Designing nanoparticles for membrane fusion

Sofía Blasco[1,3], Lukáš Sukeník[1,2], Robert Vácha[1,2,3]

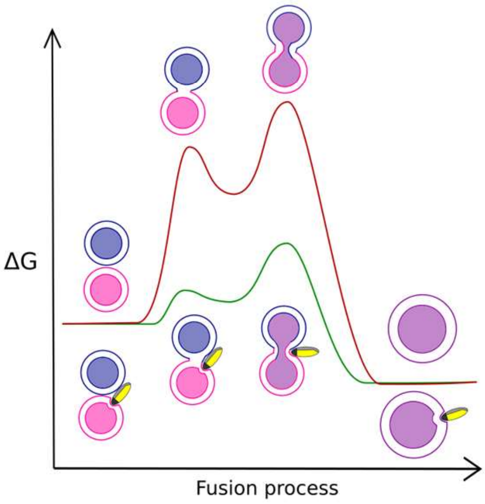
[1]CEITEC -- Central European Institute of Technology, Masaryk University, Kamenice 753/5, 625 00 Brno, Czech Republic

[2]Department of Condensed Matter Physics, Faculty of Science, Masaryk University, Kotlářská 267/2, 611 37 Brno , Czech Republic

[3] National Centre for Biomolecular Research, Faculty of Science, Masaryk University, Kamenice 5, 625 00 Brno, Czech Republic

VÁCHA LAB

INTRODUCTION

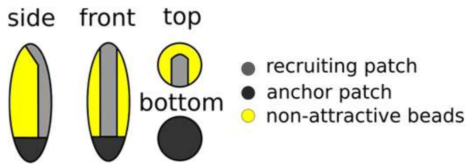


The process of membrane fusion occurs in two main steps:

- **Stalk formation**: lipid mixing without content mixing
- **Pore opening**: content mixing

This steps also correspond with the energy barriers of the process.

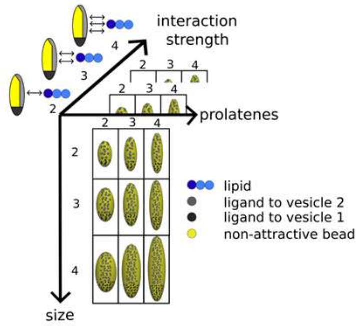
The aim of the project is **to design a nanoparticle (NP)** that would **promote membrane fusion**, by lowering said energy barriers.



Anchor patch: create membrane curvature
Recruiting patch: bring second vesicle to contact

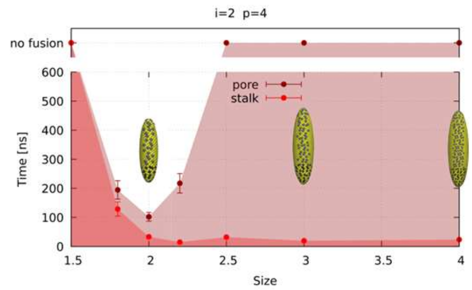
METHODS

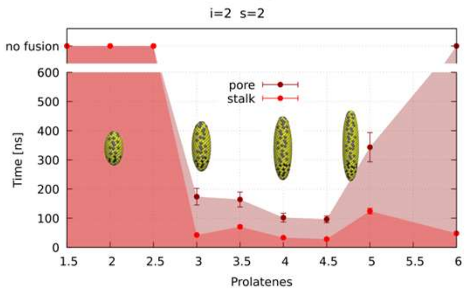
We varied three parameters: **size** (s), **prolateness** (p), **ligand interaction strength** (i).

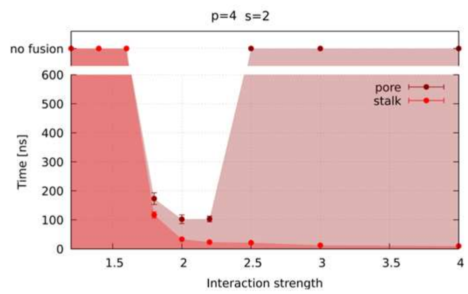


- We performed **coarse grained molecular dynamics** simulations with LAMMPS.
- Each **lipid** is composed of **three beads**: two tails and one head bead.
- Nanoparticle has **two types of ligands**, each binding one vesicle.
- Anchor patch i is not varied (4kT) to allow complete NP embedding.

RESULTS

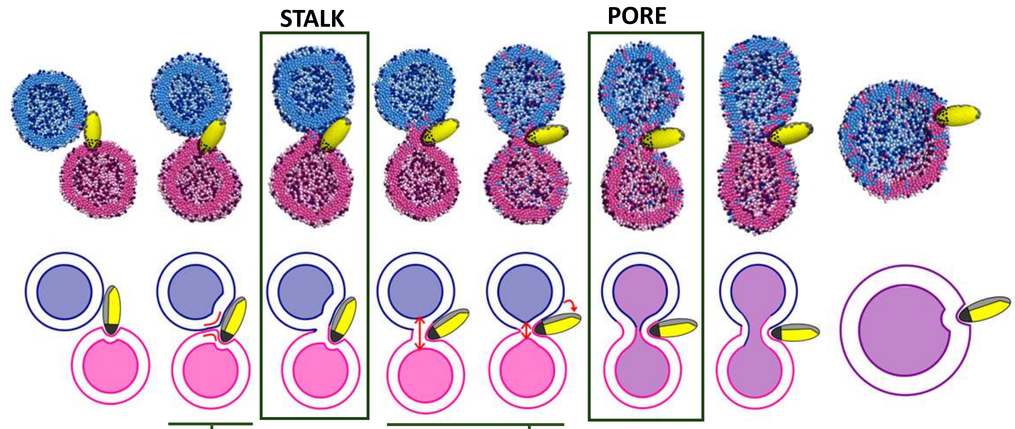






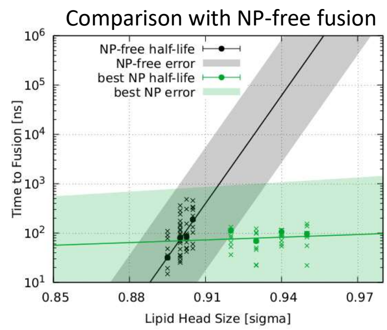
By varying the above-mentioned nanoparticle parameters, we found the optimal ranges for which fusion is achievable.

Nanoparticles need to promote stalk formation without stabilizing it, and then be able to produce pore opening between the vesicles.



The vesicles make contact in a point of high membrane curvature.

The partly unbinding of the nanoparticle produces a shortening in the distance between vesicle contents.



CONCLUSIONS

- We found an optimal parameter combination of a prolate nanoparticle to promote fusion between vesicles.
- Nanoparticle induced fusion successfully lower the energy barriers of the process, allowing faster fusion than NP-free vesicles.
- Possible applications include drug delivery with liposomes.
- New nanoparticle designs can be explored with the knowledge obtained.

National Institute of Virology and Bacteriology
No. LX22NPO5103

Funded by the European Union NextGenerationEU

erc European Research Council
No. 101001470

CEITEC

MUNI

MINISTRY OF EDUCATION, YOUTH AND SPORTS

CZECH RECOVERY PLAN

This work was supported by the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 101001470) and the project National Institute of virology and bacteriology (Programme EXCELES, ID Project No. LX22NPO5103) - Funded by the European Union - Next Generation EU. Computational resources were provided by the CESNET, CERIT Scientific Cloud, and IT4 Innovations National Supercomputing Center by MEYS CR through the e-INFRA CZ (ID:90254).