SYCO 1: The Physics of CoViD Infections

Time: Monday 13:30–16:15 Location: Audimax 1

Invited Talk SYCO 1.1 Mon 13:30 Audimax 1

A Tethered Ligand Assay to Probe SARS-CoV-2:ACE2 Interactions — Magnus Bauer[1], Sophia Gruber[1], Adina Hausch[1], Lukas Milles[2], Thomas Nicolaus[1], Leonard Schendel[1], Pilar Lopez Navajas[3], Erik Procko[4], Daniel Lietha[3], Rafael Bernadi[5], Hermann Gaub[1], and •Jan Lipfert[1] — [1]LMU Munich — [2]University of Washington — [3]Spanish National Research Council — [4]University of Illinois — [5]Auburn University

SARS-CoV-2 attaches to the ACE2 receptor on human hosts cells via its receptor-binding domain (RBD) on the Spike protein. This critical first step occurs in dynamic environments, where external forces act on the binding partners, creating an urgent need for assays that can quantitate SARS-CoV-2 interactions with ACE2 under mechanical load. We present a tethered ligand assay that comprises the RBD and the ACE2 ectodomain joined by a flexible peptide linker. Using magnetic tweezers and atomic force spectroscopy, we investigate the RBD:ACE2 interaction over the whole physiologically relevant force range. Combined with steered molecular dynamics simulations, we observe and assign fully consistent unbinding and unfolding events across the three techniques and establish ACE2 unfolding as a molecular fingerprint. We quantify the force dependence and kinetics of the RBD:ACE2 bond in equilibrium and find significant differences between SARS-CoV-1 and 2, which helps to rationalize the different infection patterns of the two viruses. Finally, we probe how different RBD mutations affect force stability and speculate how mechanical coupling promotes increased transmissibility in variants of concern.

Invited Talk SYCO 1.2 Mon 14:00 Audimax 1

From molecular simulations towards antiviral therapeutics against COVID-19 — •Rebecca Wade — Heidelberg Institute for Theoretical Studies — ZMBH, Heidelberg University, Germany

Despite advancing vaccination campaigns against COVID-19, the emergence of new variants of SARS-CoV-2 and the difficulties of achieving high vaccination levels demonstrate the importance of developing antiviral therapeutics. During the pandemic, the international computational molecular biophysics community has worked towards this goal by applying simulation techniques to study viral infection and to discover new antiviral agents. One of the challenges for such studies is the highly dynamic nature of virus protein drug targets, such as the main protease and the spike glycoprotein.

To identify inhibitors of the main protease, we applied our TRAPP toolbox (1) to analyze the druggability of ca. 30000 protein conformations and found that small structural variations in the binding site dramatically impact ligand binding (2). Virtual screening against selected conformations led to the prediction and experimental validation of novel inhibitors.

Heparin is used to prevent thrombosis in COVID-19 patients but also has antiviral activity. We are carrying out simulations to investigate how heparin polysaccharide binds to the spike and to design of new heparin derivatives for antiviral therapy. Our results reveal three mechanisms by which heparin can exert its antiviral effects (3).

(1) https://trapp.h-its.org/ (2) Gossen et al., ACS Pharmacol. Transl. Sci. 2021, 4, 1079 - 1095. (3) Paiardi et al., arXiv:2103.07722

15 min. break

Invited Talk SYCO 1.3 Mon 14:45 Audimax 1

The physical phenotype of blood cells is altered in COVID-19 — Markéta Kubánková[1], Martin Kräter[1], Bettina Hohberger[2], and •Jochen Guck[1,3] — [1]Max Planck Institute for the Science of Light & Max Planck Zentrum für Physik und Medizin, Erlangen, Germany — [2]Department of Ophthalmology, Friedrich-Alexander-Universität, Erlangen, Germany — [3]Department of Physics, Friedrich-Alexander-Universität, Erlangen, Germany

The clinical syndrome coronavirus disease 2019 (COVID-19) induced by SARS-CoV-2 continues to be a major health concern worldwide. While the pathology is not yet fully understood, a hyper-inflammatory response and thrombotic events leading to congestion of microvessels are key signatures of disease pathogenesis. Until now, the physical changes of blood cells have not been considered in the context of COVID-19 related vascular occlusion and organ damage. Here we report an evaluation of multiple physical parameters including the mechanical features of five frequent blood cell types, namely erythrocytes, lymphocytes, monocytes, neutrophils, and eosinophils. In total, more than 4 million blood cells of 17 COVID-19 hospitalized patients at different levels of severity, 24 volunteers free from infectious or inflammatory diseases, and 14 recovered COVID- 19 patients were analyzed. We found significant changes in lymphocyte stiffness, monocyte size, neutrophil size and deformability, and heterogeneity of erythrocyte deformation and size. While some of these changes reverted to normal values after hospitalization, others persisted for months after hospital discharge, evidencing the long-term imprint of COVID-19 on the body.

Invited Talk SYCO 1.4 Mon 15:15 Audimax 1

Extended lifetime of respiratory droplets in a turbulent vapor puff and its implications on airborne disease transmission — •Detlef Lohse, Kai Leong Chong, Chong Shen Ng, Naoki Hori, Morgan Li, Rui Yang, and Roberto Verzicco — Physics of Fluids Group, University of Twente, Enschede, The Netherlands

Long-range airborne transmissions of viruses encapsulated in droplets play a major role in the transmission of respiratory diseases. I will show direct numerical simulations of a typical respiratory aerosol within a Lagrangian-Eulerian approach, coupled to the ambient velocity, temperature, and humidity fields to allow for exchange of mass and heat and to realistically account for the droplet evaporation. We found that for an ambient relative humidity of 50% the lifetime of the smallest droplets of our study with initial diameter of 10 μm gets extended by a factor of more than 30 as compared to what is suggested by the classical picture of Wells, mainly due to the role of the respiratory humidity, while the larger droplets basically behave ballistically. With increasing ambient relative humidity the extension of the lifetimes of the small droplets further increases and goes up to 150 times for 90% relative humidity, implying more than two meters advection range of the respiratory droplets within one second. For low ambient temperatures the problem is even more serious, as the humidity saturation level of air goes down with decreasing temperature. We anticipate our approach to be a starting point for larger parameter studies and for optimizing ventilation and indoor humidity controlling concepts, which both will be key in mitigating the COVID-19 pandemic.

Invited Talk SYCO 1.5 Mon 15:45 Audimax 1

Beyond the demographic vaccine distribution: Where, when and to whom should vaccines be provided first? — •Benno Liebchen[1], Jens Grauer[2], Fabian Schwarzendahl[2], and Hartmut Löwen[2] — [1]Technische Universität Darmstadt, Hochschulstr. 8, 64289 Darmstadt — [2]Heinrich-Heine-Universität Düsseldorf, Universitätsstrasse 1, 40225 Düsseldorf

Once vaccines become available in a pandemic disease they are typically distributed demographically. This is in line with vaccination guidelines which largely focus on the question "to whom first?". In this talk we explore if lives could potentially be saved by asking also "where and when to provide vaccines first". To answer this question we propose alternative (non-demographic) vaccine distribution strategies and test their impact on the disease evolution within a newly developed nonuniform statistical mean-field model [1]. We find that a sequential prioritization of regions where infection numbers currently spread fastest is generically more effective than distributing vaccines demographically. These results are meant as a starting point to inspire systematic explorations of non-demographic vaccine distribution strategies aiming to find the optimal compromise between the prioritization of risk groups and highly affected regions. Towards the end of the talk we discuss recent results on possible mutation-induced phenomena in infectious-diseases and their response to vaccination [2].

[1] J. Grauer, H. Löwen, B. Liebchen, Sci. Rep. 10, 1 (2020)

[2] F. Schwarzendahl, J. Grauer, B. Liebchen, H. Löwen, medRxiv (2021)