INSTITUT Pasteur

Computational Biology DEPARTMENT

SEMINAR

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« Decoding the Dark Genome: How Computational Biology is Democratizing Long-Read Sequencing »

Monday 2 february 2026, at 2:00 pm

Auditorium Agnès Ullmann

Hosted by Rayan Chikhi: rayan.chikhi@pasteur.fr

Abstract : Long-read sequencing is revolutionizing human genomics and genetics by elucidating novel mechanisms concealed from previous technologies. This is highlighted more and more by large population studies such as AllofUs and others. Nevertheless, its transition into the clinical space has not yet occurred due to limitations in the cost and scalability of parts.

To overcome these limitations, we introduce TBAS, a new approach for cost-efficient long-read sequencing for rare diseases, combined with new analysis methods. TBAS achieves a 76% solving rate in our study of trios, providing double the coverage on important regions while halving the cost of sequencing. This represents a scalable approach to identify SNVs, indels, SVs, TRs, and methylation variations in one go. Furthermore, it elucidates the important interactions between variants highlighting the need for comprehensive genomics at scale.

Beyond germline diagnosis, a fundamental limiting factor in human genomics is the detection of cell type-specific mutations at scale. To facilitate a broader understanding of the impact and occurrence of these mosaic/somatic structural variants (SVs) across diverse human tissues, particularly in contexts like neurological diseases or cancer, we present our newest computational method. This approach enables the detection of subtle, cell-type-specific mutations using inexpensive bulk sequencing data. This computational approach facilitates the study of mosaic SVs across human tissues, ultimately improving our understanding of the occurrence and impact of mosaic mutations in healthy aging and disease.

This talk will detail novel methodology that enable novel insights into biology and medical research. Furthermore, I will discuss the remaining computational and algorithmic challenges necessary to fully democratize long-read sequencing and foster its applications across clinical and population genomics.

Biography :

Dr. Fritz Sedlazeck is an Associate Professor at Baylor College of Medicine and an adjunct Associate Professor at Rice University. He has led a research group at the Human Genome Sequencing Center at Baylor since 2018, where his work has become central to advancing bioinformatics approaches for the detection and analysis of genomic variation, particularly structural variants (SVs). These complex genomic events span multiple positions in the genome and are critical to understanding evolution, disease mechanisms, gene regulation, and phenotypic diversity. Dr. Sedlazeck is widely recognized for developing cutting-edge computational tools, including the popular Sniffles SV caller, and for his leadership in benchmarking methods to ensure robust and reproducible variant detection. His group has been instrumental in uncovering the mechanisms of SV formation across species and in diverse human populations, participating in major international efforts such as TOPMed, CCDG, CARD, and All of Us. Through this work, he has helped set standards for the field while deepening our understanding of how complex alleles evolve and contribute to human biology.