ULB UNIVERSITÉ LIBRE DE BRUXELLES

Faculty of Sciences ULB

Dynamics of functionalised particles diffusing through reversible ligand-receptor bridges

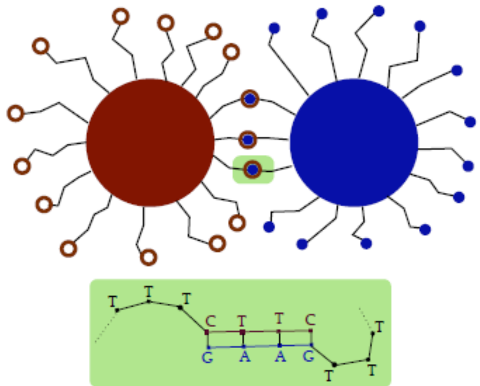
Bortolo Matteo Mognetti

Université libre de Bruxelles, *Interdisciplinary Center for Nonlinear Phenomena and Complex Systems, Belgium*

Nanoparticle assemblies: 6 April 2023

Kavli Institute for Theoretical Physics
University of California, Santa Barbara

Ligand-receptor-mediated interactions



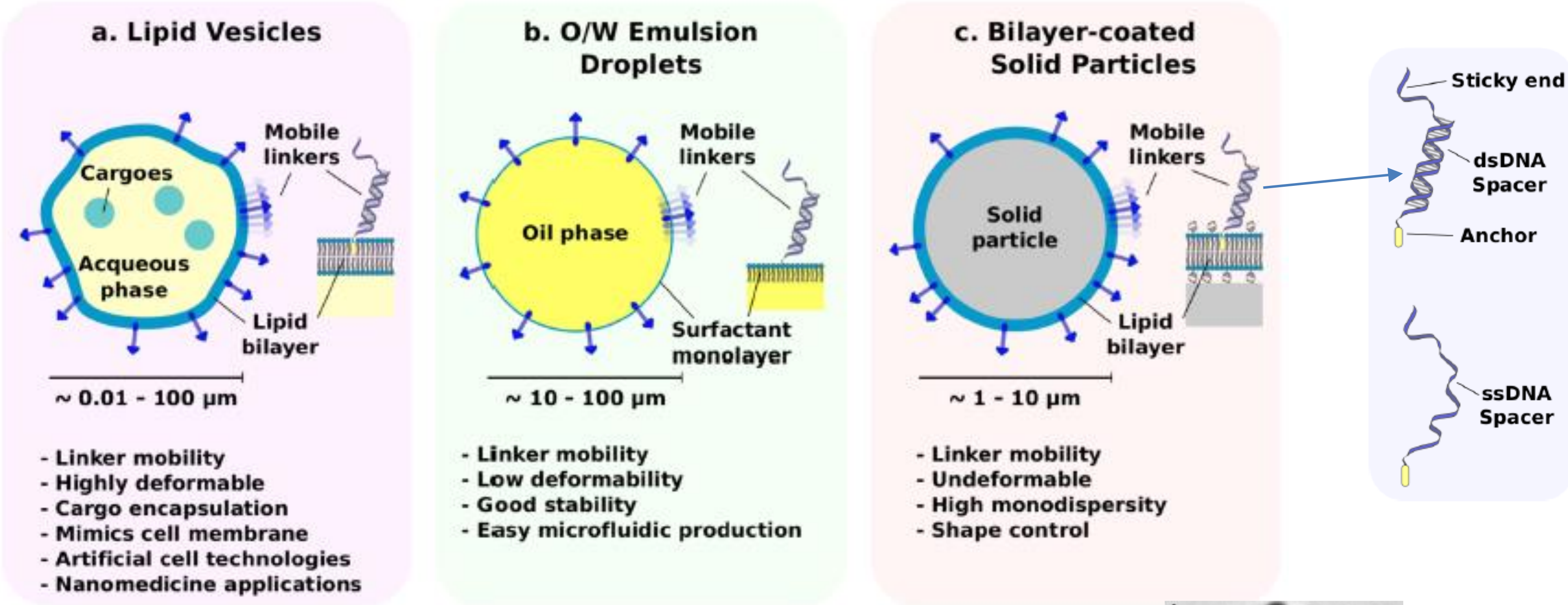
Mirkin *et al*, Nature **1996**
Alivisatos et al, Nature **1996**

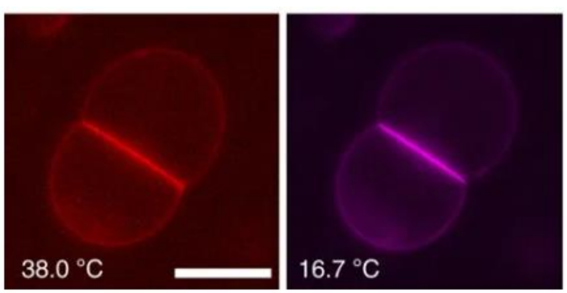
- Reversible supramolecular reaction
  (proteins, DNA/RNA, chemical complexes)

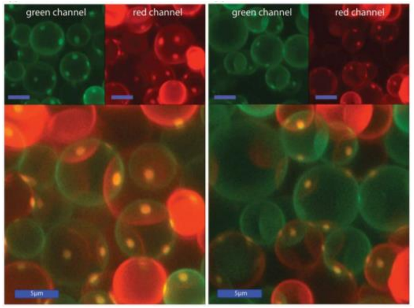
- Programmable self-assembly

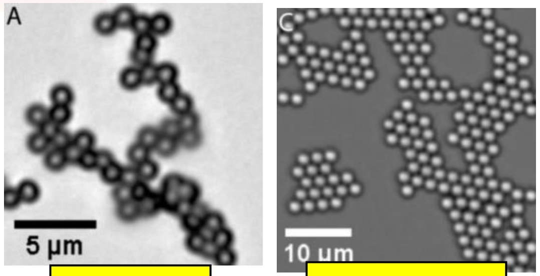
Particles functionalized by mobile linkers

Mognetti *et al*, Rep. Progr. Phys. **2019**









FIXED

MOBILE

Parolini *et al*, Nat. Comm. **2015**;
ACS Nano **2016**
Bachmann *et al*, Soft Matter **2016**

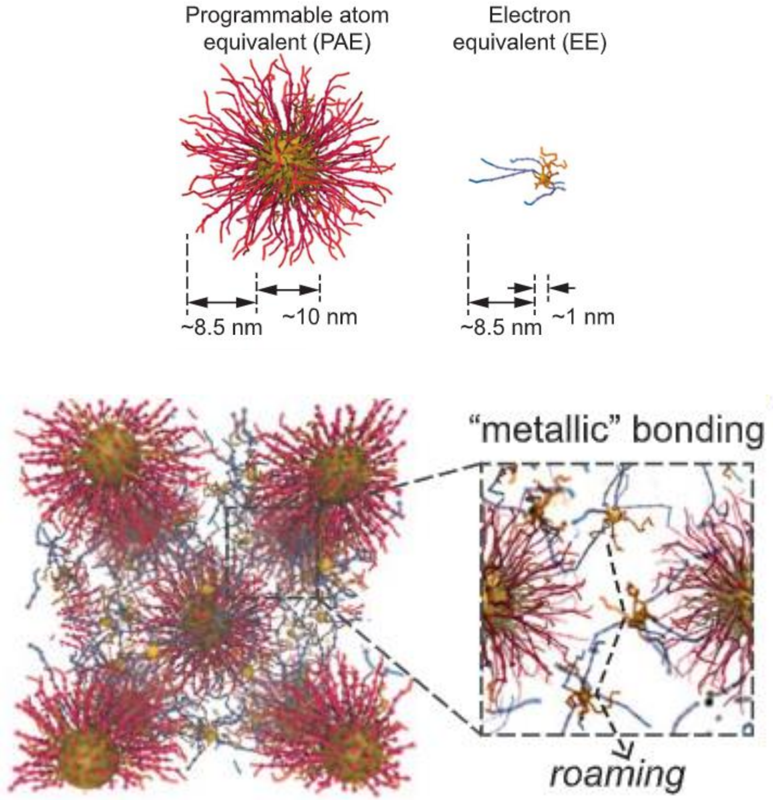
Feng *et al*, Soft Matter **2013**
Zhang *et al*, Nat. Comm. **2018**;
PNAS **2019**

Van der Meulen *et al*, JACS **2013**
Rinaldin *et al*, Soft Matter **2019**

Building multivalent models

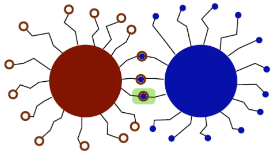
- Sticky ends continuously bind/unbind

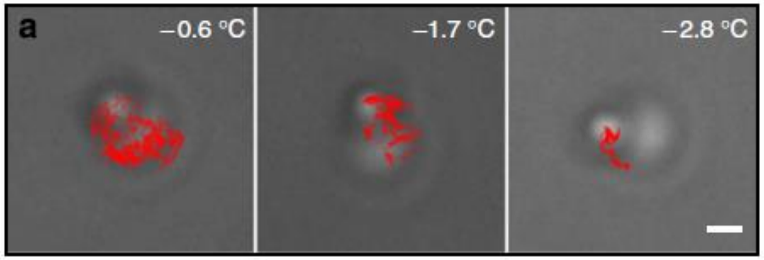
  - Particles acting as electrons



Girard *et al*, Science **2019**

  - DNA coated colloids can roll without detaching





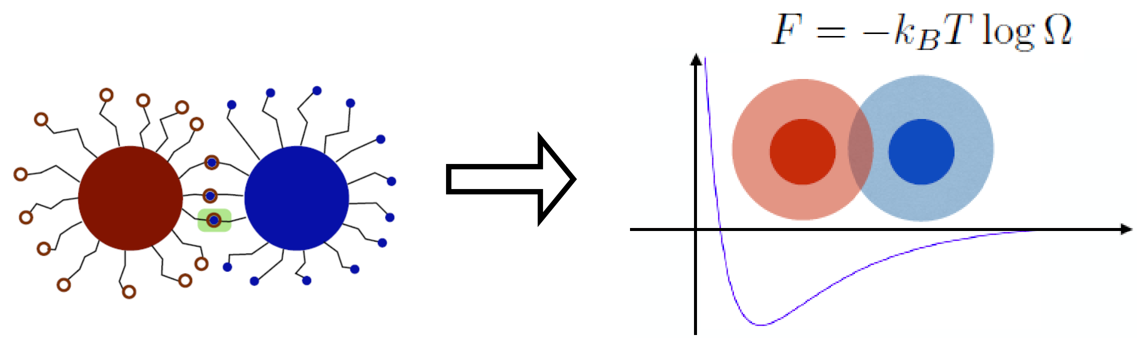
Wang *et al*, Nat. Commun. **2015**

- We need computational platforms capable of performing many reactions between sticky ends

Equilibrium models

- Effective interactions

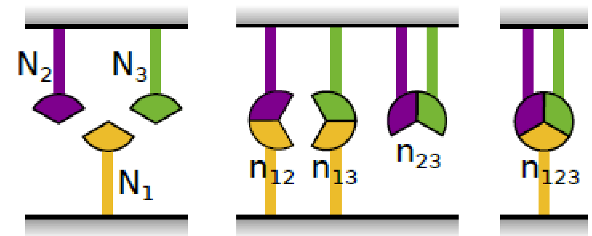
Bell *et al*, Biophys. J. **1984**



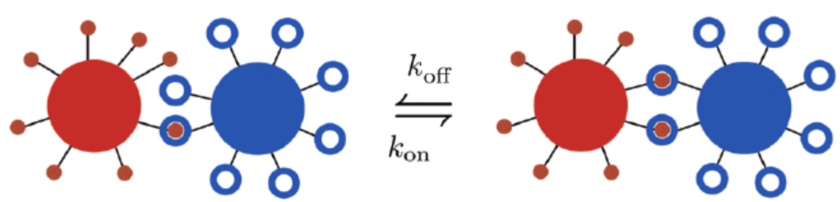
- Sampling over all possible ligand-receptor reactions

$$\frac{F}{k_B T} = \sum_i N_i \log \frac{\overline{n}_i}{N_i} + \sum_{i \leq j} \overline{n}_{ij} + 2 \sum_{i \leq j \leq k} \overline{n}_{ijk} + 3 \cdots$$

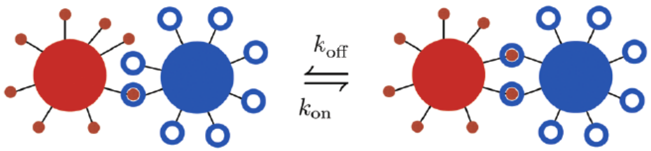
Di Michele *et al*, J. Chem. Phys. **2016;** Angioletti-Uberti *et al*, J. Chem. Phys. **2013**; Varilly *et al*, J. Chem. Phys. **2013**



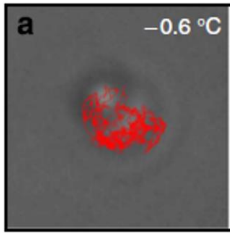
- Effective interactions based on the assumption that the reaction timescales are small



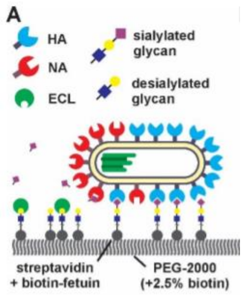
Plan of the talk



- Dynamics of particles moving through reversible ligand-receptor contacts

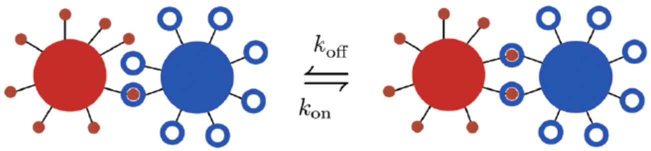


  - Predicting the emerging diffusion constant *D* in reaction-limited conditions
  - Comparison with simulations and experiments
  - Increasing the motility of the particles using enzymes (Influenza A Virus)

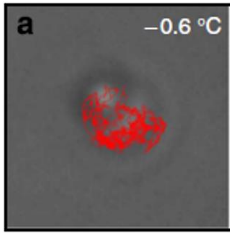


- Self-assembly dynamics
  - Finite reaction rates alter the morphology of steady aggregates

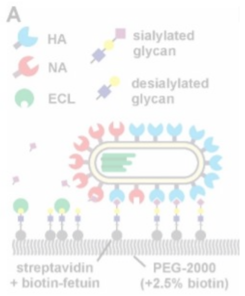
Plan of the talk



- Dynamics of particles moving through reversible ligand-receptor contacts
  - Predicting the emerging diffusion constant *D* in reaction-limited conditions

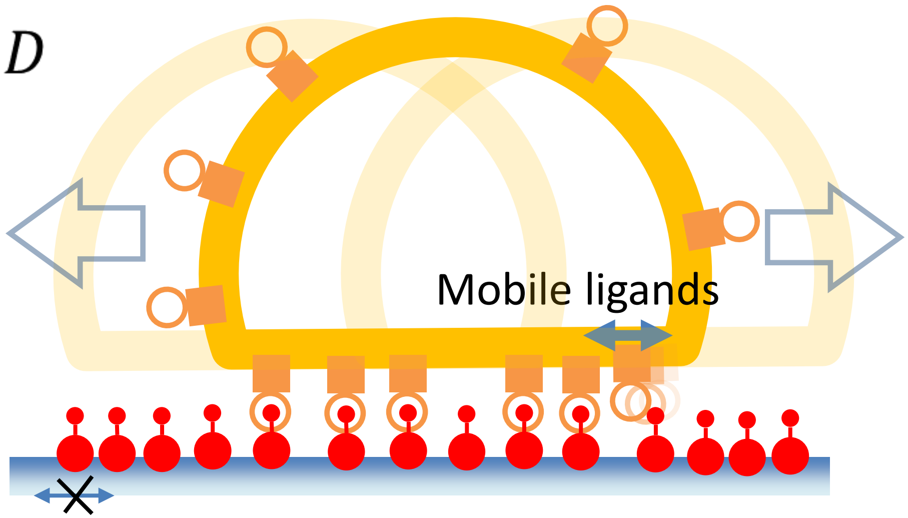


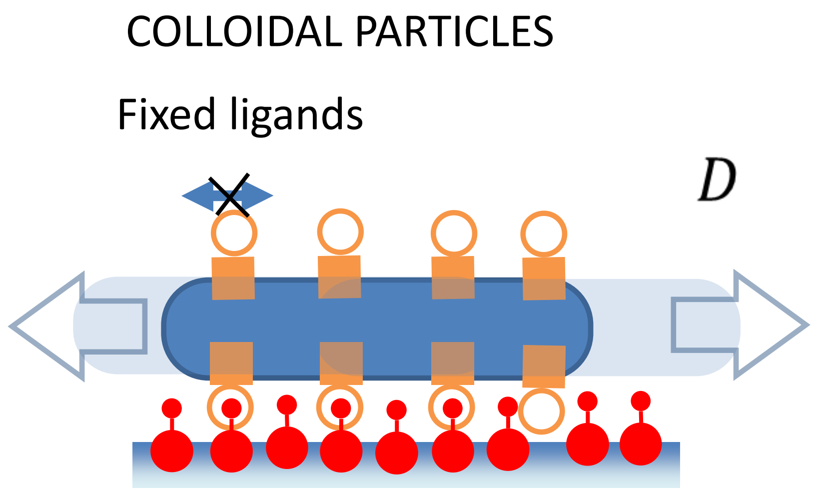
  - Comparison with simulations and experiments
  - Increasing the motility of the particles using enzymes (Influenza A Virus)

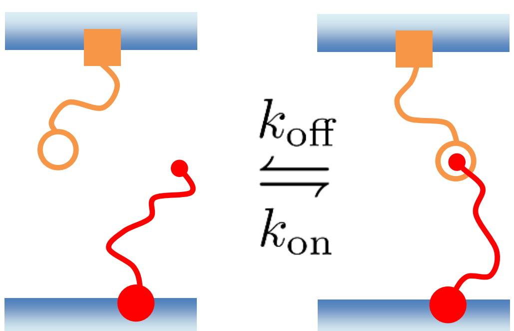


- Self-assembly dynamics
  - Finite reaction rates alter the morphology of steady aggregates

Sliding across functionalised surfaces





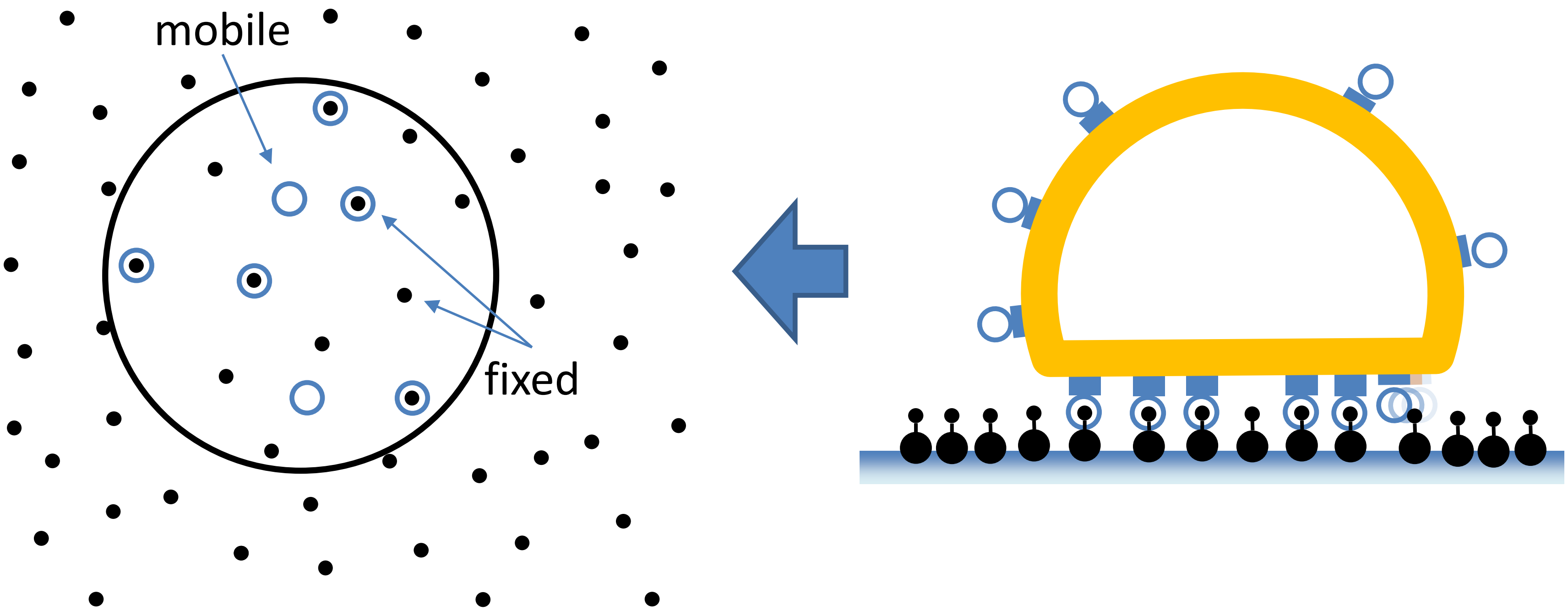


- We aim to predict the emerging diffusion constant of the particle, D, from the reaction rates, k_{on} and k_{off}, and the number of ligand-receptor bridges, n_b

Lowensohn, Stevens *et al.*, J. Chem. Phys. **2022**

Coarse-graining the diffusion dynamics

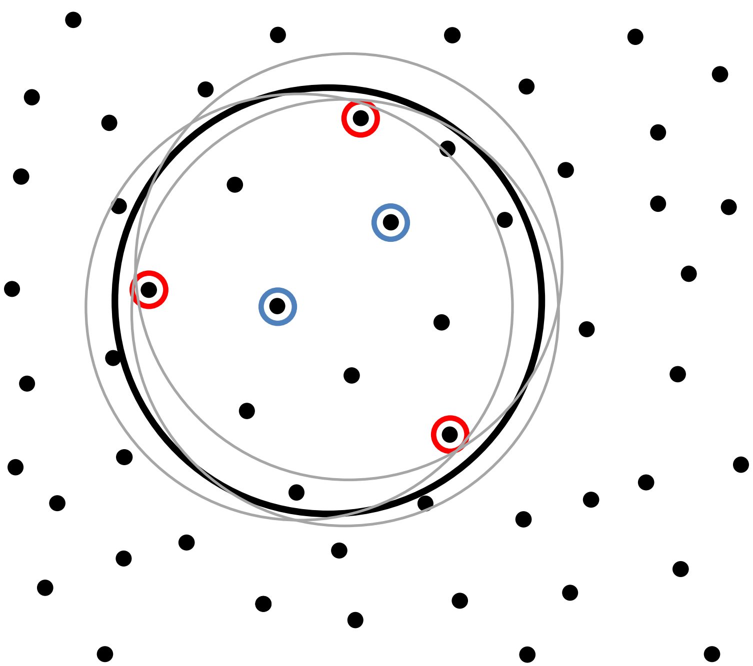
- 2D representation with fixed receptors and mobile ligands



- Receptors
- Ligand-receptor bridges
- Ligands

Coarse-graining the diffusion dynamics

- Short timescales: the particle rattles around the current set of constraining bridges



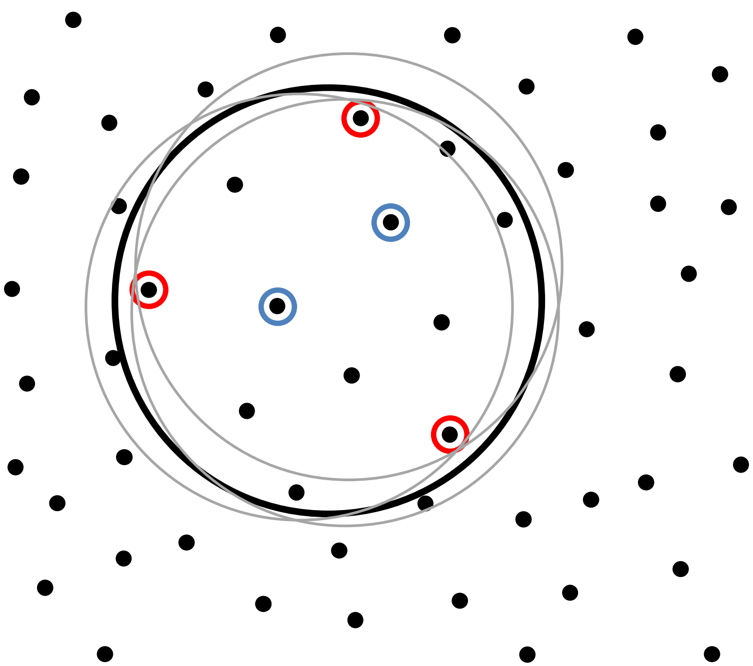
- Receptors

Ligand-receptor (non constraining) bridges

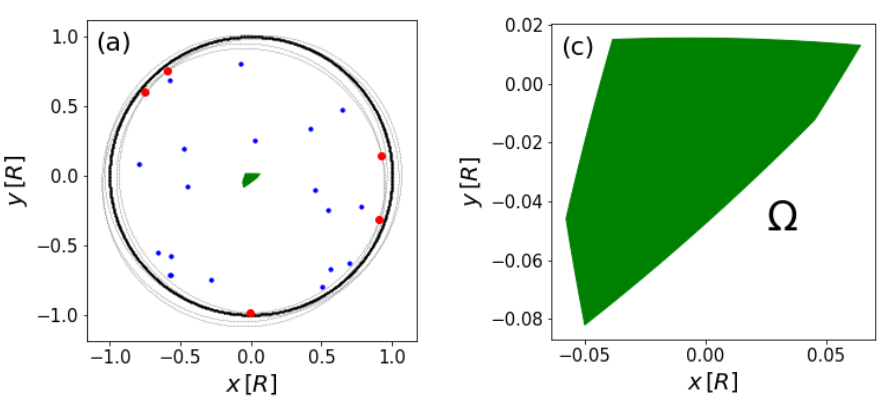
Constraining bridges (CBs)

Coarse-graining the diffusion dynamics

- Short timescales: the particle rattles around the current set of constraining bridges



- Ω: configurational region available to the particle's centre at a given set of CBs



• Receptors

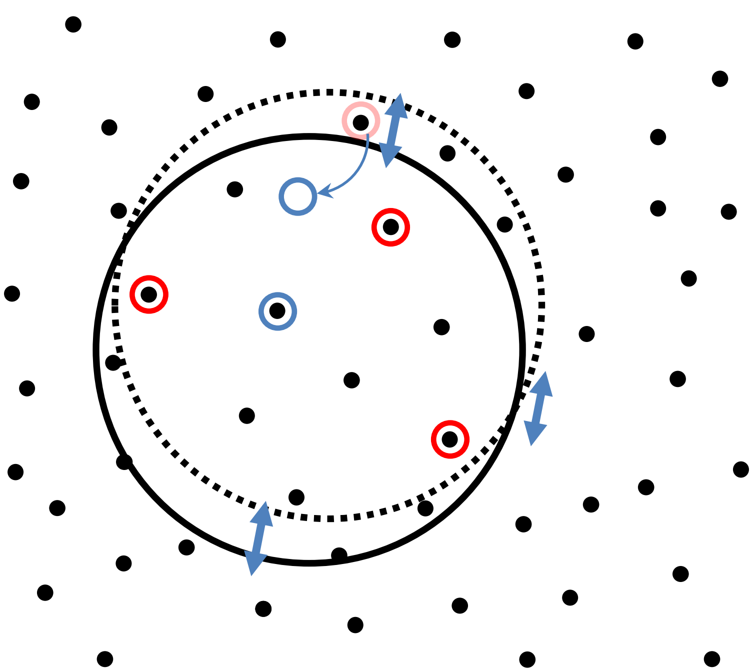
Ligand-receptor (non constraining) bridges

Constraining bridges (CBs)

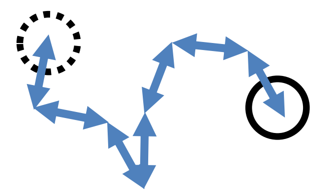
Coarse-graining the diffusion dynamics

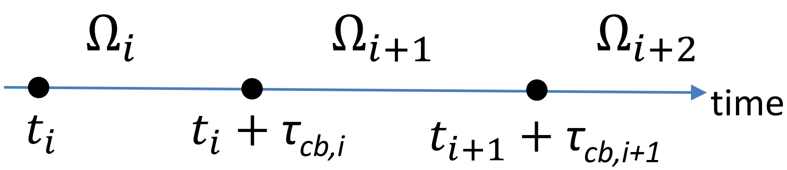
- Emerging diffusion controlled by the evolution of the set of CBs:

$$\ldots, \Omega_i, \Omega_{i+1} \ldots$$



- Receptors
- Ligand-receptor bridges
- Constraining bridges (CBs)



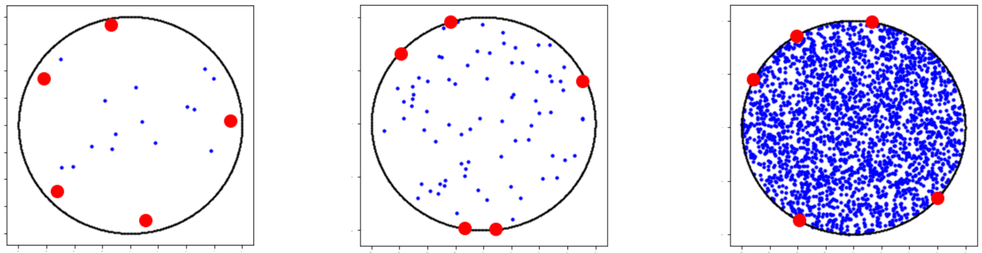


- Time to update the set of CBs: τ_{cb}
- Average displacement following an update of the CBs: δ_{cb}
- Emerging sliding diffusion constant, D

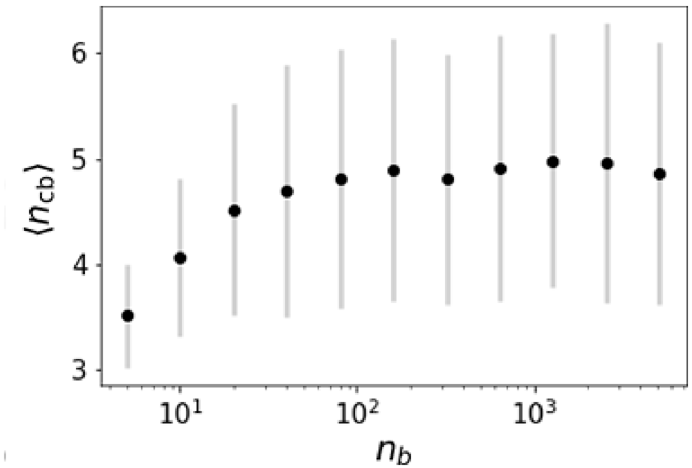
$$D = \frac{\langle \delta_{cb} \rangle^2}{2 < \tau_{cb} >}$$

Constraining bridges

- The number of constraining bridges is finite

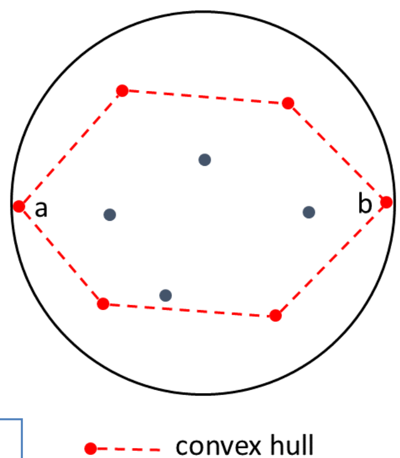


$\langle n_b \rangle = 20$ $\langle n_b \rangle = 80$ $\langle n_b \rangle = 2560$

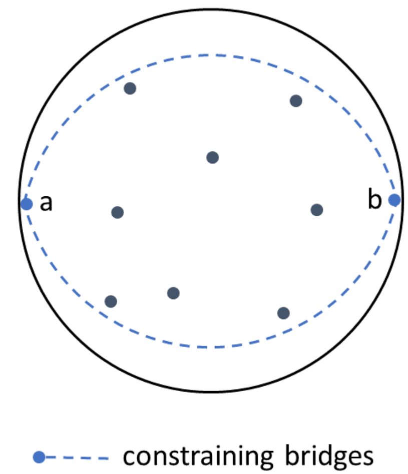


- Not all bridges on the border of the particle (e.g., vertices of the convex hull) are CBs

Efron, Biometrika **1965**



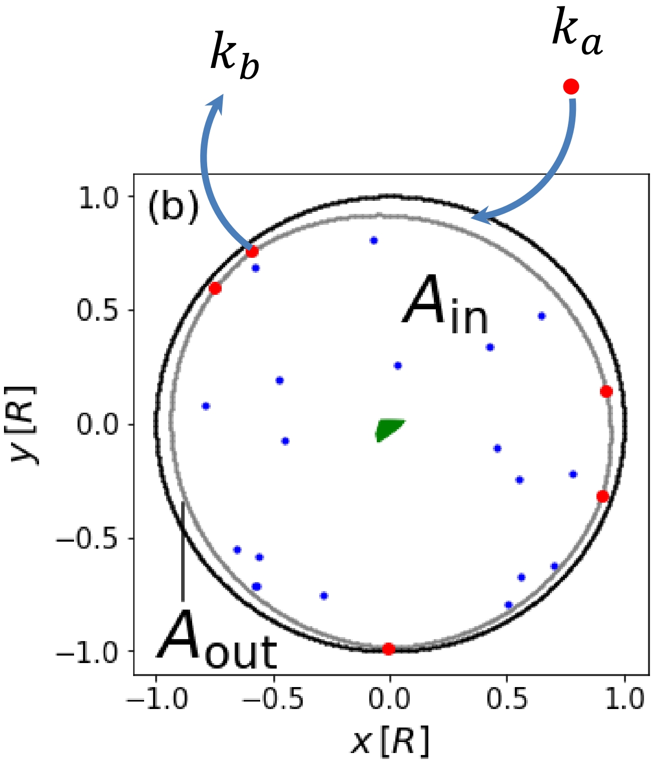
$\langle n_{\mathrm{ch}} \rangle \approx \log n_b$



$\langle n_{cb} \rangle \approx 4.9$

Updating sets of CBs: τ_{cb}

- Ω_i changes when (*a*) a bridge appears in A_{out} or (*b*) an existing CB is removed



  - k_a: rate at which a bridge appears in A_{out}

$$k_{\text{a}} = n_L n_R k_{\text{on}} \frac{A_{\text{out}}}{\pi R^2}$$

  - k_b: rate at which a constraining bridge is removed

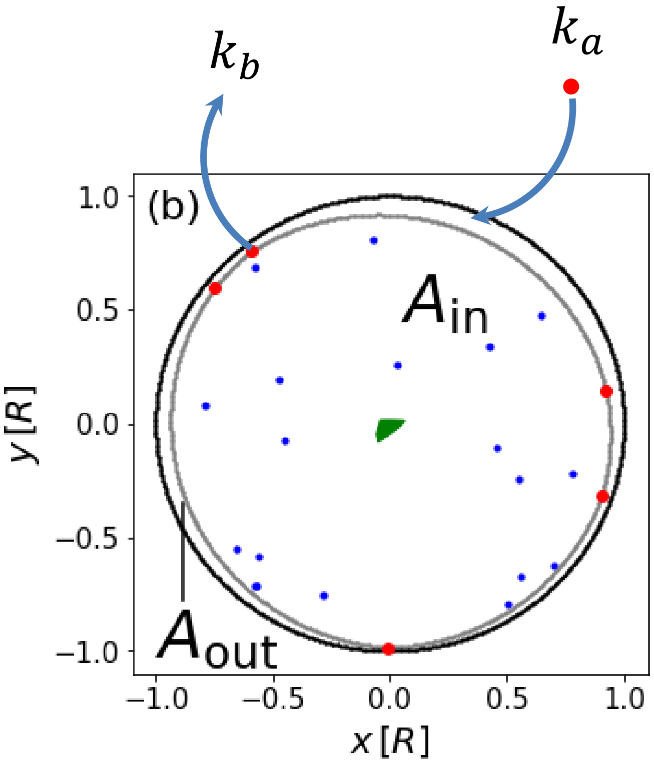
$$k_{\text{b}} = n_{cb} k_{\text{off}}$$

  - In steady conditions, $\langle k_a \rangle = \langle k_b \rangle \rightarrow$

$$\langle \tau_{cb} \rangle = \frac{1}{\langle k_a \rangle + \langle k_b \rangle} = \frac{1}{2 k_{\text{off}} \langle n_{cb} \rangle}$$

Updating sets of CBs: τ_{cb}

- Ω_i changes when (*a*) a bridge appears in A_{out} or (*b*) an existing CB is removed



- k_a: rate at which a bridge appears in A_{out}

$$k_{\text{a}} = n_L n_R k_{\text{on}} \frac{A_{\text{out}}}{\pi R^2}$$

- k_b: rate at which a constraining bridge is removed

$$k_{\text{b}} = n_{cb} k_{\text{off}}$$

- In steady conditions, $\langle k_a \rangle = \langle k_b \rangle \rightarrow$

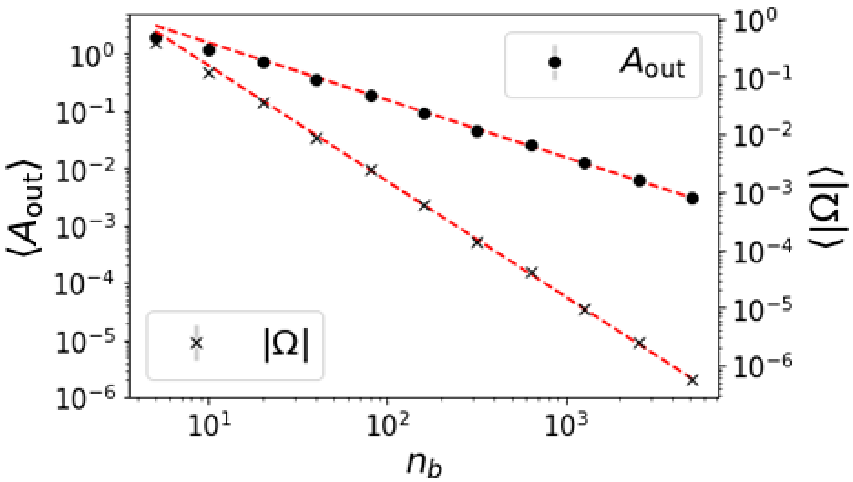
$$\langle \tau_{cb} \rangle = \frac{1}{\langle k_a \rangle + \langle k_b \rangle} = \frac{1}{2k_{\text{off}} \langle n_{cb} \rangle}$$

- In steady conditions, $\frac{d\langle n_b \rangle}{dt} = 0 \rightarrow$

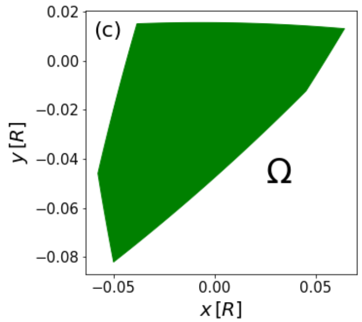
$$\langle A_{\text{out}} \rangle = \pi \frac{R^2 < n_{cb} >}{\langle n_b \rangle}$$

Updating sets of CBs: τ_{cb}

- Ω_i changes when (*a*) a bridge appears in A_{out} or (*b*) an existing CB is removed



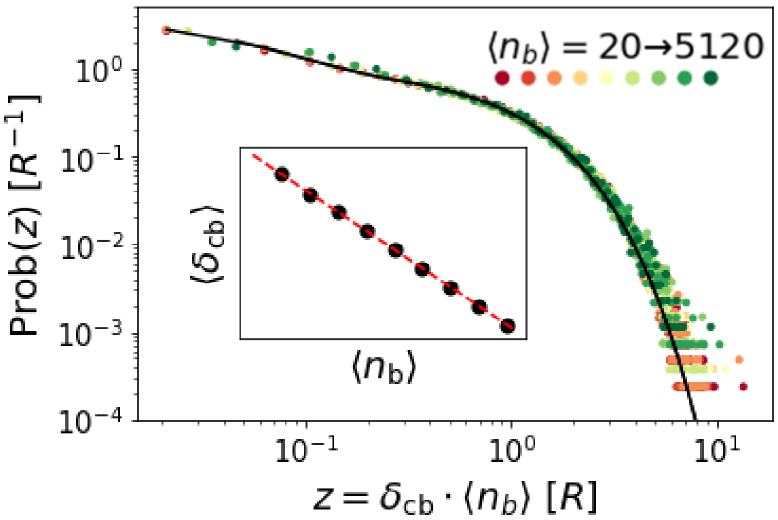
$$\langle|\Omega|\rangle = \frac{\langle A_{out} \rangle}{\langle n_b \rangle}$$
(fitted)



- k_a: rate at which a bridge appears in A_{out}
$$k_{\text{a}} = n_L n_R k_{\text{on}} \frac{A_{\text{out}}}{\pi R^2}$$
- k_b: rate at which a constraining bridge is removed
$$k_{\text{b}} = n_{cb} k_{\text{off}}$$
- In steady conditions, $\langle k_a \rangle = \langle k_b \rangle \rightarrow$
$$\langle \tau_{cb} \rangle = \frac{1}{\langle k_a \rangle + \langle k_b \rangle} = \frac{1}{2k_{\text{off}} \langle n_{cb} \rangle}$$
- In steady conditions, $\frac{d\langle n_b \rangle}{dt} = 0 \rightarrow$
$$\langle A_{\text{out}} \rangle = \pi \frac{R^2 < n_{cb} >}{\langle n_b \rangle}$$

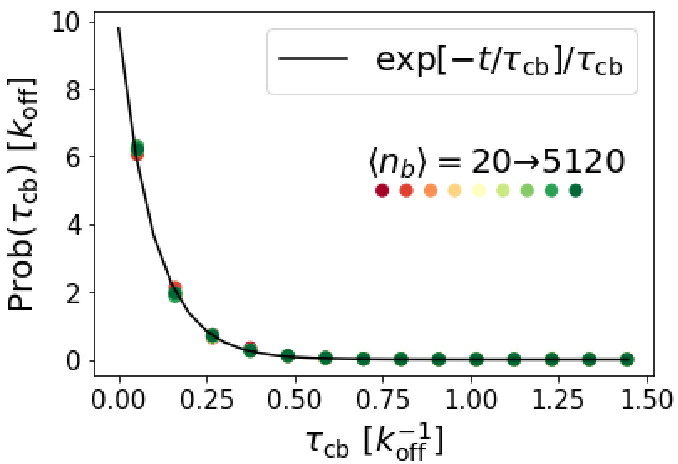
Updating sets of CBs: δ_{cb}

- Average displacement following an update of the CBs, δ_{cb}



$$\langle \delta_{cb} \rangle = \sqrt{\frac{\pi}{\langle n_{cb} \rangle} \frac{R}{\langle n_b \rangle}} \quad \text{(fitted)}$$

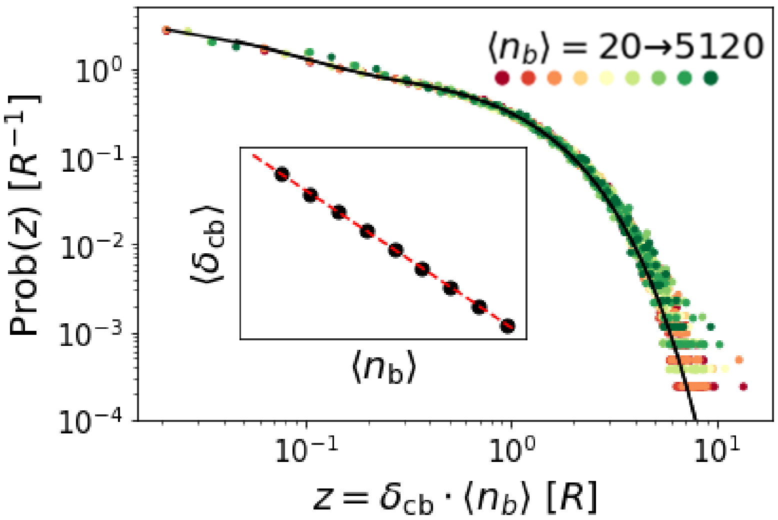
- δ_{cb} sampled using MC simulations in which we add/remove bridges while rattling the disk



- We verify that τ_{cb} follows the expected Poisson distribution

Updating sets of CBs: δ_{cb}

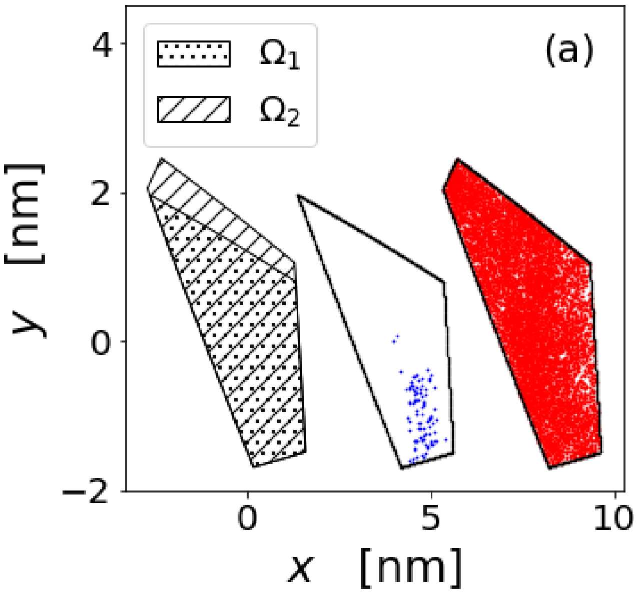
- Average displacement following an update of the CBs, δ_{cb}



$$\langle \delta_{cb} \rangle = \sqrt{\frac{\pi}{\langle n_{cb} \rangle}} \frac{R}{\langle n_b \rangle} \quad \text{(fitted)}$$

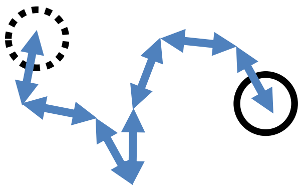
- δ_{cb} sampled using MC simulations in which we add/remove bridges while rattling the disk

- $\langle \delta_{cb} \rangle = \frac{\sqrt{\langle |\Omega| \rangle}}{\langle n_{cb} \rangle} \rightarrow$ Subsequent configurational spaces visited by the particle overlap $\Omega_i \cap \Omega_{i+1} \neq \emptyset$

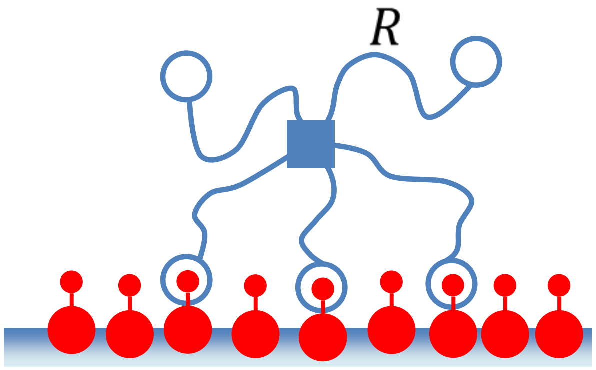


Emerging sliding diffusion constant

- Emerging diffusion constant, **mobile ligands**, $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi R^2 k_{\text{off}}}{\langle n_b \rangle^2}$



$$\langle \delta_{cb,i} \delta_{cb,i+1} \rangle = \langle \delta_{cb,i} \rangle \langle \delta_{cb,i+1} \rangle$$



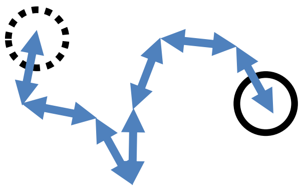
MOLECULAR WALKER

$$D = \frac{1}{2} \frac{k_{on} k_{off}}{k_{on} + k_{off}} \frac{R^2}{\langle n_b \rangle^2}$$

Kowalewski *et al*, J. Phys. Chem. B **125**, 6857 (2021)

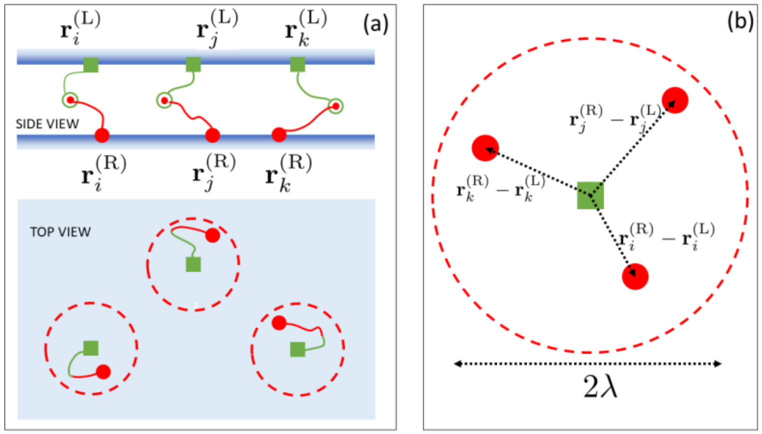
Emerging sliding diffusion constant

- Emerging diffusion constant, **mobile ligands**, $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi R^2 k_{\mathrm{off}}}{\langle n_b \rangle^2}$



$$\langle \delta_{cb,i} \delta_{cb,i+1} \rangle = \langle \delta_{cb,i} \rangle \langle \delta_{cb,i+1} \rangle$$

- Emerging sliding diffusion constant, **fixed ligands**, $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi \lambda^2 k_{\mathrm{off}}}{\langle n_b \rangle^2}$



$$\langle \tau_{cb} \rangle = \frac{1}{2 k_{\mathrm{off}} \langle n_{cb} \rangle}$$

$$\langle \delta_{cb} \rangle = \sqrt{\frac{\pi}{\langle n_{cb} \rangle}} \frac{\lambda}{\langle n_b \rangle}$$

- λ: extensibility of a bridge

Simulation validation

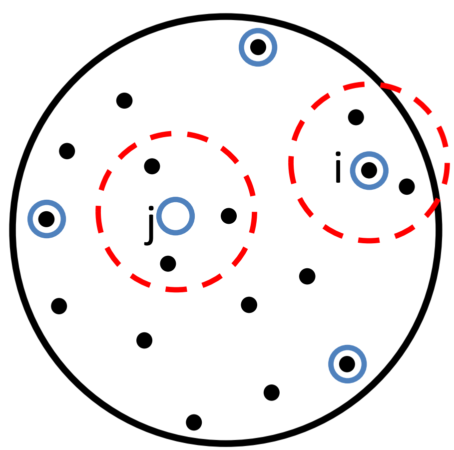
- **Mobile ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi R^2 k_{\text{off}}}{\langle n_b \rangle^2}$ **Fixed ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi \lambda^2 k_{\text{off}}}{\langle n_b \rangle^2}$

- Simulations (reaction-diffusion dynamics) validate the theory

```
t ← 0
while t < t_E do
    Fire Reactions(Δt)
    i_B = 0
    while i_B < N_B do
        Brownian Diffusion(Δt/N_B)
        i_B ← i_B + 1
    end while
    t ← t + Δt
end while
```

- The reaction algorithm (Gillespie) samples the type of reaction to be implemented and the time for it to happen t_{reac}

$$a_{on}^T = \Sigma_i a_{on}(\text{i}) \quad a_{off}^T = k_{off} n_b$$



$$a_{on}(\text{i}) = 0$$
$$a_{on}(\text{j}) = 3k_{\text{on}}$$

https://github.com/bmognetti/SlidingDiffusionConstant_Mobile.git
https://github.com/StevensLaurie/Disk_Diffusion

Simulation validation

- **Mobile ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi R^2 k_{\text{off}}}{\langle n_b \rangle^2}$ **Fixed ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi \lambda^2 k_{\text{off}}}{\langle n_b \rangle^2}$

○ Simulations (reaction-diffusion dynamics) validate the theory

```
t ← 0
while t < t_E do
    Fire Reactions(Δt)
    i_B = 0
    while i_B < N_B do
        Brownian Diffusion(Δt / N_B)
        i_B ← i_B + 1
    end while
    t ← t + Δt
end while
```

○ The reaction algorithm (Gillespie) samples the type of reaction to be implemented and the time for it to happen t_{reac}

$$a_{on}^T = \Sigma_i a_{on}(\mathrm{i}) \qquad a_{off}^T = k_{off} n_b$$

$$P(t_{reac}) = \left(a_{on}^T + a_{off}^T\right) \mathrm{e}^{-\left(a_{on}^T + a_{off}^T\right) t_{reac}}$$

○ If $t_r + t_{reac} < \Delta t$, we update the affinity lists, implement a reaction, and select a new t_{reac}

https://github.com/bmognetti/SlidingDiffusionConstant_Mobile.git
https://github.com/StevensLaurie/Disk_Diffusion

Simulation validation

- **Mobile ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \boxed{\frac{\pi R^2 k_{\text{off}}}{\langle n_b \rangle^2}}$ **Fixed ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \boxed{\frac{\pi \lambda^2 k_{\text{off}}}{\langle n_b \rangle^2}}$

  - Simulations (reaction-diffusion dynamics) validate the theory

```
t ← 0
while t < t_E do
    Fire Reactions(Δt)
    i_B = 0
    while i_B < N_B do
        Brownian Diffusion(Δt/N_B)
        i_B ← i_B + 1
    end while
    t ← t + Δt
end while
```

- Brownian Dynamics diffusion of the particle's position $r(t+\Delta t) = r(t) + \Delta r$

$$\Delta r = \frac{f D_0 \Delta t}{k_B T} + \delta r \qquad \langle \delta r^2 \rangle = 2 D_0 \Delta t$$

$$\Delta \varphi = \frac{\tau D_0^R \Delta t}{k_B T} + \delta \varphi \qquad \langle \delta \varphi^2 \rangle = 2 D_0^R \Delta t$$

- If a bridge becomes overstretched the BD update is rejected

- To limit the rejection rate, we divide the BD update into N_B sub-steps

https://github.com/bmognetti/SlidingDiffusionConstant_Mobile.git
https://github.com/StevensLaurie/Disk_Diffusion

Simulation validation

- **Mobile ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \boxed{\frac{\pi R^2 k_{\text{off}}}{\langle n_b \rangle^2}}$ **Fixed ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \boxed{\frac{\pi \lambda^2 k_{\text{off}}}{\langle n_b \rangle^2}}$

○ Simulations (reaction-diffusion dynamics) validate the theory

```
t ← 0
while t < t_E do
    Fire Reactions(Δt)
    Static Update()
    t ← t + Δt
end while
```

○ In the reaction-limited regime, we update the position of the particle by sampling Ω statically

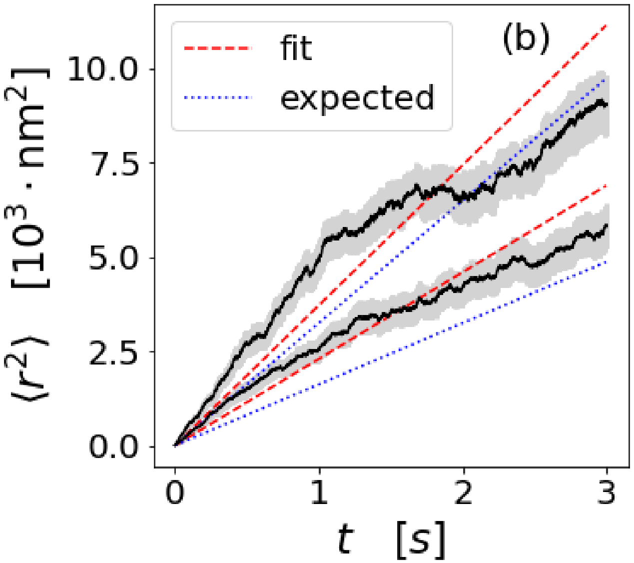
https://github.com/bmognetti/SlidingDiffusionConstant_Mobile.git
https://github.com/StevensLaurie/Disk_Diffusion

Simulation validation

- **Mobile ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \boxed{\frac{\pi R^2 k_{\text{off}}}{\langle n_b \rangle^2}}$ **Fixed ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \boxed{\frac{\pi \lambda^2 k_{\text{off}}}{\langle n_b \rangle^2}}$

○ Simulations (reaction-diffusion dynamics) validate the theory

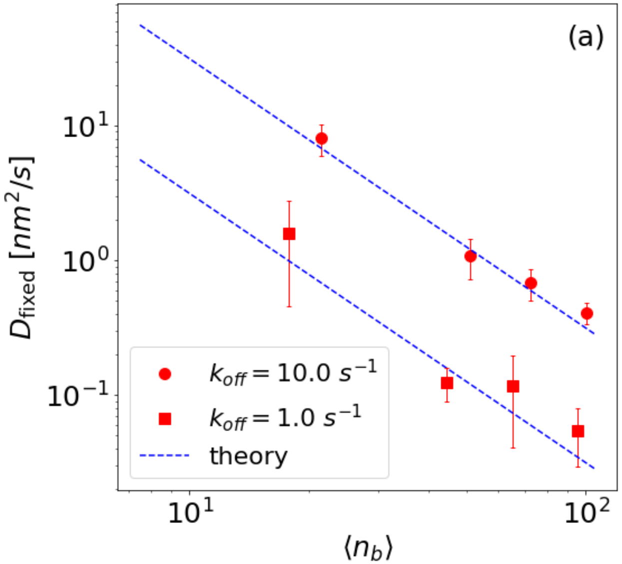
MOBILE



$k_{\text{off}} = 318 \cdot s^{-1}; 636 \cdot s^{-1}$

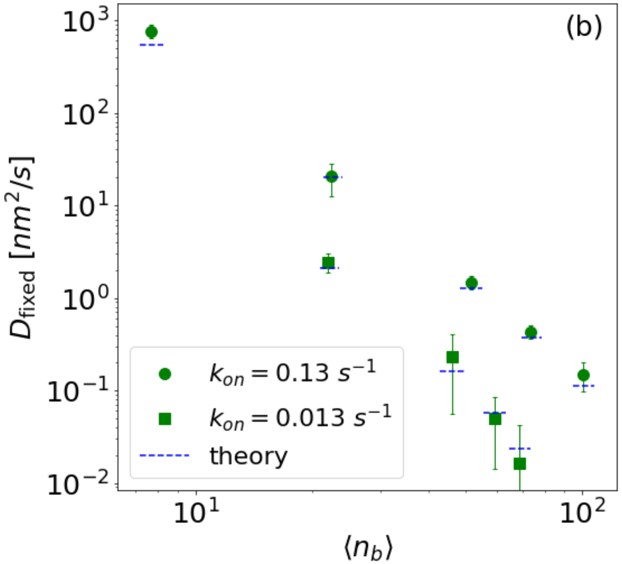
$\langle n_b \rangle \approx 110$

FIXED



○ Different values of k_{on}

FIXED

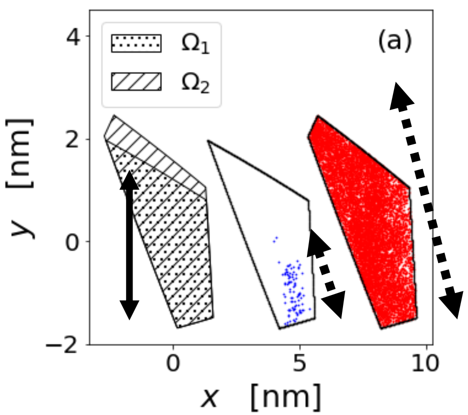


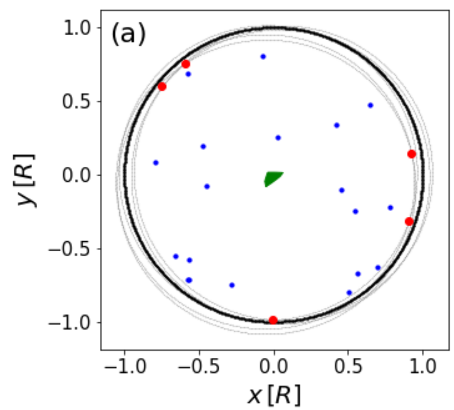
○ Different values of k_{off}

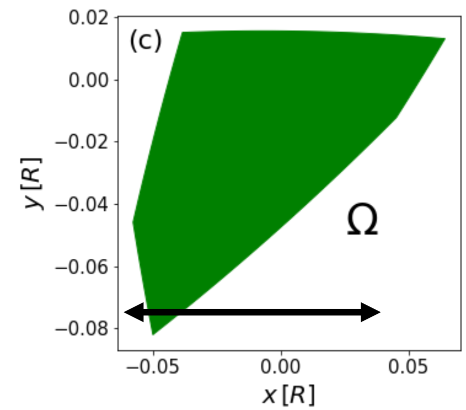
Discussion: possible limitations

- **Mobile ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi R^2 k_{\text{off}}}{\langle n_b \rangle^2}$ **Fixed ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi \lambda^2 k_{\text{off}}}{\langle n_b \rangle^2}$

  - The theory neglects that D may be limited by hydrodynamic friction. Predictions are reliable if $D_0 \langle \tau_{cb} \rangle \geq |\Omega|$ (reaction-limited diffusion)







- $\sqrt{D_0 \cdot \tau_{cb}}$: potential distance explored by the trajectory while rattling
- $\sqrt{|\Omega|}$: typical linear extension of the configurational space

  $\sqrt{|\Omega|} \sim \frac{R}{\langle n_b \rangle}$ (mobile) $\sim \frac{\lambda}{\langle n_b \rangle}$ (fixed)

Discussion: possible limitations

- **Mobile ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi R^2 k_{\text{off}}}{\langle n_b \rangle^2}$ **Fixed ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi \lambda^2 k_{\text{off}}}{\langle n_b \rangle^2}$

  - The theory neglects that D may be limited by hydrodynamic friction. Predictions are reliable if $D_0 \langle \tau_{cb} \rangle \geq |\Omega|$ (reaction-limited diffusion)

  - Static and dynamic correlations between stochastic variables (e.g., $\langle A_{out} n_{cb} \rangle$, $\langle \delta_{cb} \cdot n_{cb} \rangle$, $\langle \delta_{cb,i} \cdot \delta_{cb,i+1} \rangle$, …)

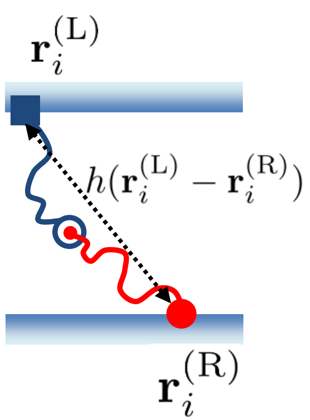
Discussion: possible limitations

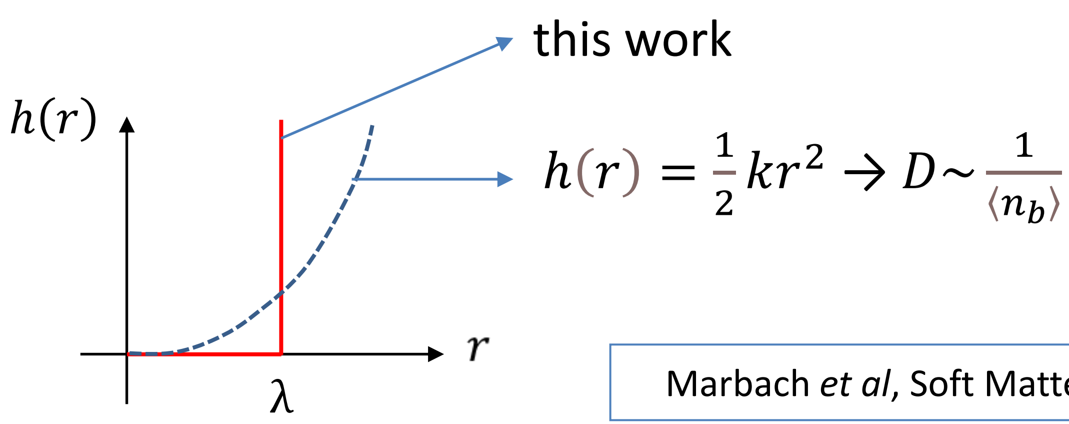
- **Mobile ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi R^2 k_{\text{off}}}{\langle n_b \rangle^2}$ **Fixed ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi \lambda^2 k_{\text{off}}}{\langle n_b \rangle^2}$

  - The theory neglects that D may be limited by hydrodynamic friction. Predictions are reliable if $D_0 \langle \tau_{cb} \rangle \geq |\Omega|$ (reaction-limited diffusion)

  - Static and dynamic correlations between stochastic variables (e.g., $\langle A_{out} n_{cb} \rangle$, $\langle \delta_{cb} \cdot n_{cb} \rangle$, $\langle \delta_{cb,i} \cdot \delta_{cb,i+1} \rangle$, …)

  - Results based on a particular choice of the bond potential $h(r)$



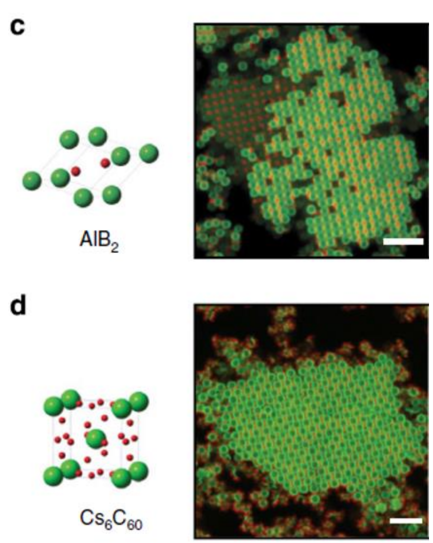


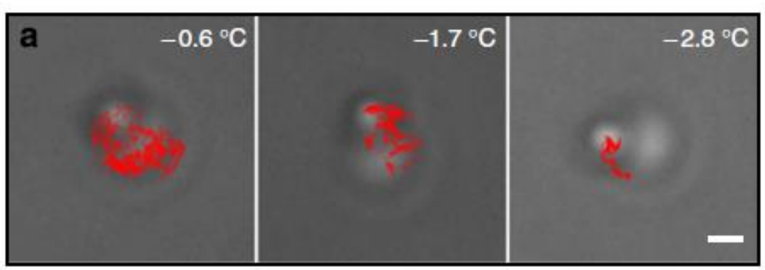
Marbach *et al*, Soft Matter **2022**

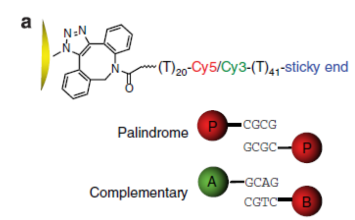
Discussion: experimental predictions

- **Mobile ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi R^2 k_{\mathrm{off}}}{\langle n_b \rangle^2}$ **Fixed ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi \lambda^2 k_{\mathrm{off}}}{\langle n_b \rangle^2}$

  - DNA coated colloids with a high grafting density crystallize







Wang *et al*, Nat. Commun. **2015**; Kim *et al*, Langmuir. **2006**

$$\langle n_b \rangle \sim \rho_R \rho_L \mathrm{e}^{-\beta \Delta G(T)}$$

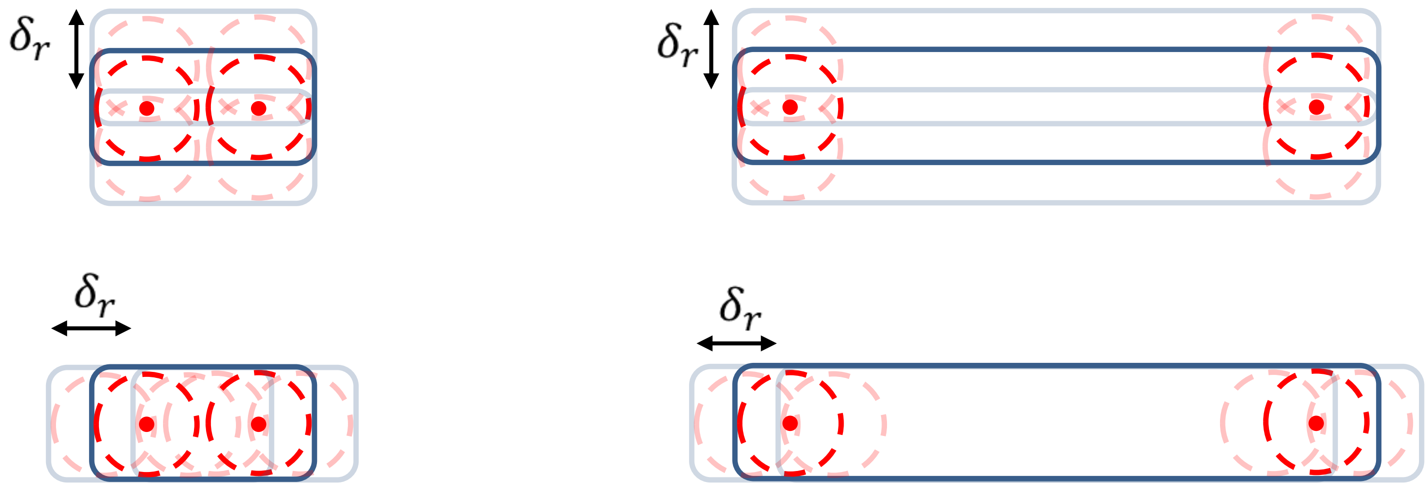
$$k_{\mathrm{off}} \sim \mathrm{e}^{\beta \Delta G(T)}$$

  - Higher values of ρ_{R} or ρ_{L} will increase the value of the hybridisation free energy $\Delta G(T)$ (at a given $\langle n_b \rangle$) and therefore increase k_{off}

Jana, Mognetti, PRE **2019**

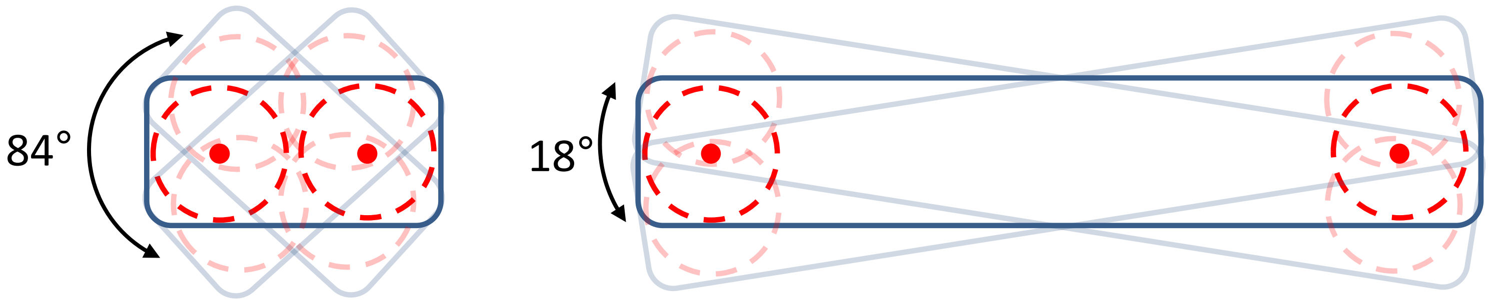
Discussion: experimental predictions

- **Mobile ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi R^2 k_{\text{off}}}{\langle n_b \rangle^2}$ **Fixed ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi \lambda^2 k_{\text{off}}}{\langle n_b \rangle^2}$
  - DNA coated colloids with a high grafting density crystallize
  - The translational diffusion constant is not a function of the particle shape



Discussion: experimental predictions

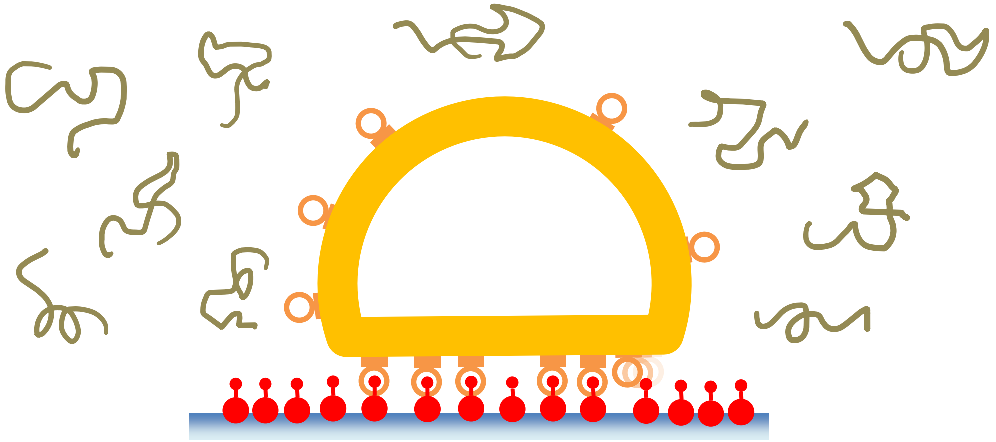
- **Mobile ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi R^2 k_{\text{off}}}{\langle n_b \rangle^2}$ **Fixed ligands**: $D = \frac{\langle \delta_{cb} \rangle^2}{2\langle \tau_{cb} \rangle} = \frac{\pi \lambda^2 k_{\text{off}}}{\langle n_b \rangle^2}$
  - DNA coated colloids with a high grafting density crystallize
  - The translational diffusion constant is not a function of the particle shape



(the rotational diffusion constant is affected by the particle shape)

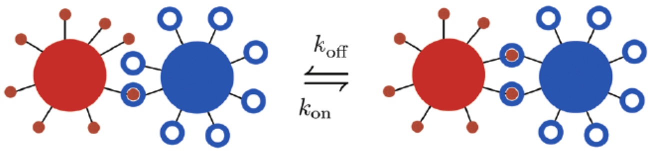
Discussion: experimental predictions

- **Mobile ligands**: $D = \frac{\langle\delta_{cb}\rangle^2}{2\langle\tau_{cb}\rangle} = \frac{\pi R^2 k_{\mathrm{off}}}{\langle n_b\rangle^2}$ **Fixed ligands**: $D = \frac{\langle\delta_{cb}\rangle^2}{2\langle\tau_{cb}\rangle} = \frac{\pi \lambda^2 k_{\mathrm{off}}}{\langle n_b\rangle^2}$
  - DNA coated colloids with a high grafting density crystallize
  - The translational diffusion constant is not a function of the particle shape
  - The emerging mobility is not a function of the hydrodynamic friction

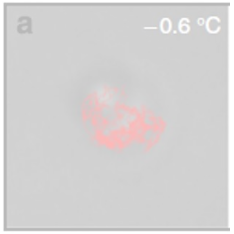


D is not affected by crowders

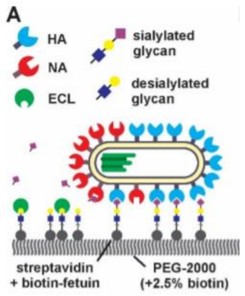
Plan of the talk



- Dynamics of particles moving through reversible ligand-receptor contacts
  - Predicting the emerging diffusion constant *D* in reaction-limited conditions



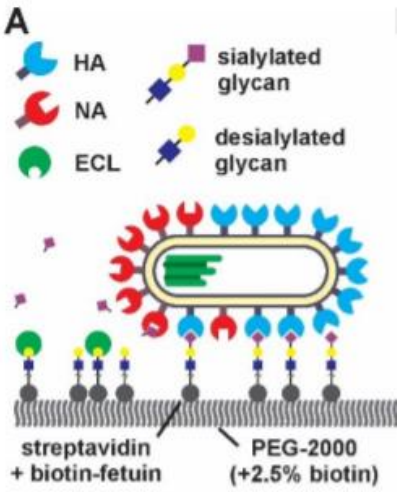
  - Comparison with simulations and experiments
  - Increasing the motility of the particles using enzymes (Influenza A Virus)

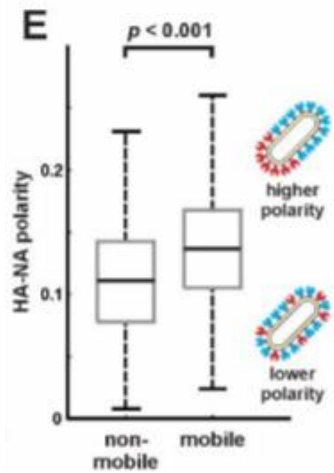


- Self-assembly dynamics
  - Finite reaction rates alter the morphology of steady aggregates

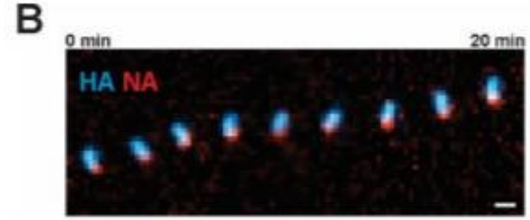
Mobility of IAV virions

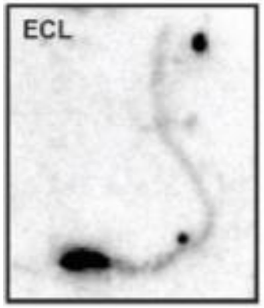
- IAV virions carry receptor-binding (HA) and receptor-cleaving (NA) proteins





persistent motion towards the HA-rich pole





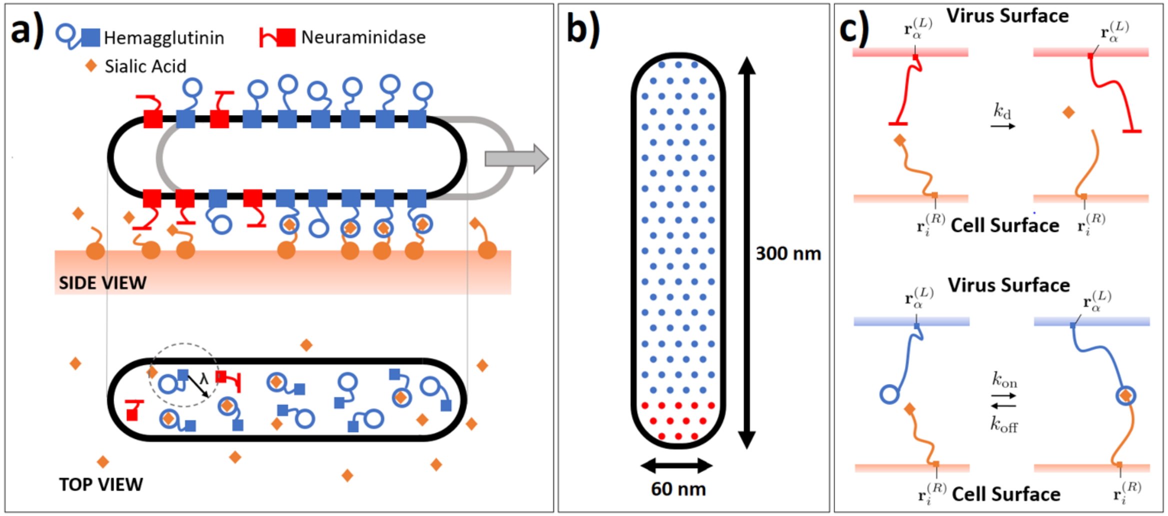
trails of passivated receptors

Vahey, Fletcher eLife **2019**

- ○ Hemagglutinin (HA) binds to receptors presenting sialic acid (SA) residues
- ○ Receptor-cleaving protein neuraminidase (NA) passivates receptors
- ○ The reduced number of HA-SA contact increases the motility of IAV virions

Mobility of IAV virions

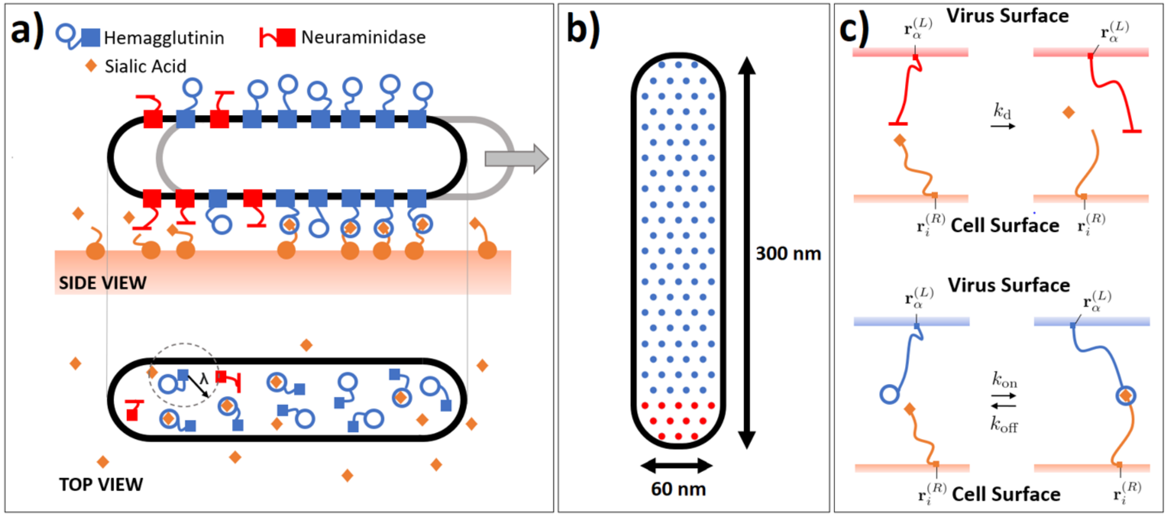
- Polarised IAV virions (in which NA ligands are clustered)



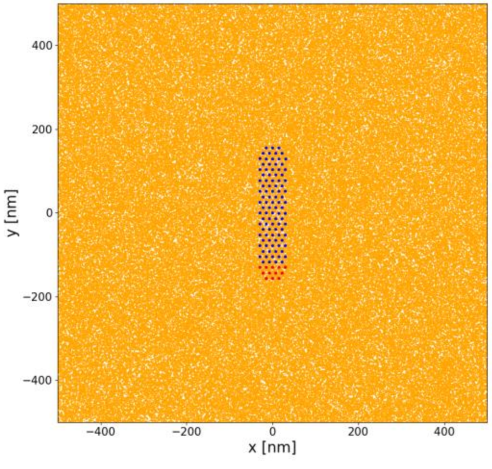
Stevens *et al*, submitted

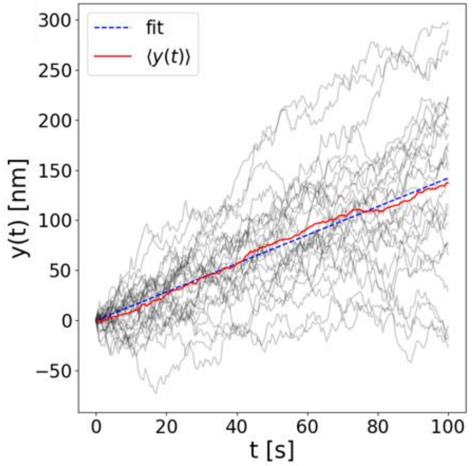
Mobility of IAV virions

- Polarised IAV virions (in which NA ligands are clustered)



- At short timescales, the virion drifts in the direction opposite to the NA ligands

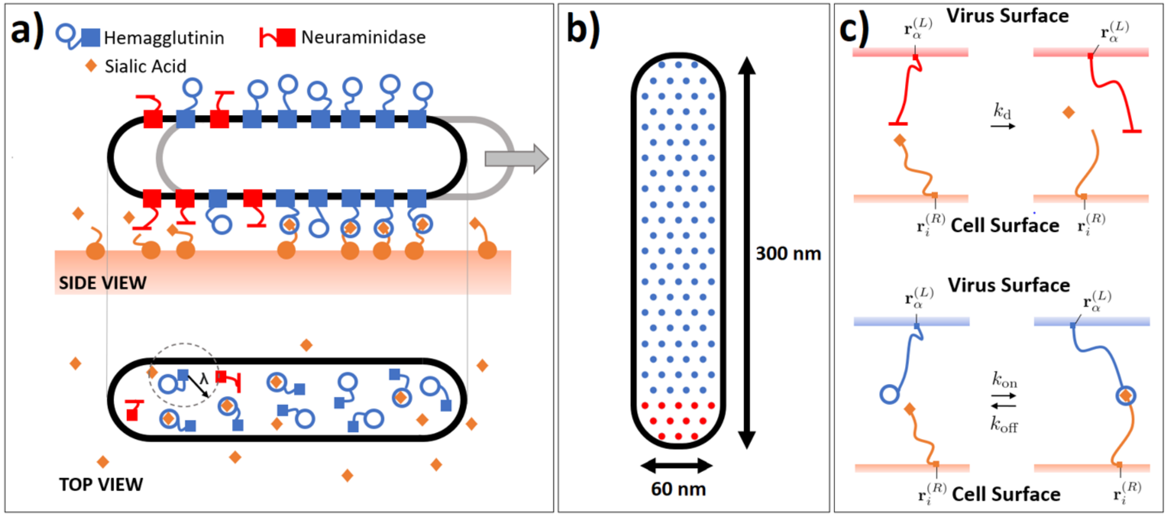




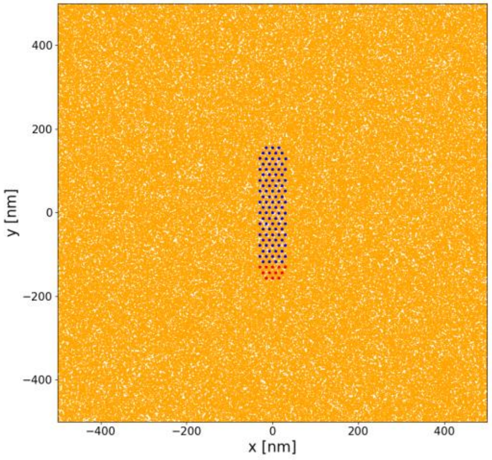
Stevens *et al*, submitted

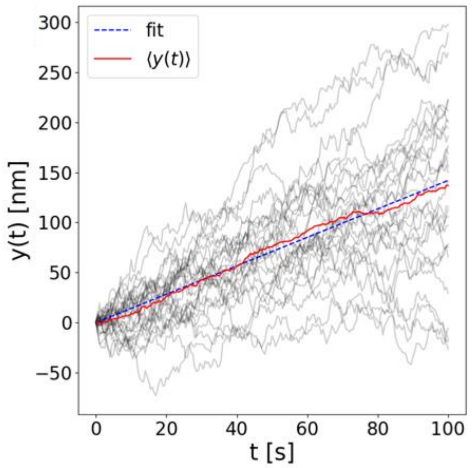
Mobility of IAV virions

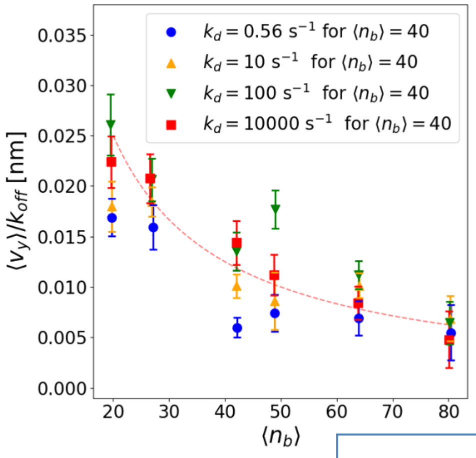
- Polarised IAV virions (in which NA ligands are clustered)



- At short timescales, the virion drifts in the direction opposite to the NA ligands
- The drifting velocity scales like $\langle v_y \rangle \sim 1/\langle n_b \rangle$ and is weakly affected by k_d





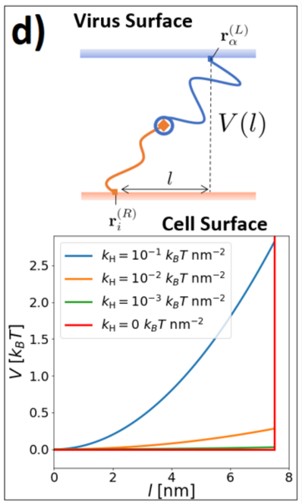


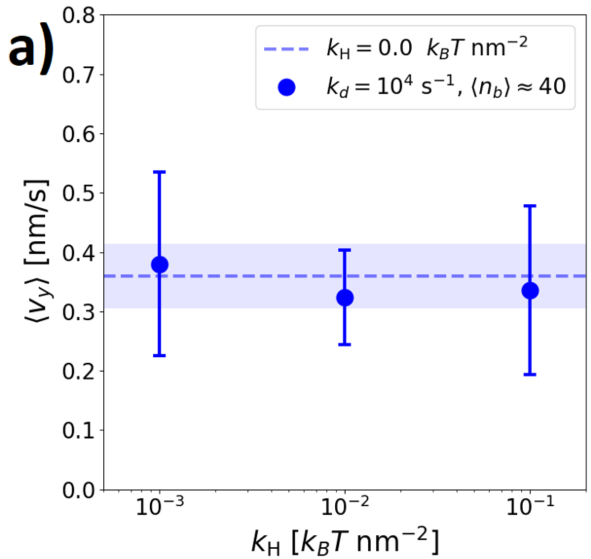
Stevens *et al*, submitted

Mobility of IAV virions

- IAV virions in which NA ligands are clustered

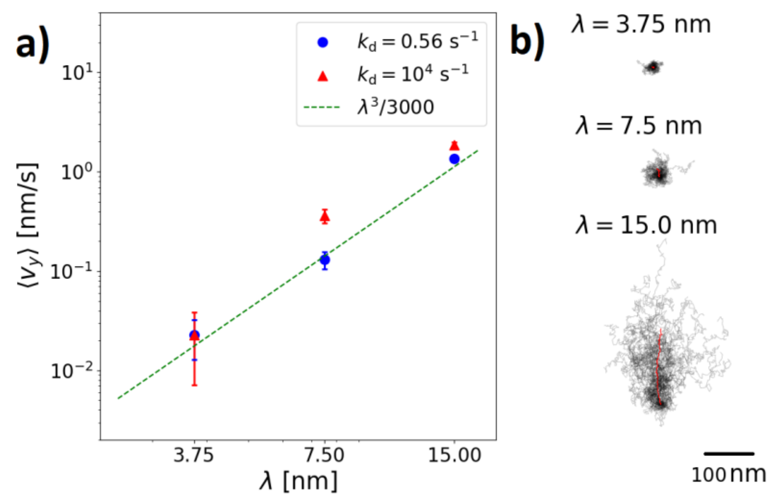
Stevens *et al*, submitted





- Configurational forces do not affect v_y (consistent with reaction-limited dynamics)

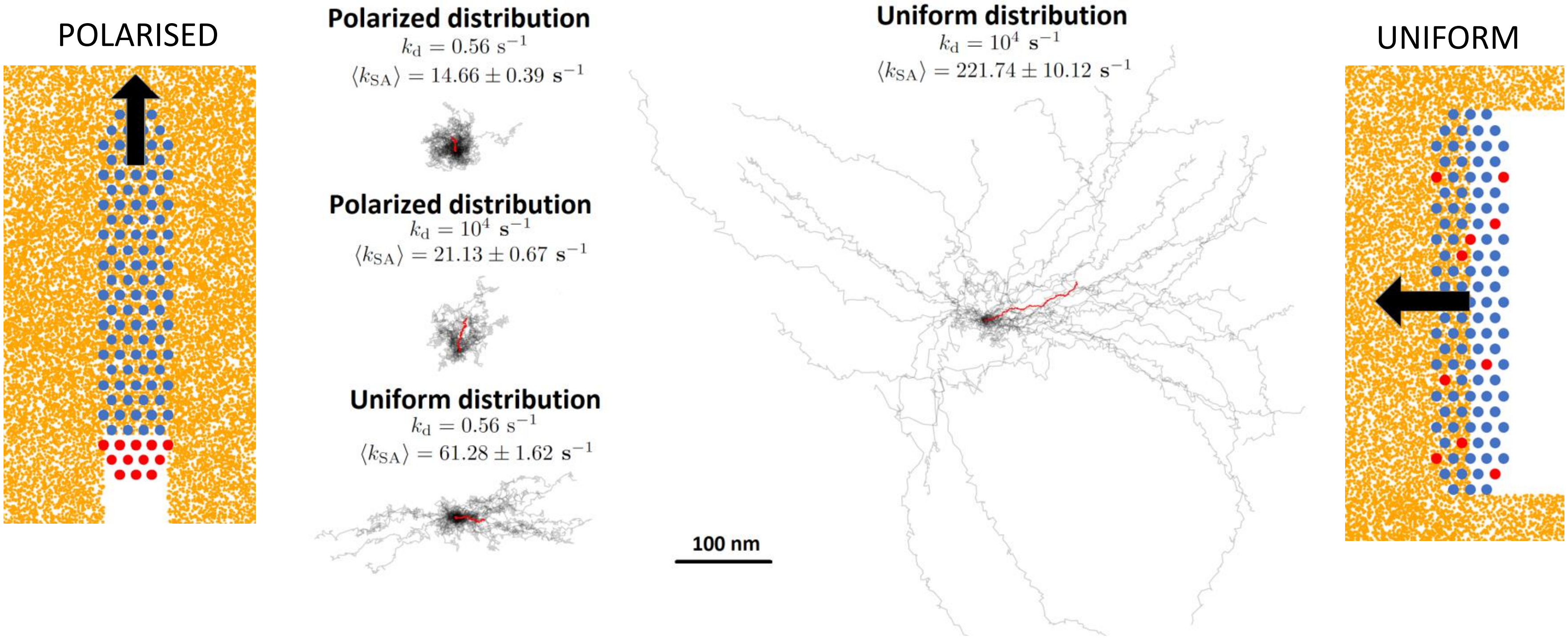
- The maximal lateral distance at which a pair of ligand-receptor molecules can form a bridge (λ) greatly affects v_y



Mobility of IAV virions

- Comparing different NA distributions

Stevens *et al*, submitted

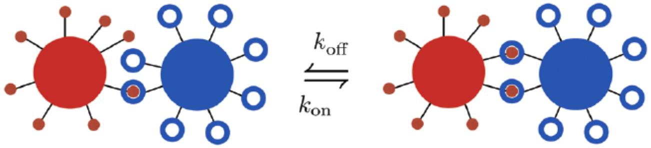


- Virions with uniformly distributed NA ligands move orthogonally to the particle's axis

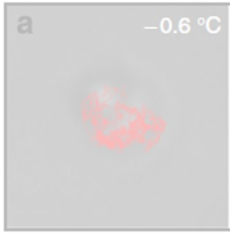
Sakai *et al*, J. Virol. **2018**; Bazrafshan *et al,* Angew. Chem. Int. Ed. **2020**

- The motility of virions with uniformly distributed ligands is more sensitive to variations in the catalytic rate (k_d)

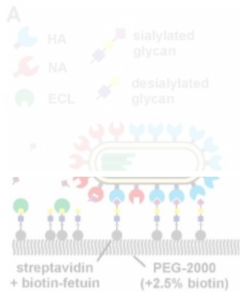
Plan of the talk



- Dynamics of particles moving through reversible ligand-receptor contacts
  - Predicting the emerging diffusion constant *D* in reaction-limited conditions



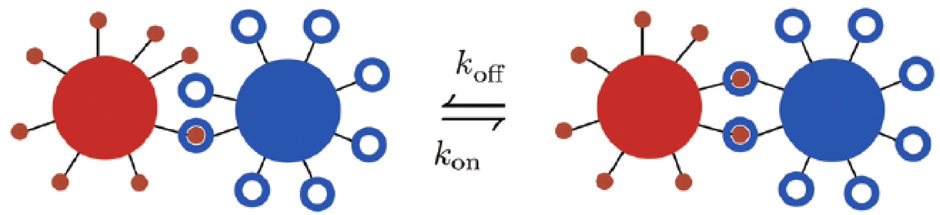
  - Comparison with simulations and experiments
  - Increasing the motility of the particles using enzymes (Influenza A Virus)

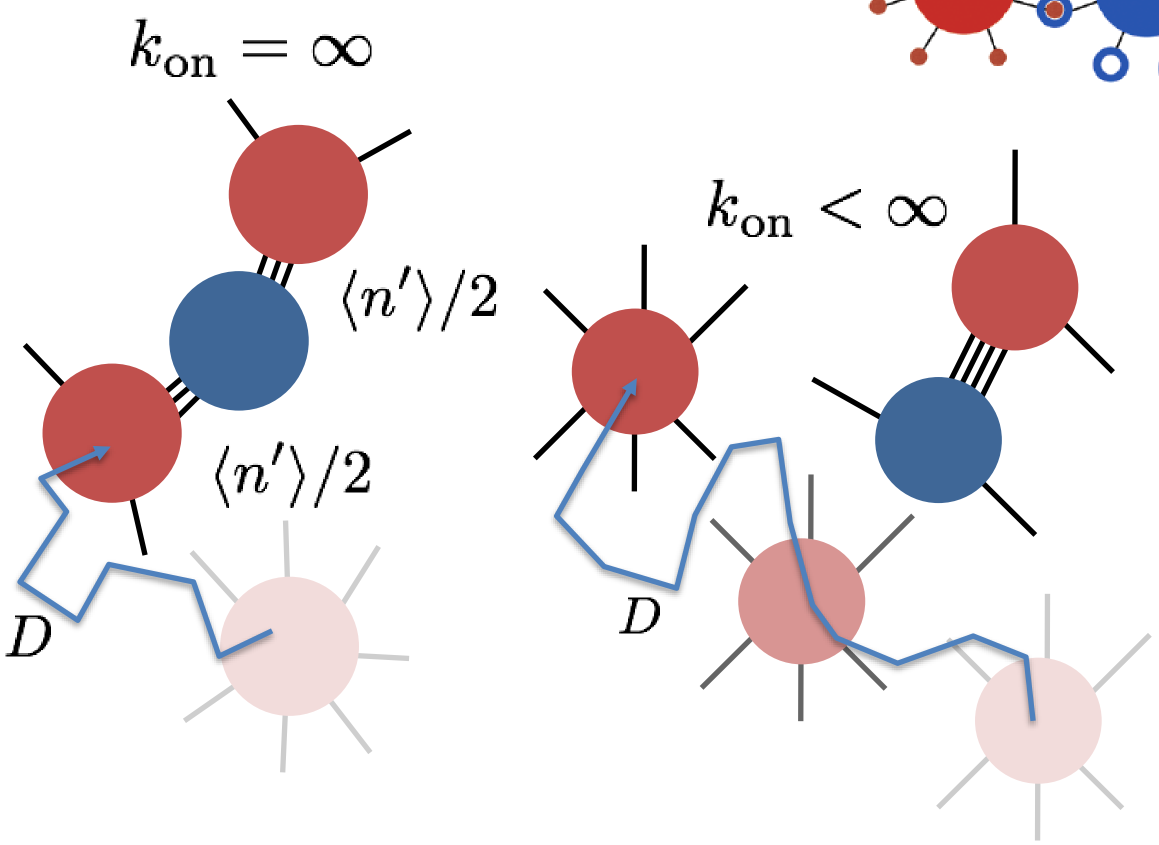


- Self-assembly dynamics
  - Finite reaction rates alter the morphology of steady aggregates

Particles functionalized by mobile linkers

- Finite reaction rates drastically affect self-assembly





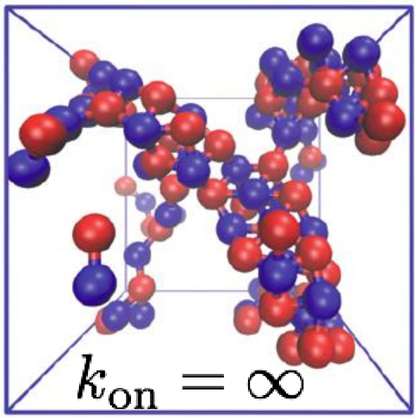
- Linkers segregate in the interaction patch
- Formation of new colloid-colloid contacts is limited by *on/off* reactions
- Kinetic control of the valency used to assemble *colloidomers*

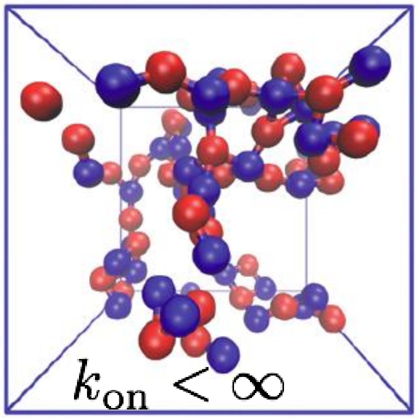
Bachmann, Petitzon *et al,* Soft Matter **2016**

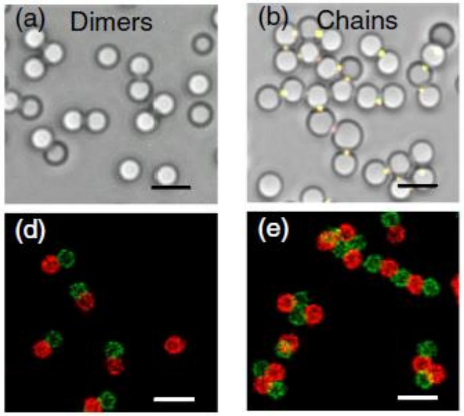
McMullen *et al,* PRL **2018**

Particles functionalized by mobile linkers

- Finite reaction rates drastically affect self-assembly

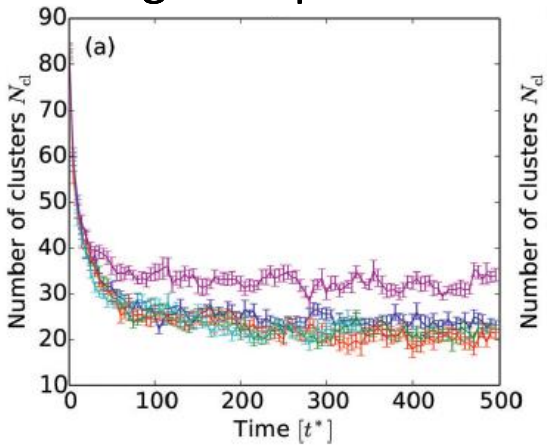




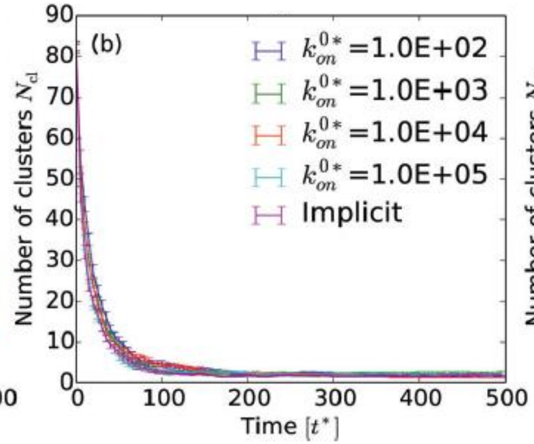


McMullen *et al,* Phys. Rev. Lett. **2019**; Feng *et al*, Soft Matter **2013**

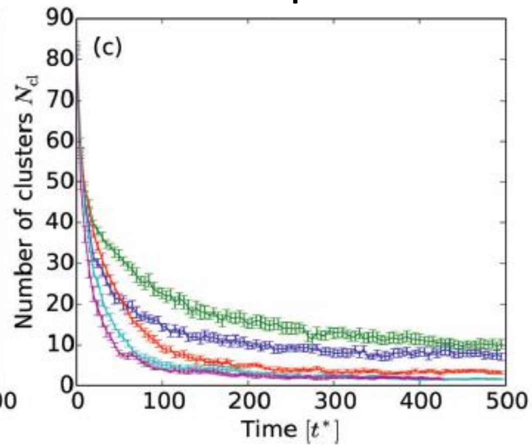
High temperature



Int. temperature



Low temperature



Bachmann, Petitzon *et al,* Soft Matter **2016**

Acknowledgements

- Coauthors
  - Janna Lowenshon (ULB, Belgium)
  - Laurie Stevens (VUB-ULB, Belgium)
  - Sophie de Buyl (VUB, Belgium)
  - Pritam Kumar Jana (BITS Pilani, India)
  - Marius Petitzon (VUB, Belgium)
  - Stephan Bachmann (BASF, Germany)
- Funding
- Computing