Bulletin 2FDN-SFN
Mai 2022

Rubriques:

- **Actualités**
- **Actualité scientifique du mois**
- **Evènements à venir**
- **Publications du mois**

Actualités

▸ La SFN a sa chaîne You Tube, avec déjà cinq vidéos en ligne : "nanocomposites", "loops currents" "SANS under electric field", "coupling neutrons with other techniques" et "gas hydrates" ! Abonnez-vous https://www.youtube.com/channel/UC12MNaOsS8G81duGl_pyQdA ou envoyez-nous des vidéos (mangin-throl@ill.fr).

▸ La conférence **QENS-WINS2022** s'est tenue en mode hybride la semaine dernière, en ligne et dans la superbe baie de San Sébastien. Avec plus de 120 participants, la communauté du quasi-élastique et de la diffusion inélastique a profité d'excellentes présentations et d'échanges riches autour de thématiques scientifiques dans lesquelles les neutrons apportent des informations indispensables. Des questions fondamentales sur les liquides et les verres, des problèmes de diffusions ioniques dans les batteries ou de fonctionnalité de systèmes biologiques… grâce, entre autres, à 50 ans de spin-écho ! De nombreuses présentations ont montré les dernières avancées en instrumentation à tous les niveaux : nouveaux instruments, nouvelles sources… la diffusion quasi-élastique et inélastique est un domaine d'excellence bien vivant pour les neutrons.

► Le colloque dédié à ***la structure extraordinaire des choses ordinaires*** organisé à l'ILL du 18 au 20 mai a été l'occasion de rendre un hommage émouvant à la carrière trop courte de notre amie et collègue Isabelle Grillo. Les exposés scientifiques ont permis de retracer ses apports importants sur l'effet Ouzo, la physique des liposomes, le traitement de données de diffusion aux petits angles ou la construction du diffractomètre D33.

Innauguration de la salle Isabelle Grillo à l'ILL. Crédit photo : Stéphanie Monfront, ILL

Actualité scientifique du mois :

Strikingly Different Roles of SARS-CoV-2 Fusion Peptides Uncovered by Neutron Scattering

Armando Maestro[1,2] and Nathan Zaccai[3]

[1] Centro de Física de Materiales (CSIC, UPV/EHU) - Materials Physics Center MPC, Paseo Manuel de Lardizabal 5, E-20018 San Sebastián, Spain.

[2] IKERBASQUE—Basque Foundation for Science, Plaza Euskadi 5, Bilbao, 48009 Spain

[3] Cambridge Institute for Medical Research, University of Cambridge, Cambridge CB22 7QQ, United Kingdom.

En raison de la pandémie du COVID-19, il est devenu important de comprendre les mécanismes moléculaires à la base de l'infection par les coronavirus. Une étape critique dans la pénétration du virus SARS-CoV-2 dans la cellule se produit lorsque la protéine virale Spike sert de médiateur de la fusion entre les membranes du virus et de son hôte. Notre récente publication dans le Journal of the American Chemical Society présente une étude du rôle joué par certaines régions de la protéine Spike et de l'influence du calcium et du cholestérol dans le processus de fusion par diffusion des neutrons. Nos résultats ont révélé

que des fonctions étonnamment différentes sont codées dans cette protéine.

Due to the COVID-19 pandemic, a thorough understanding of the molecular mechanisms of cellular infection by coronaviruses has become imperative. A critical stage in cell entry by the SARS-CoV-2 virus occurs when its Spike protein mediates fusion between viral and host membranes. Recently published in the Journal of the American Chemical Society, we presented a detailed investigation of the role of selected regions of the Spike protein, and the influence of calcium and cholesterol, in this fusion process.

Importantly, in order to gain insights about how the fusion proceeds in vivo, we recreated important elements of the fusion mechanism by simplifying the system down to its core elements, amenable to experimental analysis by neutron scattering. In our in vitro models, cellular membranes were mimicked with hydrogenated and deuterated lipid monolayers and bilayers, produced in a recently set-up facility within the Partnership for Soft Condensed Matter at the ILL (www.ill.eu/L-Lab), while different sections of the Spike protein's unstructured region, crucial for viral fusion, were synthesised as (fusion) peptides.

Structural information from specular neutron reflectometry[1] and small angle neutron scattering[2], complemented by dynamical information from quasi-elastic and spin–echo neutron spectroscopy[3], was therefore employed to study the interaction of fusion peptides with model membrane. Neutrons are particularly well suited for the study of soft and biological matter since they allow measurements at room-temperature with better than nanometer resolution and at energies corresponding to thermal fluctuations. They are non-destructive and highly penetrating, thus allowing work in physiological conditions. Furthermore, as neutrons interact very differently with hydrogen (^{1}H) and deuterium (^{2}H), it is possible through isotopic substitution, for example in lipids, to observe hydrogen atoms and water molecules in biological samples, and therefore highlight structural and chemical differences in specific regions of interest.

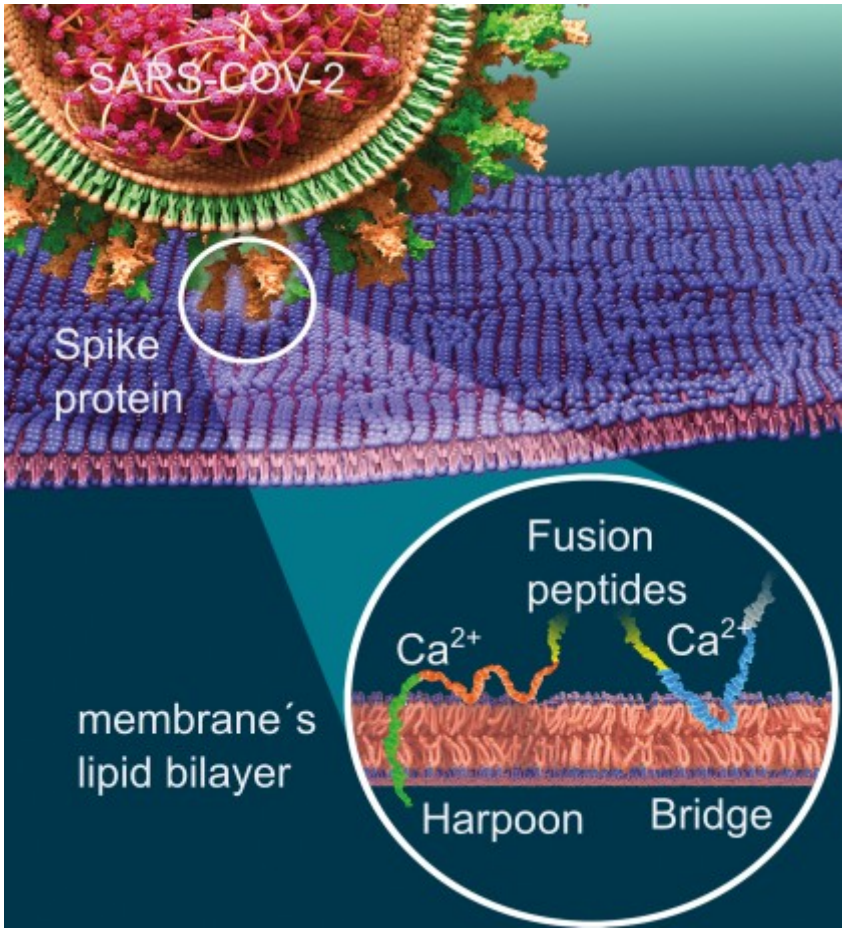
Our experiments revealed strikingly different functions encoded in the Spike fusion domain. Calcium drives the N-terminal of the Spike fusion domain to fully cross the host plasma membrane. Removing calcium, however, reorients the peptide back to the lipid leaflet closest to the virus, leading to significant changes in lipid fluidity and rigidity. In conjunction with other regions of the fusion domain, which are also positioned to bridge and dehydrate viral and host membranes, the molecular events leading to cell entry by SARS-CoV-2 are proposed.

The data are of interest not only in the context of the current COVID-19 pandemic, but they also provide a powerful interdisciplinary framework for future investigations of eukaryotic and viral fusion

1 FIGARO reflectometer, ILL, Grenoble, France
2 D22, ILL
3 IN5 and IN15 spectrometers, ILL

mechanisms. For example, it remains to be discovered if other viral fusion peptides can also harpoon through cellular membranes during infection. Our comprehensive study will also interest a wider audience, since this scientific approach, combining structural and dynamics characterization by neutrons under physiological conditions, can be readily applied to many biological questions.

Reference : Santamaria A, Batchu KC, Matsarskaia O, Prévost SF, Russo D, Natali F, Seydel T, Hoffmann I, Laux V, Haertlein M, Darwish TA, Russell RA, Corucci G, Fragneto G, Maestro A, Zaccai NR. Strikingly Different Roles of SARS-CoV-2 Fusion Peptides Uncovered by Neutron Scattering. ***J Am Chem Soc.*** **(2022) 144(7):2968-2979. DOI: 10.1021/jacs.1c09856.**



Schematic view of how during SARS-Cov-2 infection, the critically important fusion of human and viral membranes is induced by the viral Spike protein. The presence of calcium (Ca+) drives the fusion peptides of the Spike protein to harpoon through the host cell membrane's lipid bilayer, while other regions of the Spike protein help bridge viral and host membranes, thereby facilitating fusion.

Evènements à venir (voir aussi https://neutronsources.org/calendar.html)

- **International meeting on challenges and opportunities for HiCANS : June 20th 2022.**
- **15th Bombannes summer school on scattering applied to soft condensed matter**, 20-28 june 2022 - https://workshops.ill.fr/event/219/
- **ICNS 2022 — 12TH INTERNATIONAL CONFERENCE ON NEUTRON SCATTERING, 21 Aug 2022 - 25 Aug 2022 • Buenos Aires, Argentina -** https://www.sni-portal.de/en/files/FlyerICNS2022B.pdf
- **ECM33**, 33rd European Crystallographic Meeting, Versailles, France, 23-27 August 2022. https://www.ecm33.fr/
- **JCM18, 22-26 août 2022**, http://jmc2022.univ-lyon1.fr/fr.
- **Third ESS and ILL European Users Meeting,** Oct. 5th to 7th 2022 http://www.neutrons4europe.com/ - **Abstract submission by June 8th**
- CONFIT - **5th International Workshop on Dynamics in Confinement**, Oct 11th-13th, Grenoble, France - **Abstract submission by June 19th.**
- **MATERIAUX 2022**, 24-28 octobre 2022, Lille - https://materiaux2022.org/
- **DYNAmics of FUNctional materials** workshop (**DYNAFUN**). **12th-15th of September 2022,** in Saint-Jorioz, Annecy, France. We invite you to visit our website HERE for more information
- **"Synchrotron and neutron studies of glasses and melts",** 13-14 octobre 2022, synchrotron SOLEIL. Workshop parrainé par la SFN dans le cadre de l'année internationale du verre. **https://www.iyog2022.org/.**
- **JdN2022**, Biarritz, France, du 14 au 17 novembre 2022. **https://jdn-conference.net/**

Publications du mois (ordonnées par thématiques : magnétisme, matériaux, matière molle, biophysique, autres)

1 Coey, J., Givord, D. & Fruchart, D. Metallic Nitride and Carbide Perovskites: History and Prospects. *ECS Journal of Solid State Science and Technology* 11 055002 doi:https:/doi.org/10.1149/2162-8777/ac6695 (2022).

2 Khan, N. *et al.* Combined inelastic neutron scattering and ab initio lattice dynamics study of FeSi.*Physical Review B* 105 134304 doi:https:/doi.org/10.1103/PhysRevB.105.134304 (2022).

3 Turchenko, V. A. *et al.* Impact of In3+ cations on structure and electromagnetic state of M−type hexaferrites. *Journal of Energy Chemistry* 69 667-676 doi:https:/doi.org/10.1016/j.jechem.2021.12.027 (2022).

4 Cheikh Sleiman, H., Tengattini, A., Briffaut, M., Huet, B. & Dal Pont, S. Drying of mortar at ambient temperature studied using high resolution neutron tomography and numerical modelling. *Cement and Concrete Composites* 104586 doi:https://doi.org/10.1016/j.cemconcomp.2022.104586 (2022).
5 Joubert, J.-M. Intermetallic compounds of the Cr–Mn system investigated using in situ powder neutron diffraction: The reported order-disorder transformation of the σ phase elucidated. *Intermetallics* 146 107580 doi:https://doi.org/10.1016/j.intermet.2022.107580 (2022).
6 Pineda-Romero, N., Witman, M., Stavila, V. & Zlotea, C. The effect of 10 at.% Al addition on the hydrogen storage properties of the Ti0.33V0.33Nb0.33 multi-principal element alloy. *Intermetallics* 146 107590 doi:https:/doi.org/10.1016/j.intermet.2022.107590 (2022).
7 Poree, V. *et al.* Crystal-field states and defect levels in candidate quantum spin ice Ce2Hf2O7. *Physical Review Materials* 6 doi:https:/doi.org/10.1103/PhysRevMaterials.6.044406 (2022).
8 Soloy, A. *et al.* Effect of Particle Size on LiNi0.6Mn0.2Co0.2O2 Layered Oxide Performance in Li-Ion Batteries. *ACS Applied Energy Materials* doi:https:/doi.org/10.1021/acsaem.1c03924 (2022).
9 Vottero, E. *et al.* Evidence for H2-Induced Ductility in a Pt/Al2O3 Catalyst. *ACS Catalysis* 5979-5989 doi:https:/doi.org/10.1021/acscatal.2c00606 (2022).
10 Zhang, X. L. *et al.* Unconventional twin deformation of Ni-Mn-Ga 7M martensite under tension mediated by the collective lattice reorientation from a-c twin to b-c twin. *Acta Materialia* 227 doi:https:/doi.org/10.1016/j.actamat.2022.117729 (2022).
11 Denk, P. *et al.* Cloud point, auto-coacervation, and nematic ordering of micelles formed by ethylene oxide containing carboxylate surfactants. *Journal of colloid and interface science* 621 470-488 doi:https:/doi.org/10.1016/j.jcis.2022.04.046 (2022).
12 Liu, C. *et al.* Chain Conformation and Liquid-Crystalline Structures of a Poly(thieno)thiophene br. *Macromolecules* 55 2892-2903 doi:https:/doi.org/10.1021/acs.macromol.2c00143 (2022).
13 Bicout, D. J., Cisse, A., Matsuo, T. & Peters, J. The dynamical Matryoshka model: 1. Incoherent neutron scattering functions for lipid dynamics in bilayers. *Biochimica et biophysica acta. Biomembranes* 183944 doi:https:/doi.org/10.1016/j.bbamem.2022.183944 (2022).
14 Cisse, A. *et al.* The dynamical Matryoshka model: 2. Modeling of local lipid dynamics at the sub-nanosecond timescale in phospholipid membranes. *Biochimica et biophysica acta. Biomembranes* 1864 183950 doi:https:/doi.org/10.1016/j.bbamem.2022.183950 (2022).
15 Clavier, B. *et al.* Revisiting Mg solubility in CuO nanorods: limit probed by neutron diffraction and effect on the particle toxicity towards bacteria in water. *Dalton transactions (Cambridge, England : 2003)* doi:https:/doi.org/10.1039/d2dt00352j (2022).
16 Drago, V. N. *et al.* Microgravity crystallization of perdeuterated

tryptophan synthase for neutron diffraction. *NPJ microgravity* 8 13 doi:https:/doi.org/10.1038/s41526-022-00199-3 (2022).
17 Pounot, K. *et al.* High-resolution Neutron Spectroscopy to Study Picosecond-nanosecond Dynamics of Proteins and Hydration Water. *J Vis Exp* doi:https:/doi.org/10.3791/63664 (2022).
18 Martell, J. *et al.* The scale of a martian hydrothermal system explored using combined neutron and x-ray tomography. *Science advances* 8 eabn3044 doi:https:/doi.org/10.1126/sciadv.abn3044 (2022).
19 Tengattini, A. *et al.* Compact and versatile neutron imaging detector with sub-4μm spatial resolution based on a single-crystal thin-film scintillator. *Opt. Express* 30 14461-14477 doi:https:/doi.org/10.1364/OE.448932 (2022).