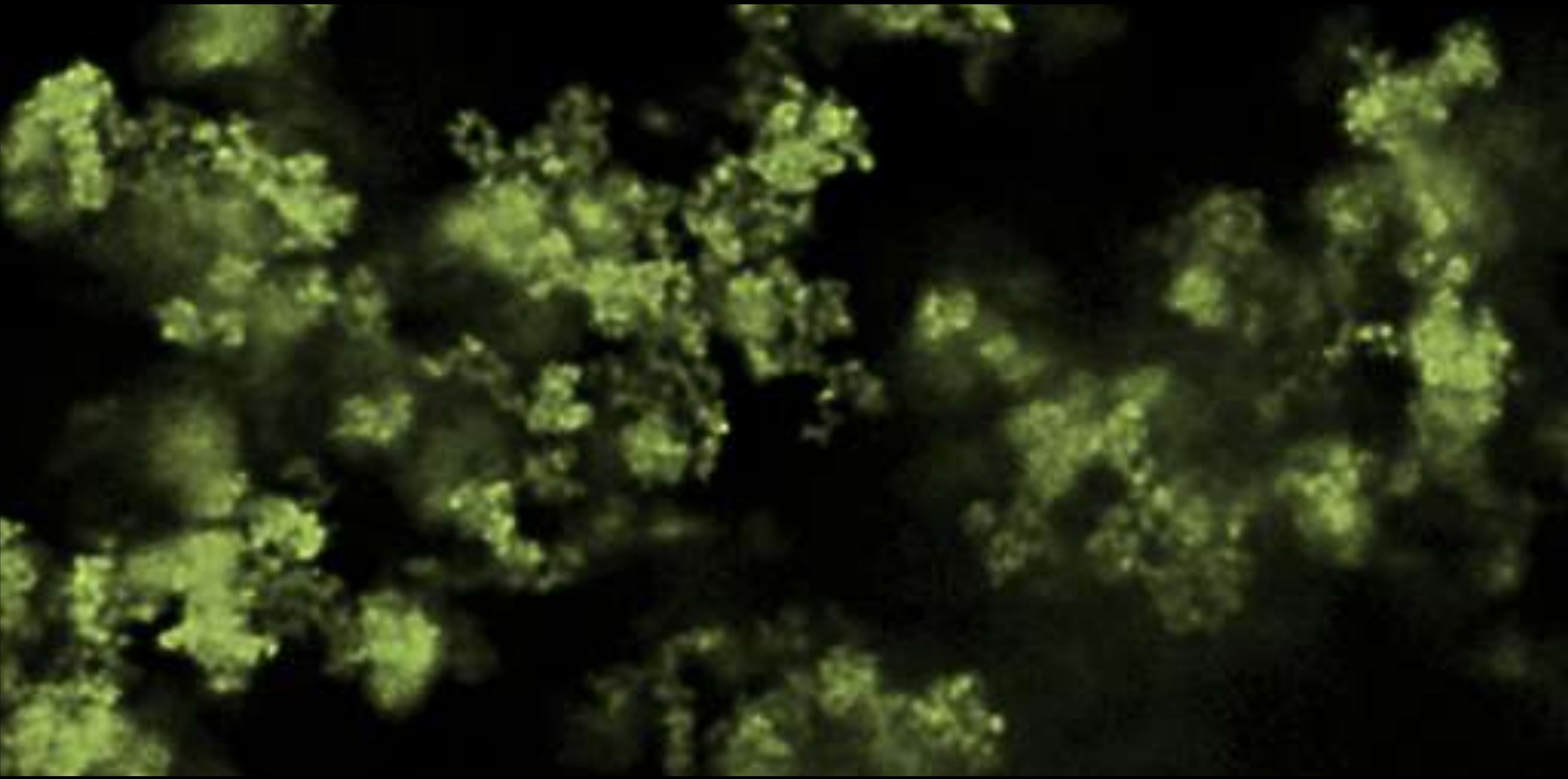
cnrs
Gulliver UMR 7083
ESPCI PARIS
ÉCOLE SUPÉRIEURE DE PHYSIQUE ET DE CHIMIE INDUSTRIELLES DE LA VILLE DE PARIS



Resolving Challenges in Self-Assembly with Nano Real Space Analysis

C. Patrick Royall

Rui Cheng

Ioatzin Rios de Anda

Ross Anderson

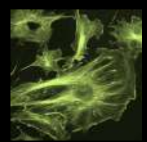
Angelique Coutable

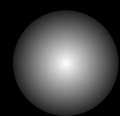
Annela Seddon
Tom Taylor
Jingwen Li

Molecular Foundry

Steve Whitelam

Lengthscales in Soft Matter



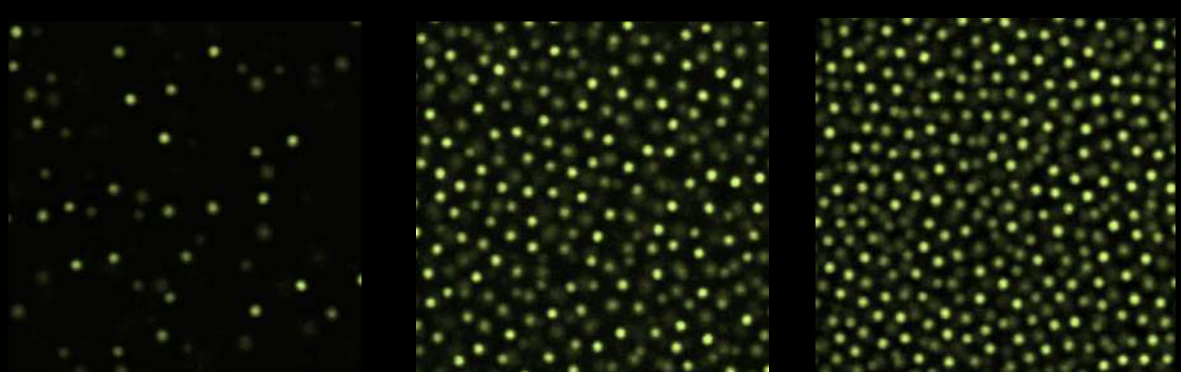


smaller

cells
~10 μm

colloids
~30-3000 nm

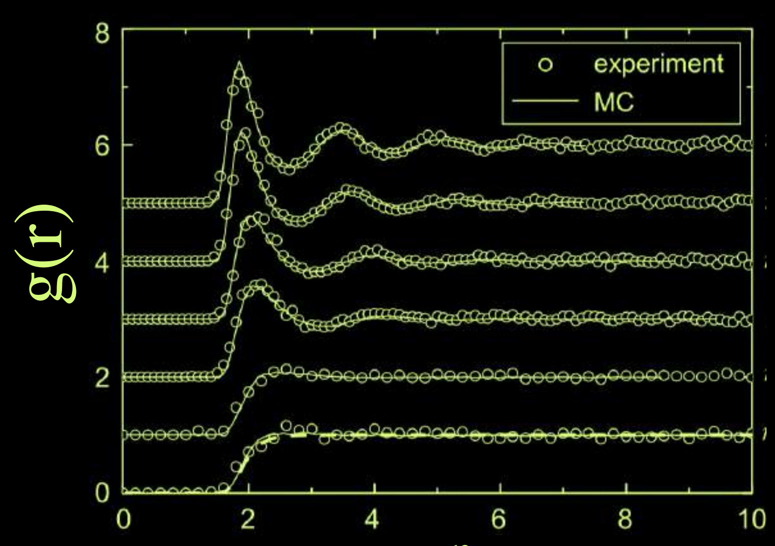
(Quantitative) real space imaging to date has focused on colloids whose interactions can be manipulated at will (salt, polymers...)



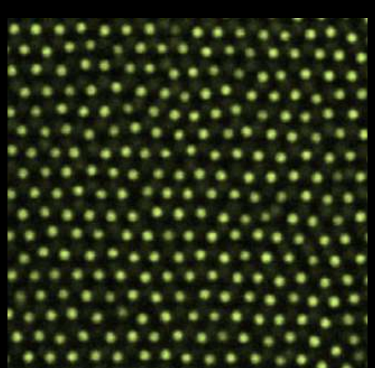
density

measure radial distribution function g(r)

uniquely defined by particle interactions



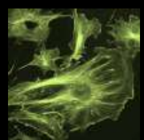
particle separation

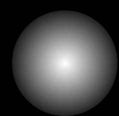


with interactions can predict conditions for crystallisation

"complex plasmas and colloidal dispersions: particle-resolved studies of classical liquids and solids", 2012

Lengthscales in Soft Matter





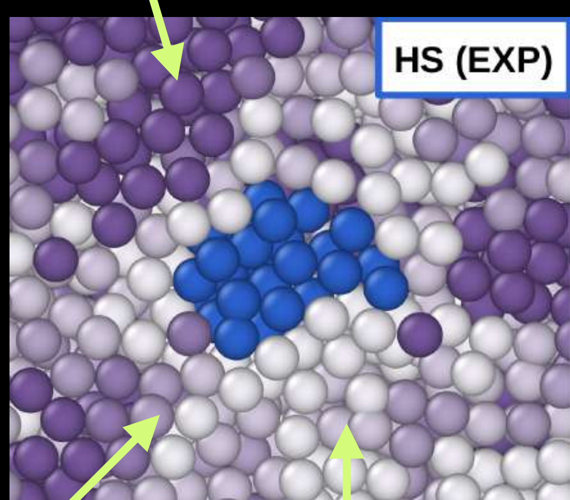
smaller

cells
~10 μm

colloids
~30-3000 nm

(Quantitative) real space imaging to date has focused on colloids whose interactions can be manipulated at will (salt, polymers...)

Many PB

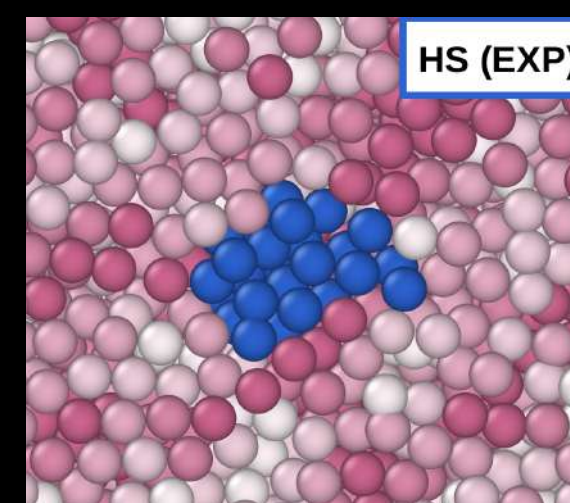


PB density

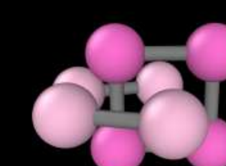
FCC nucleus

Few PB

Pentagonal bipyramid PB



SD density



Same snapshot

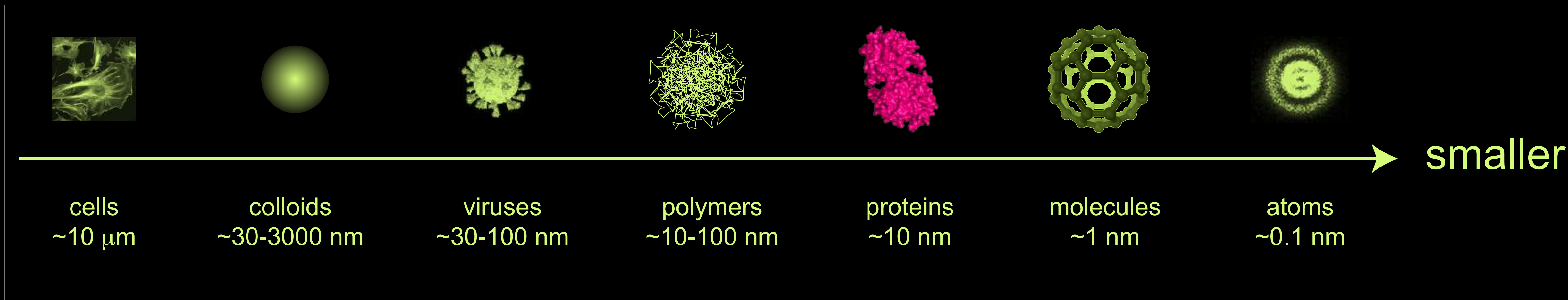
Siamese dodecahedron SD

Understand why FCC nuclei are favored over HCP
(free energy difference is negligible)

SD form a link between FCC crystal and PB rich fluid

ACS Nano 17 8807 (2023)

Lengthscales in Soft Matter



but STED super-resolution “nanoscopy” means that it doesn’t always have to be like this

Nature Commun. 14 2621 (2023); 9 3272 (2018)

can we use the kind of methods that work for colloids for proteins?

Soft Matter Physics
Self-assembly
Interactions~structure
super-resolution imaging

← Space! →

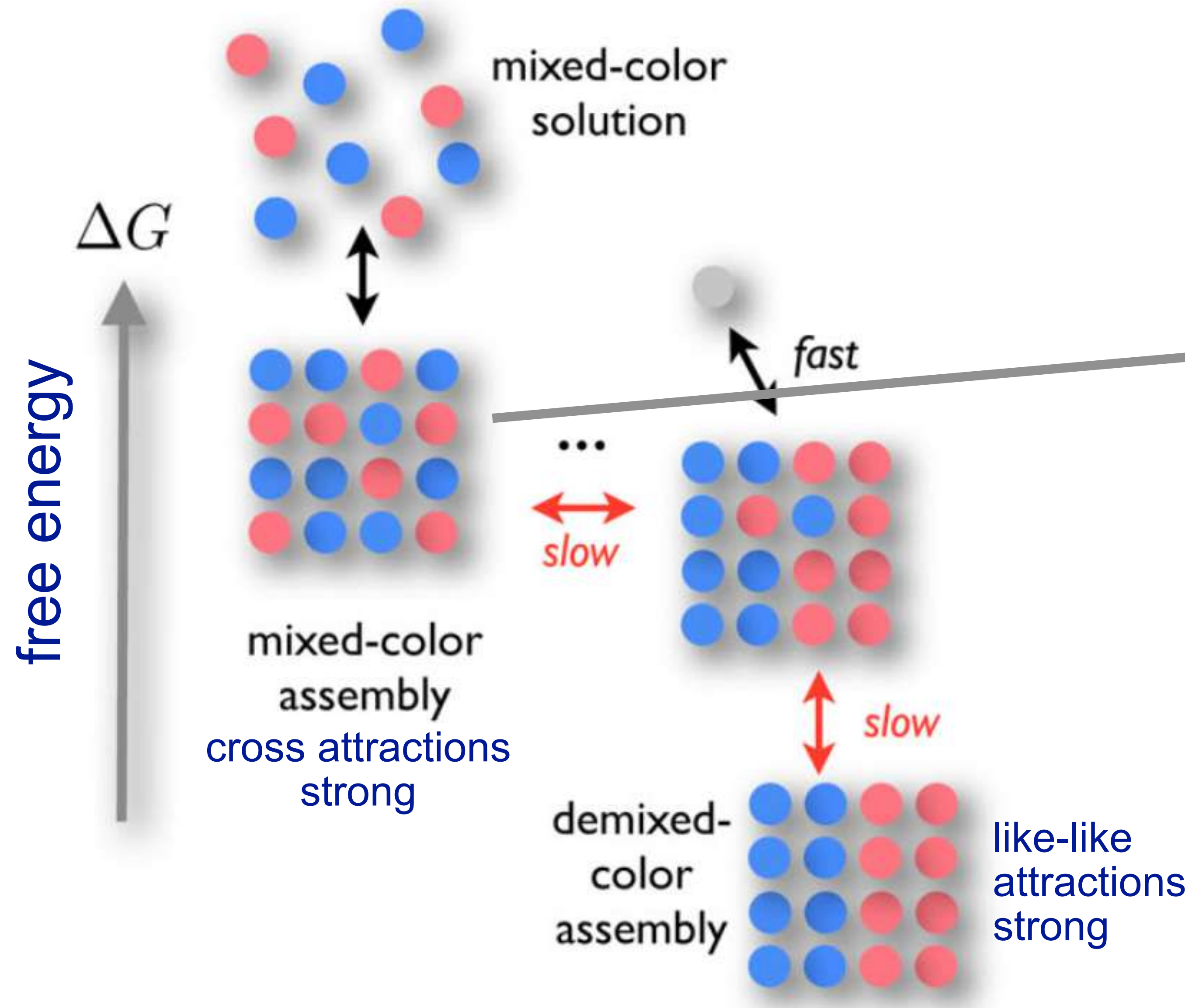
Biochemistry
enzymology
design of
de novo
proteins with
light-harvesting
electron-transfer
catalytic properties

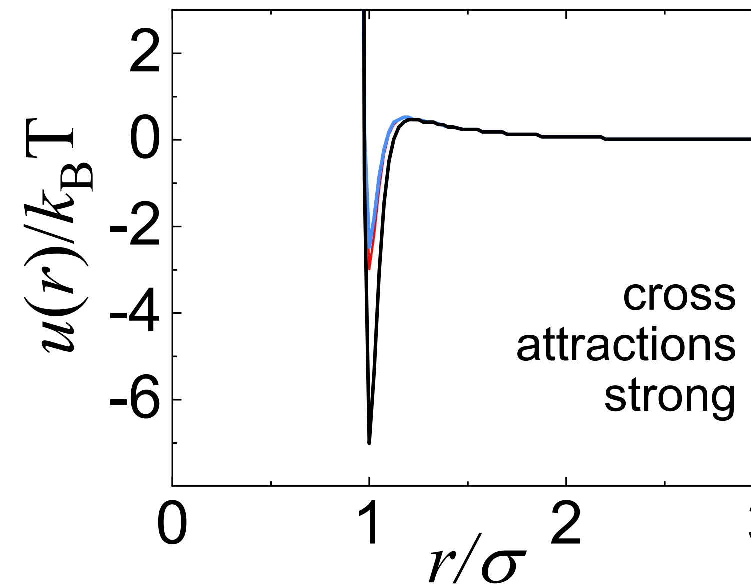
Strategy for Protein Assembly: Critical Soft Matter

Collaboration with Steve Whitelam,
Molecular Foundry, Berkeley CA

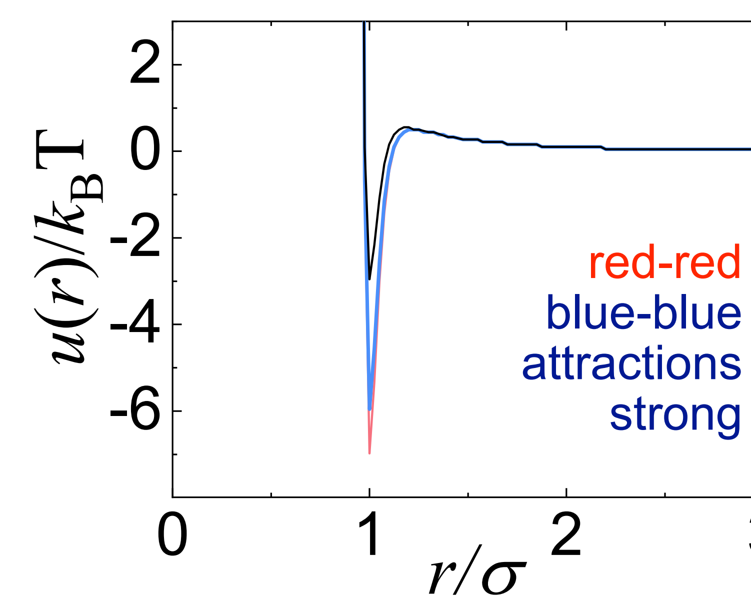
How to realise CSM with proteins?

first-order approximation:
"mermaid" interactions (soft matter)





small domains
(far from criticality)

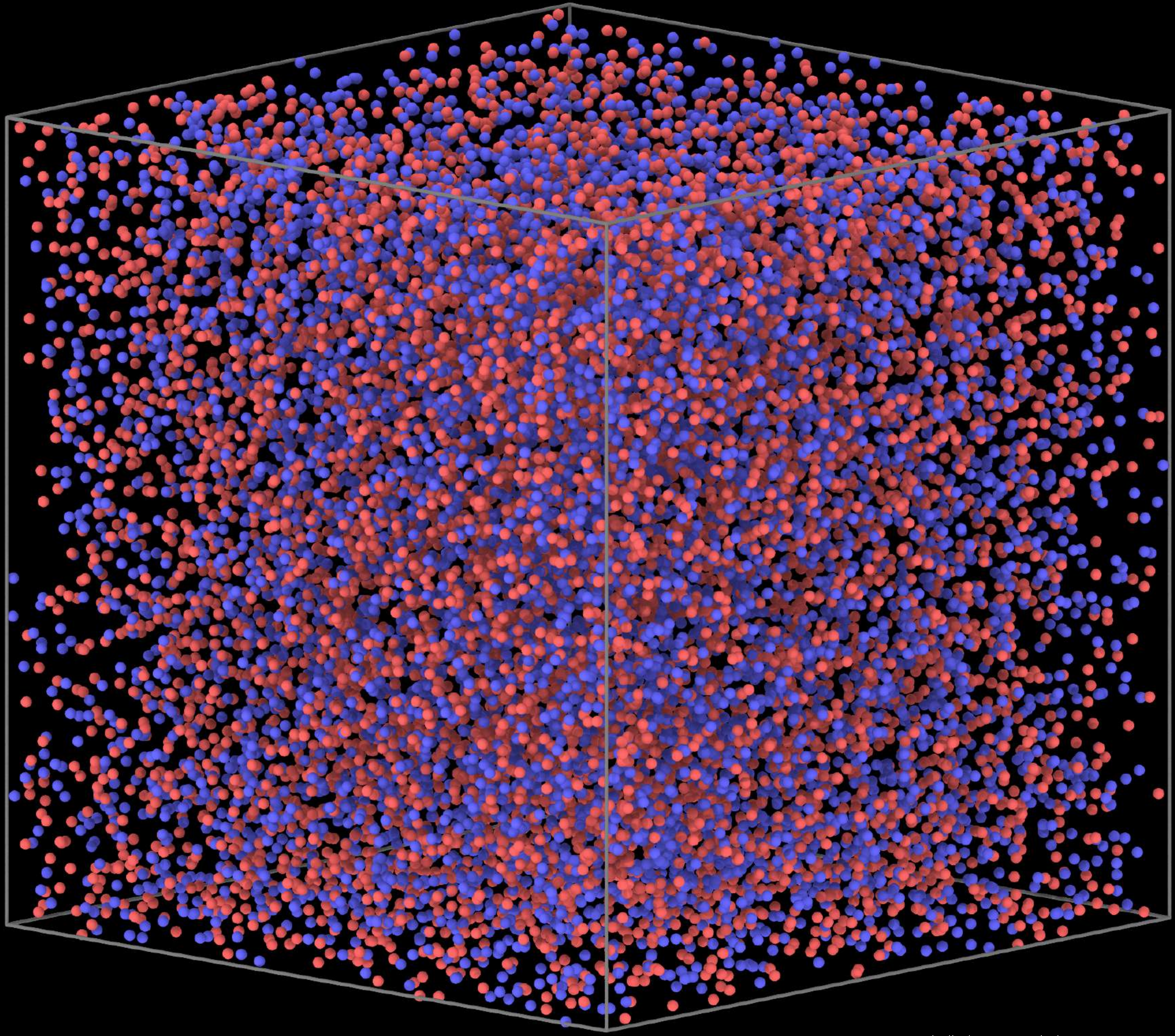


large domains
(close to criticality)

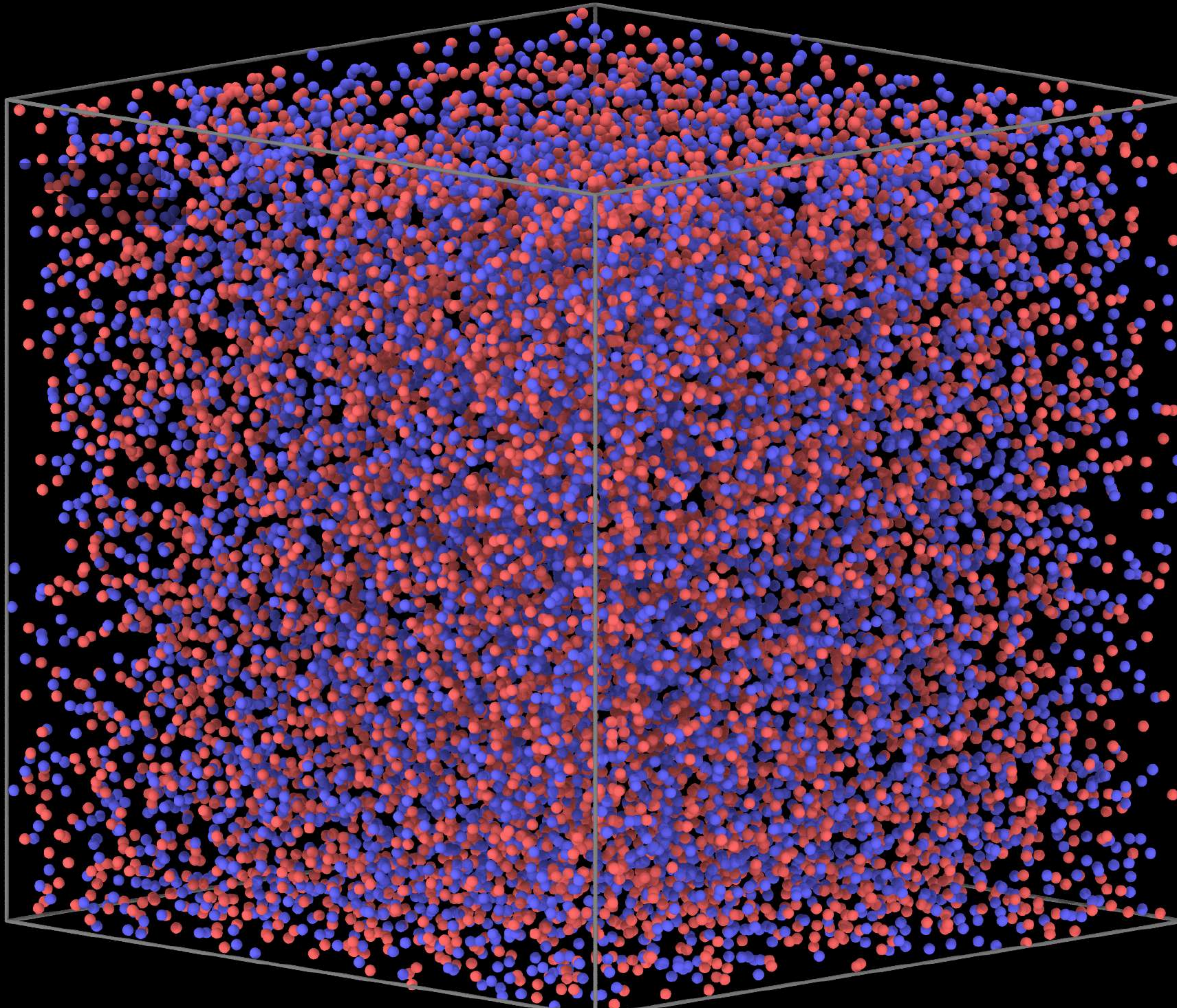
concept:
competition between (equilibrium) demixing and "locking in" structure during self-assembly
red and blue are identical but tune like-like and red-blue attractions

Whitelam and co *PRL* **112** 155504 (2014)

"Hunting Mermaids in Real Space", *Soft Matter* **14** 4020 (2018)



CROSS ATTRACTIONS STRONG



LIKE-LIKE ATTRACTIONS STRONG

IS THERE ANY REASON TO SUPPOSE THAT THIS MIGHT WORK?

A LITTLE BIT:

SOME PROTEINS HAVE "COLLOID-LIKE" PHASE BEHAVIOUR/SELF-ASSEMBLY

MCMANUS ET AL CURR OP COLL INTERF SCI 22 73 (2016)
FOFFI ET AL PNAS 111 16748 (2014)

Soft matter meets biochemistry

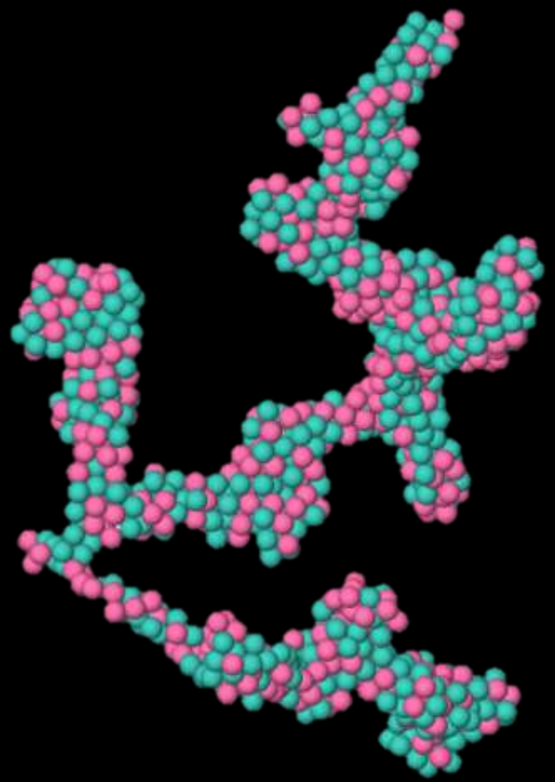
Soft matter: add polymer, ionic strength

Biochemical techniques: cationisation to control surface charge

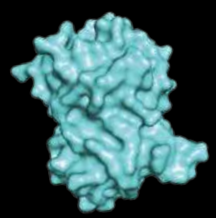
target: binary network (gel)
with tunable domain size
"critical soft matter"

towards useful materials with enzymatic properties

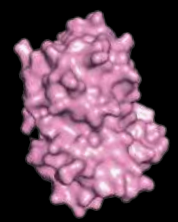
purpose of a network: flow through reactants and product



Strategy to produce network with tunable domain size



+



eGFP mCherry

Independent control of eGFP-eGFP, mCherry-mCherry interactions

eGFP-eGFP control with Y3+

mCherry-mCherry cationise (ignores Y3+)

two-step assembly: eGFP network with Y3+

decorate with mCherry upon addition of ammonium sulphate

Soft Matter 17 6873 (2021)

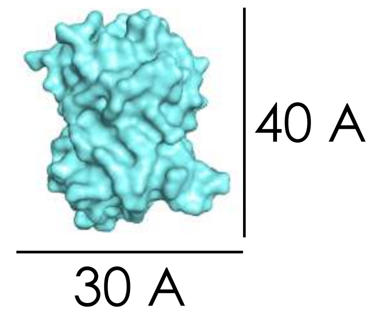
Start with eGFP

x-ray scattering for protein-protein interactions. manipulate with Y3+, polymer

scattering intensity $I(q)$

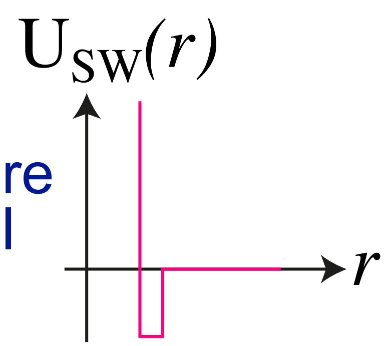
$$I(q) \sim S(q)P(q)$$

form factor $P(q)$
protein shape
(cylinder)



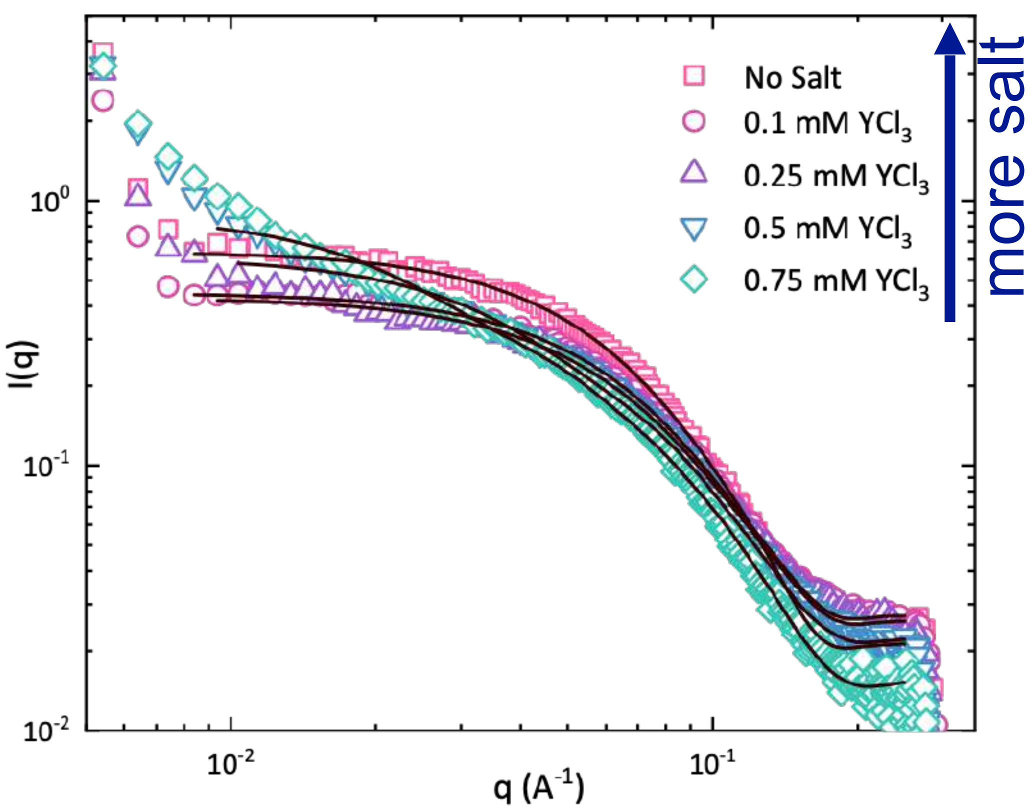
$S(q)$ Fourier transform of $g(r)$:
determine interactions as for colloids

square
well



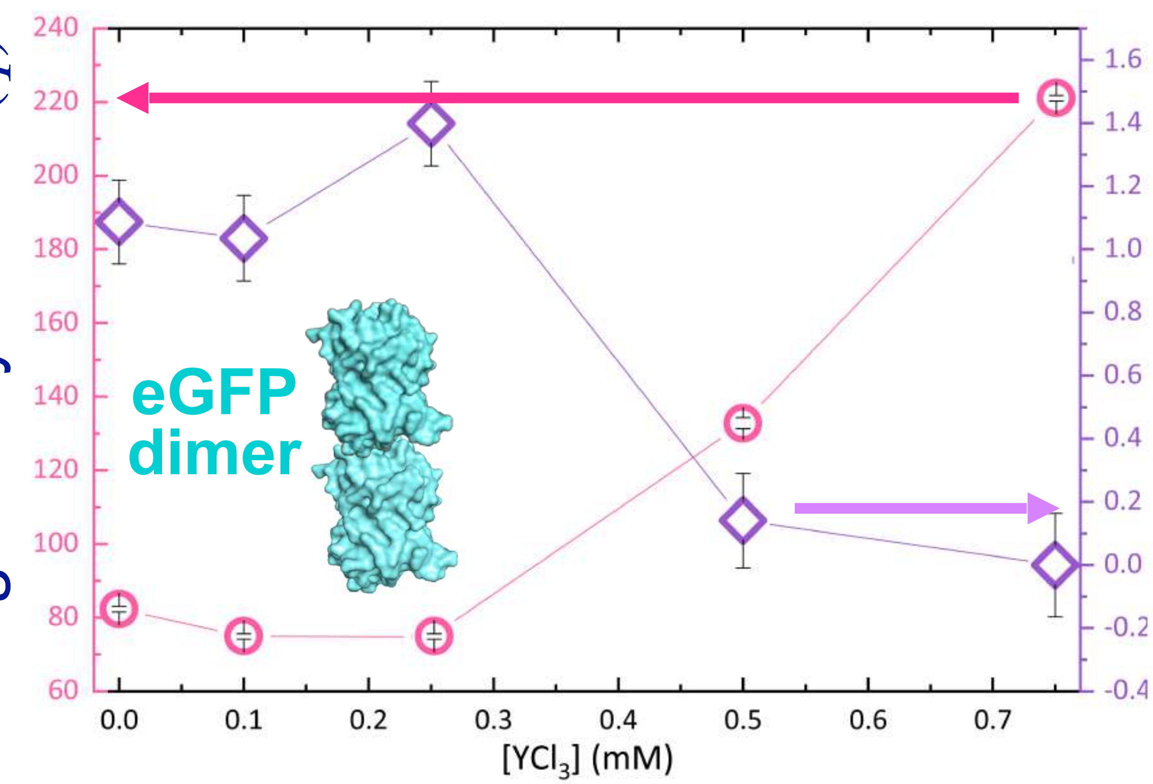
well
depth

scattering intensity $I(q)$



wavevector q

length of cylinder $P(q)$

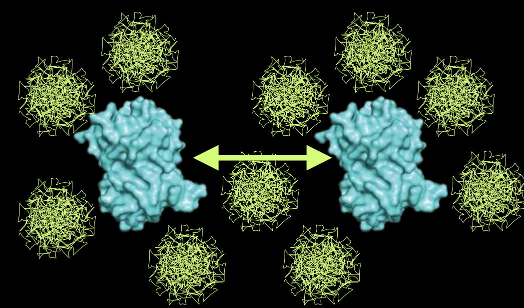


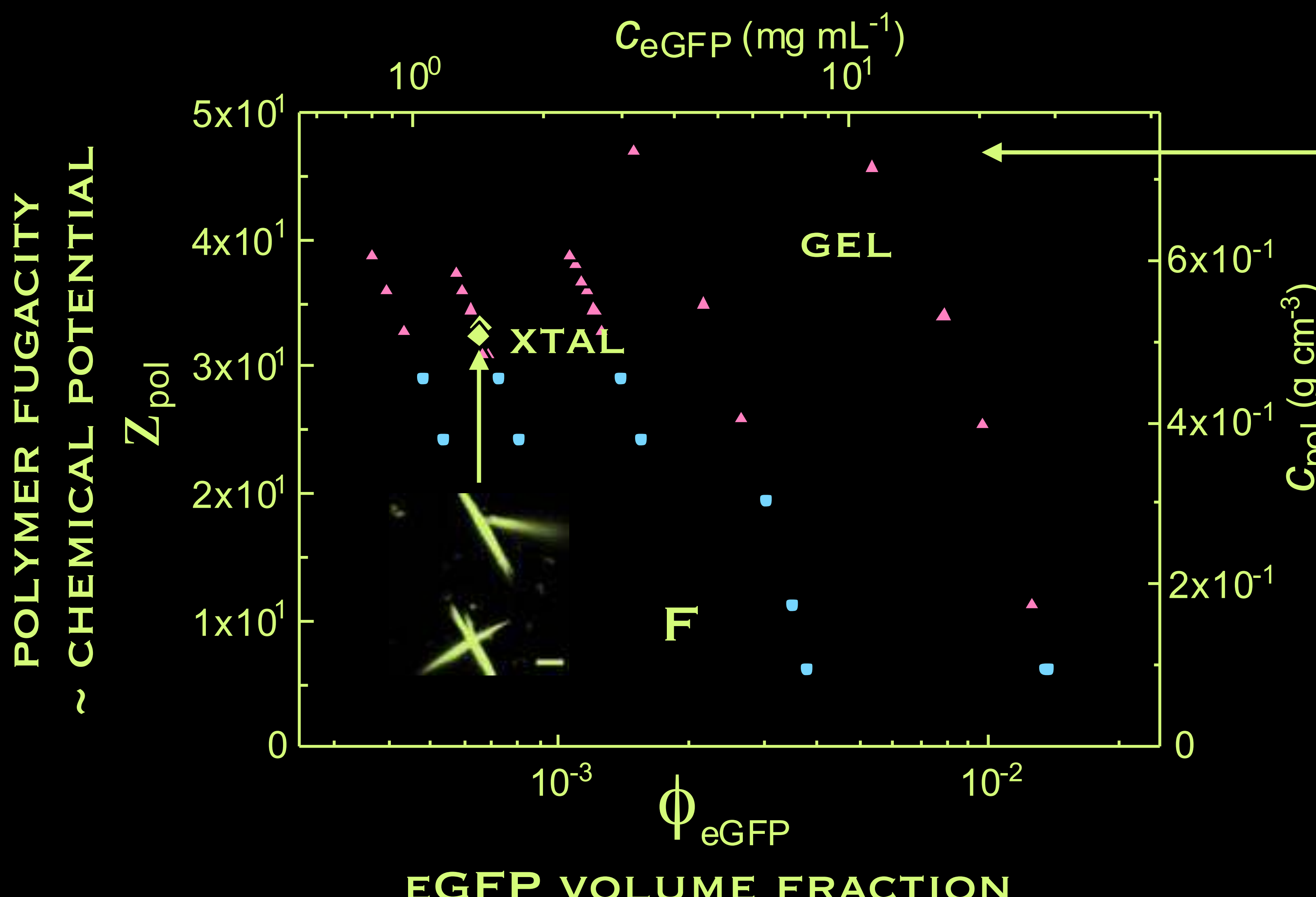
depth of square well
interaction $S(q)$

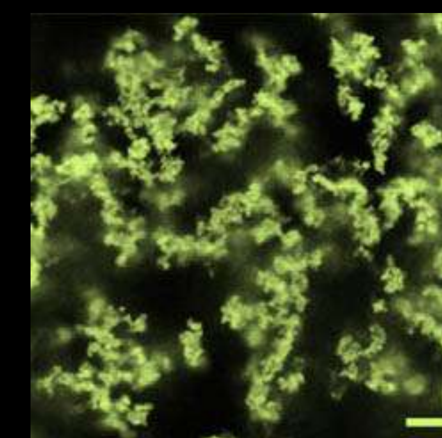
salt concentration

START WITH EGFP

eGFP+polymer (PEG)



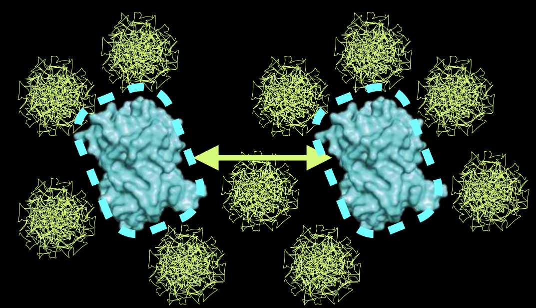


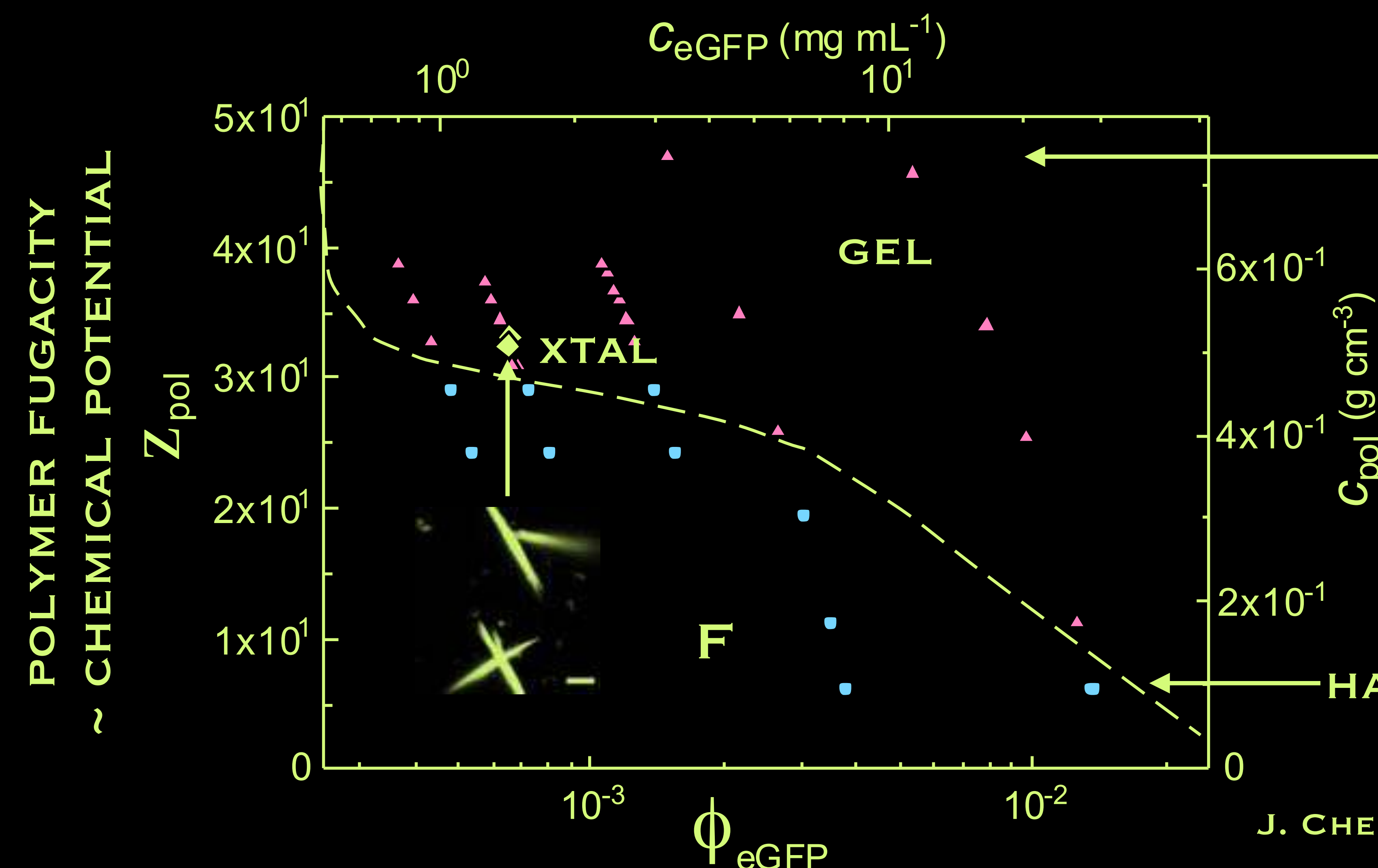


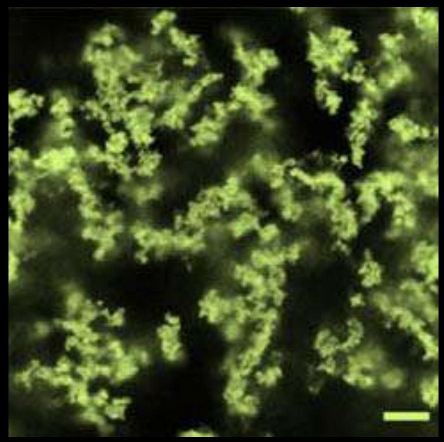
J. Chem. Phys. 155 114901 (2021)

START WITH EGFP

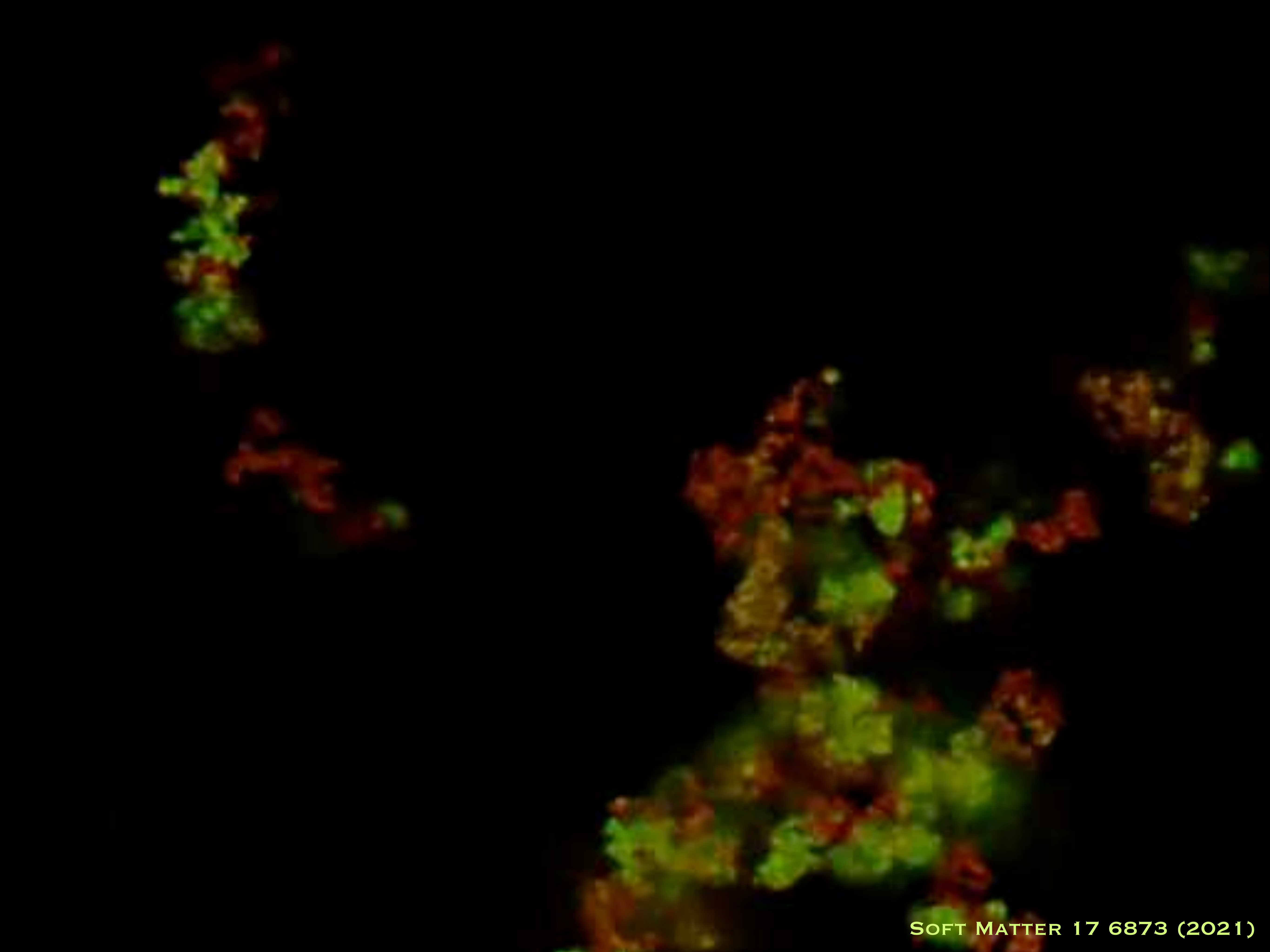
eGFP+polymer (PEG)







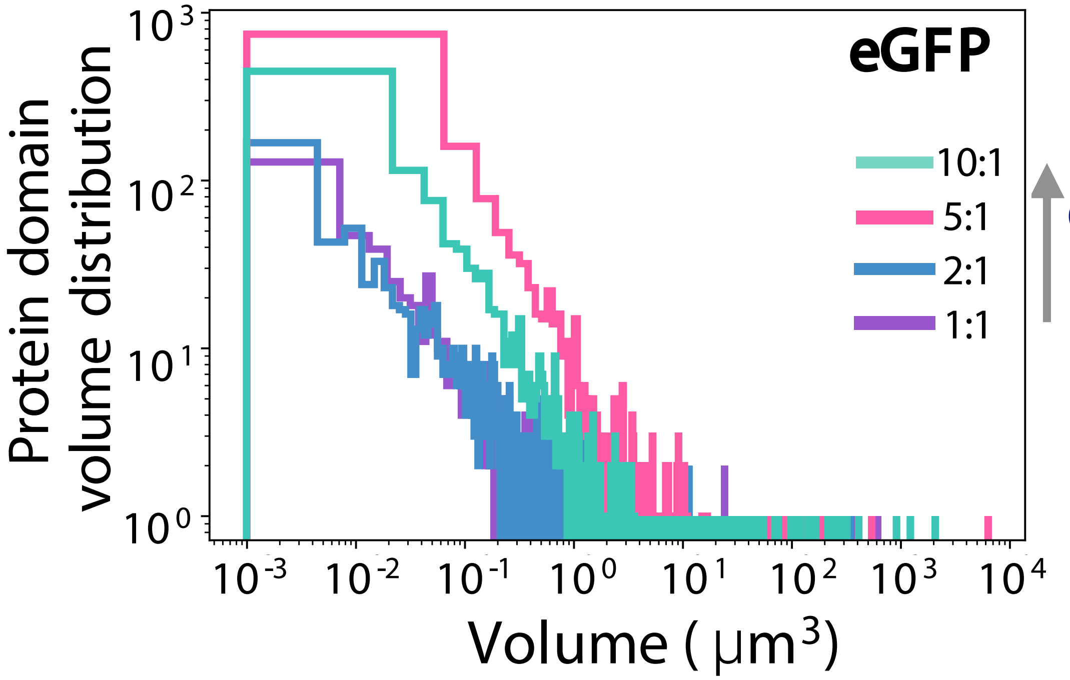
J. Chem. Phys. 155 114901 (2021)



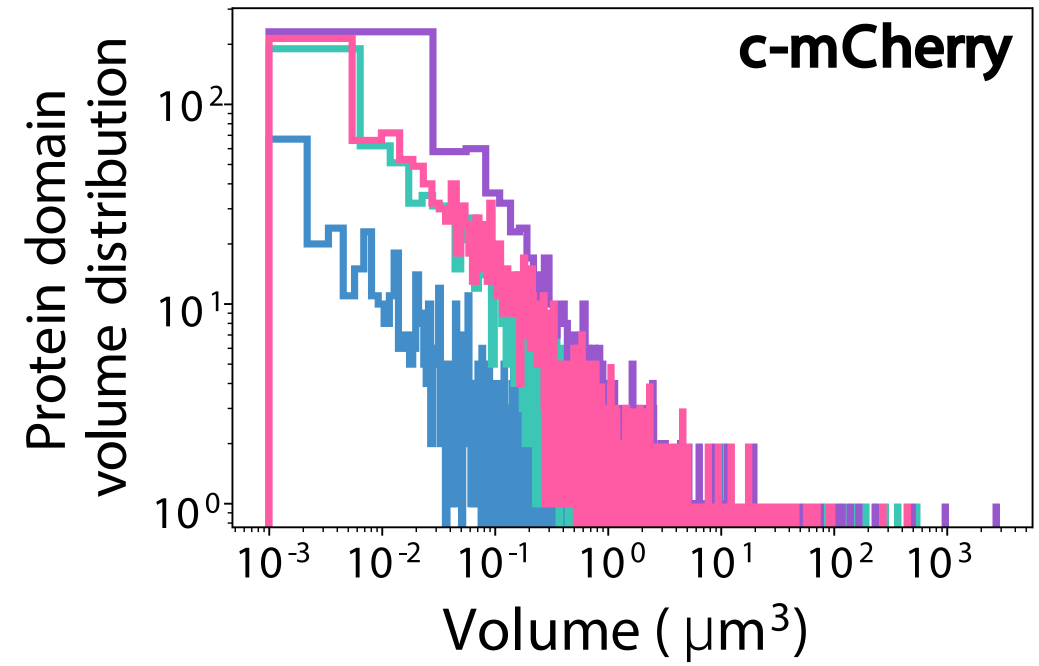
Soft Matter 17 6873 (2021)

What about controlling the domain size?

Change eGFP/mCherry composition



eGFP:mCherry up



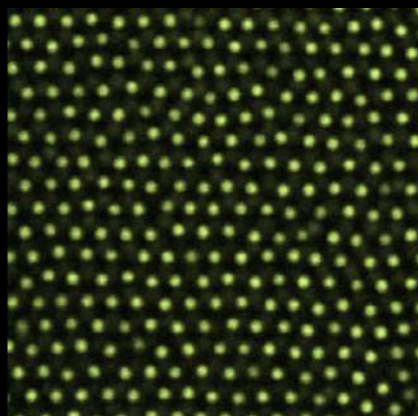
non-monotonic!

an explanation would be nice…

Soft Matter **17** 6873 (2021)

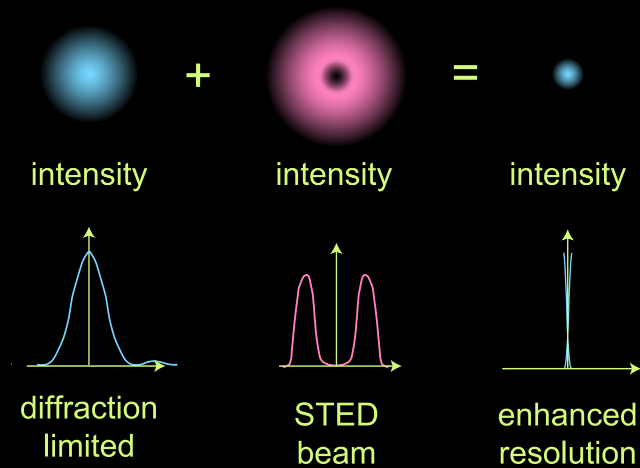
SOFT MATTER METHODS FOR PROTEIN ASSEMBLY

COLLOIDS

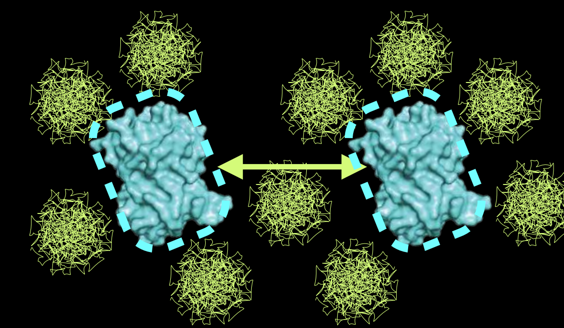


QUANTITATIVE IMAGING: PREDICT ASSEMBLY
UNDERSTAND POLYMORPH SELECTION

ACS NANO 17 8807 (2023)
"COMPLEX PLASMAS AND COLLOIDAL DISPERSIONS...", 2012



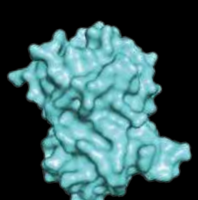
STED NANOSCOPY
SHORTER LENGTHSCALES



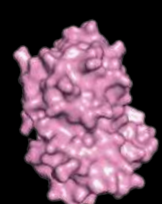
EGFP+POLYMER
BEHAVES LIKE
HARD SPHEROCYLINDERS

J. CHEM. PHYS. 155 114901 (2021)

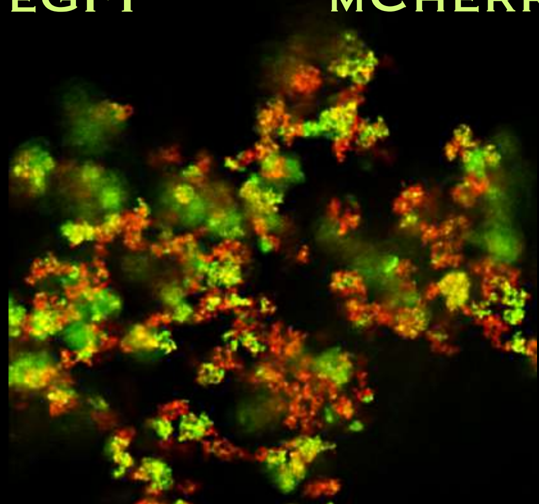
BINARY PROTEIN NETWORKS



+



EGFP MCHERRY



CONTROL OF
DOMAIN SIZE

SOFT MATTER 17 6873 (2021)