

The European Spallation Source – possibilities for life science & pharma research

Zoë Fisher Deuteration & Macromolecular Crystallization Group European Spallation Source



ESS: The Next-Generation Neutron Source

https://europeanspallationsource.se/building-ess



Aerial view 12 August 2021



ESS instruments will be very well equipped to support users from life science, chemistry, soft matter areas



ESS offers more than just neutron instruments

- Besides instruments, we are also establishing user support labs
- On-site @ ESS: several"general" user labs (chemistry, LS & SCM, characterization)
- Off-site @ MV, LU: DEMAX support labs (<u>DE</u>uteration & <u>MA</u>cromolecular <u>X</u>tallization support lab) for chemical & biological deuteration and support for protein crystal growth













Neutrons for Life Sciences



Structure

Short Article

Biophysical Journal

Article

Malleability of the SARS-CoV-2 3CL Mpro Active-Site **Cavity Facilitates Binding of Clinical Antivirals**

Graphical Abstract



Authors

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In Brief

Kneller et al used room temperature Xray crystallography and in vitro enzyme kinetics to probe the binding of hepatitis C clinical protease inhibitors and the natural aldehyde leupeptin to the SARS-CoV-2 main protease (3CL M^{pro}). The study visualized significant malleability of the enzyme active-site cavity, providing insights for drug design.

Article

cells

Hybrid Biopolymer and Lipid Nanoparticles with Improved Transfection Efficacy for mRNA

Christian D. Siewert ¹, Heinrich Haas ², Vera Cornet ¹, Sara S. Nogueira ², Thomas Nawroth ¹, Lukas Uebbing 10, Antje Ziller 1, Jozef Al-Gousous 1, Aurel Radulescu 30, Martin A. Schroer 40 Clement E. Blanchet⁴, Dmitri I. Svergun⁴, Markus P. Radsak⁵, Ugur Sahin^{2,6} and Peter Langguth 1,*

> Molecular Therapy Nucleic Acids Original Article

Functionalized lipid nanoparticles for subcutaneous administration of mRNA to achieve systemic exposures of a therapeutic protein

Nigel Davies,¹ Daniel Hovdal,² Nicholas Edmunds,^{3,9} Peter Nordberg,² Anders Dahlén,² Aleksandra Dabkowska,¹ Marianna Yanez Arteta,¹ Aurel Radulescu,⁵ Tomas Kjellman,^{1,10} Andreas Höijer,¹ Frank Seeliger,⁴ Elin Holmedal,⁴ Elisabeth Andihn,6 Nils Bergenhem,7 Ann-Sofie Sandinge,2 Camilla Johansson,4 Leif Hultin,4 Marie Johansson,4 Johnny Lindqvist,⁴ Liselotte Björsson,⁴ Yujia Jing,¹ Stefano Bartesaghi,² Lennart Lindfors,¹ and Shalini Andersson⁴



Transient and stabilized complexes of Nsp7, Nsp8,

Mateusz Wilamowski,^{1,2} Michal Hammel,³ Wellington Leite,⁴ Qiu Zhang,⁴ Youngchang Kim,^{1,5} Kevin L. Weiss,⁵ Robert Jedrzejczak,^{1,5} Daniel J. Rosenberg,^{3,6} Yichong Fan,⁴ Jacek Wower,⁷ Jan C. Bierma,³ Altal H. Sarker,⁵ Susan E. Tsutakawa,³ Sai Venkatesh Pingali,⁴ Hugh M. O'Neill,⁴ Andrzej Joachimiak,^{1,2,5,5} and Greg L. Hura^{3,5}

-10 >10

> Nsp7/8 (x²=0.6) Nsp7/8 + dsRNA

 $(65\% D_2O) (\chi^2=3.0)$

α (Å⁻¹)

0.1

0.01

and Nsp12 in SARS-CoV-2 replication

Nsp7/8 + dsRNA

Effect of Formulation Method, Lipid Composition, and PEGylation on Vesicle Lamellarity: A Small-Angle Neutron Scattering Study

Valeria Nele,^{†,‡,§} Margaret N. Holme,^{*,†,‡,§,||} Ulrike Kauscher,^{†,‡,§} Michael R. Thomas,^{†,‡,§} James J. Doutch,[⊥] and Molly M. Stevens*,^{†,‡,8,},[∥]®

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¹ISIS Neutron and Muon Source, STFC, Rutherford Appleton Laboratory, Didcot OX11 ODE, U.K.

Supporting Information

Biophysical Society

ABSTRACT: Liposomes are well-established systems for drug delivery and biosensing applications. The design of a liposomal carrier require careful choice of lipid composition and formulation method. These determine many vesicle properties including lamellarity, which can have a strong effect on both encapsulation efficiency and the efflux rate of encapsulated active compounds. Despite this, a comprehensive study on how the lipid composition and formulation method affect vesicle lamellarity is still lacking. Here, we combine small-angle neutron scattering and cryogenic transmission electron microscopy to study the effect of three different well-established formulation methods followed by extrusion through 100 nm polycarbonate membranes on the resulting



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vesicle membrane structure. Specifically, we examine vesicles formulated from the commonly used phospholipids 1-palmitoyl-2 vesice memorane structure. Specifically, we examine vesices formulated from the commonly used paosponjous 1-paintopit-oleoyl-sn-gytecro-3-phosphocholine (POPC). L2-dipaintoyl-sn-gytecro-3-phosphocholine (DPPC) and 1,2-diolooyl-sn-glycero-3-phosphocholine (DOPC) via film hydration followed by (i) agitation on a shaker or (ii) freeze-thansing, or (iii) the reverse-phase evaporation vesicle method. After extrusion, up to half of the total lipid content is still assembled into multilamellar structures. However, we achieved unilamellar vesicle populations when as little as 0.1 mol % PEG-modified lipid was included in the vesicle formulation. Interestingly, DPPC with 5 mol % PEGylated lipid produces a combination of cylindrical micelles and vesicles. In conclusion, our results provide important insights into the effect of the formulation method and lipid composition on producing liposomes with a defined membrane structure.

CHAPTER TWELVE

Proton transfer and drug binding details revealed in neutron diffraction studies of wild-type and drug resistant HIV-1 protease

Andrey Kovalevsky^{a,*}, Oksana Gerlits^b, Kaira Beltran^b, Kevin L. Weiss^a, David A. Keen^c, Matthew P. Blakeley^d, John M. Louis^e, Irene T. Weber^{f,g}



MDPI

Drug discovery and development process



How can you access ESS in the future?

- Access is managed through calls for proposals
- Since 2019 we use this portal & system to offer pilot access to our DEMAX lab services
- UPCOMING: Jan 2022 call for deuteration proposals will be issued
- Future: also used for beamtime proposals

brightness²

If you are curious:

https://useroffice.ess.eu/SignIn







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• Science using neutrons:

https://europeanspallationsource.se/science-using-neutrons

- Weekly construction updates & progress: <u>https://europeanspallationsource.se/site-weekly-updates</u>
- Scientific & publication highlights:

https://europeanspallationsource.se/article/2021/09/27/highlights-published-papers