Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
150-Plat  
**Machine learning reveals the critical interactions for SARS-CoV-2 spike protein binding to ACE2**  
Anna Pavlova¹, Zijian Zhang¹, Atanu Acharya¹, Diane L. Lynch¹, Yui Tik Pang¹, Zhongyu Mou¹, Jerry M. Parks², Christophe J. Chipot³, James C. Gumbart¹.  
¹School of Physics, Georgia Tech, Atlanta, GA, USA, ²Center for Molecular Biophysics, Oak Ridge National Laboratory, Oak Ridge, TN, USA, ³University of Lorraine, Vandoeuvre-les-Nancy, France.

A novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread throughout the world. SARS-CoV-2 is less deadly but more transmissible than SARS-CoV, which appeared in late 2002. Both viruses first engage with their host by binding to the same target protein, ACE2. Receptor-binding domain (RBD) is the key that allows the virus to dock to the targeted host protein, ACE2, to gain entry into cells. Herein, we have used molecular dynamics (MD) simulations, machine learning (ML), and free-energy perturbation (FEP) calculations to elucidate the differences in binding by the two viruses. Although only subtle differences were observed between the MD simulations of the two RBD—ACE2 complexes, three ML approaches, i.e., logistic regression (LR), random forest (RF), and multilayer perceptron (MLP) neural network, successfully identified the individual residues with the most distinctive ACE2 interactions, many of which have been highlighted in previous experimental studies. FEP calculations quantified the corresponding differences in binding free energies to ACE2, and examination of MD trajectories provided structural explanations for these differences. Lastly, the energetics of emerging SARS-CoV-2 mutations were studied, showing that the affinity of the RBD for ACE2 is increased by N501Y and E484K mutations but is slightly decreased by K417N.

151-Plat  
**Simultaneous multicolor imaging and multiscale analysis of receptor organization and actin cortex dynamics**  
Huong-Tra Ngo¹, Aparajita Dasgupta², Deryl Tschoerner¹, Nicolas Touret³, Bruno da Rocha-Azevedo¹, Khuloud Jaqaman¹.  
¹Biophysics, The University of Texas Southwestern Medical Center, Dallas, TX, USA, ²Department of Biochemistry, University of Alberta, Edmonton, AB, Canada.

Cell surface receptor organization is influenced by many components that crowd the plasma membrane, one of which is the actin cortex (AC). While the AC is a dynamic structure, most studies to date investigating how the AC influences cell surface receptor organization have not been able to access cortical actin dynamics. The reasons are that many studies perturb the actin cytoskeleton to infer its role on receptor organization, which precludes any quantification of actin dynamics in the absence of perturbational studies. We built a computational pipeline to put temporally and spatially relevant information obtained from SMI and FSM together. We then used machine learning to derive quantitative relationships between receptor behavior and AC dynamics. Application of this pipeline to the cell surface receptor CD36 and chimeric control transmembrane proteins revealed a novel biphasic relationship between receptor diffusion and AC density. Our results highlight the unique information that can be learned through direct simultaneous imaging and analysis of the dynamics of both the AC and cell surface receptor.

152-Plat  
**Accurate segmentation and tracking of single cells in complex 3D bacterial biofilms using machine learning**  
Yibo Wang¹, Ji Zhang¹, Eric D. Donarski¹, Andreas Gahlmann¹,²,³.  
¹Chemistry, University of Virginia, Charlottesville, VA, USA, ²Molecular Physiology & Biological Physics, University of Virginia, Charlottesville, VA, USA, ³Department of Physics, Northeastern University, Boston, MA, USA.

Bacterial biofilms are complex 3-dimensional structures with substantial spatial and temporal heterogeneity at the single-cell level. Simultaneous multi-cell tracking in 3D is thus critical for analyzing single-cell behaviors, such as motility and metabolism, as well as lineage tracing in biofilms. Due to phototoxicity and photobleaching concerns, fluorescence images are often characterized by having low signal-to-background ratios (SBRs). High cell density, and large relative cell movements from frame to frame add additional challenges for accurate segmentation and tracking of living biofilms. To address these problems, we used Lattice light sheet microscopy (LL-SM) to image bacterial biofilms with high spatial and temporal resolution and without substantial light-induced degradation of the SBRs. To enable accurate cell segmentation, we trained convolutional neural networks (CNNs) to perform voxel classification and to translate 3D fluorescence images into 3D intermediate image representations that are more resistant to over- and under-segmentation errors. Using this approach, improved segmentation results are obtained even for low SBRs and/or high cell density biofilm images. In order to track individual cells, we further leveraged machine learning to select cell features that facilitate linking corresponding cells between frames. We demonstrate the applications and limitations of our data processing pipeline by systematically evaluating tracking accuracy using both simulated and experimentally acquired images. Our combination of non-invasive imaging and machine-learning based computational image analysis pipeline provides new opportunities for investigating time-dependent cellular-scale phenomena in living bacterial biofilms.

Platform: Transcription and Translation

153-Plat  
**Structural basis of early translocation events on the ribosome**  
Emily J. Rundlet¹,², Mikael Holm¹, Magdalena Schacherl¹, Kundhavai Natchiar¹, Roger B. Altman¹, Christian M.T. Spahn³, Alexander G. Myerskov⁴, Scott C. Blanchard⁴, ¹Structural Biology, St. Jude Children’s Research Hospital, Memphis, TN, USA, ²Tri-Institutional PhD Program in Chemical Biology, Weill Cornell Medicine, New York, NY, USA, ³Institut für Medizinische Physik und Biophysik, Charité, Universitätmedizin Berlin, Berlin, Germany.

Peptide-chain elongation during protein synthesis entails sequential aminoacyl-tRNA selection and translocation reactions that proceed rapidly (2-20 μs per second) and with a low error rate (around 10⁻⁶ to 10⁻⁷ at each step) over thousands of cycles. The cadence and fidelity of ribosome transit through mRNA templates in discrete codon increments is a paradigm for movement in biological systems that must hold for diverse mRNAs and tRNAs across domains of life. Here we use single-molecule fluorescence methods to guide the capture of structures of early translocation events on the bacterial ribosome. Our findings reveal that the bacterial GTPase elongation factor G specifically engages spontaneously achieved ribosome conformations while in an active, GDP-bound conformation to unlock and initiate peptidyl-tRNA translocation. These findings suggest that processes intrinsic to the pre-translocation ribosome complex can regulate the rate of protein synthesis, and that energy expenditure is used later in the translocation mechanism than previously proposed.

154-Plat  
**Dependence of tRNA dynamics on subunit rotation in the ribosome**  
Sandra Byju¹, Paul C. Whitford².  
¹Department of Physics, Northeastern University, Boston, MA, USA, ²Department of Physics, University of Virginia, Charlottesville, VA, USA.

Large-scale conformational rearrangements in biomolecular assemblies can be crucial to their functional dynamics. We investigate the functional rearrangements in a massive nucleoprotein assembly present in all living cells, the ribosome. It is responsible for protein synthesis, which requires several large-scale structural rearrangements in the ribosome bound tRNA molecules. To probe the energetics of the ribosome, we employ all-atom structure-based models and molecular dynamics simulations. Structure-based models provide simplified energetic descriptions, where experimentally obtained atomic structures are defined to be potential energy minima. In our study, we used these models to investigate how inter-subunit rotation in the ribosome influences the free-energy barrier associated with P/E tRNA hybrid formation. To probe these collective dynamics, we utilize multi-basin all-atom structure-based models to simulate spontaneous P-E tRNA transitions to the P/E hybrid state for different degrees of body rotation. The study reveals the quantitative dependence of P/E tRNA hybrid formation on subunit