Stanford MEDICINE | Department of Biomedical Data Science

Inferring transcriptional activity from circulating DNA molecules

Mohammad Shahrokh Esfahani

Assistant Professor, Division of Radiation & Cancer Biology,

Department of Radiation Oncology, Stanford University

October 22, 2026

1:30PM-2:50PM

Li Ka Shing Center, Room:120

Abstract:

Liquid biopsy, a noninvasive window into whole-body cellular states, has transformed applications in prenatal screening and oncology. Cell-free DNA (cfDNA), a key component of liquid biopsy, contains information beyond sequence variation: fragmentation patterns and genomic coverage reflect the chromatin landscape of the cells from which these molecules originate.

From a statistical perspective, cfDNA represents a complex mixture: billions of short DNA fragments shed from many cell types, each potentially in a distinct cellular state. The central challenge is therefore as follows: how to recover latent transcriptional activity from sparse, noisy, and compositional measurements of DNA fragments.

In this talk, I will present a framework for inferring transcriptional activity from cfDNA profiles at the patient level. I will show how these inferred signals can be used to distinguish cancer from non-cancer and discuss how regulatory elements shape the relationship between chromatin structure and downstream RNA output. I will also highlight key challenges, including identifiability, bias, and limits of inference, and outline opportunities for integrating statistical modeling with biological priors in this setting.

Reading List:

Tsui, et al., *Cell-free DNA fragmentomics in cancer*, Cancer Cell, 2025, 10.1016/j.ccell.2025.09.006

Esfahani, et al., *Inferring gene expression from cell-free DNA fragmentation profiles*, Nature Biotechnology, 2022, https://doi.org/10.1038/s41587-022-01222-4

Ulz et al., *Inferring expressed genes by whole-genome sequencing of plasma DNA*, Nature Genetics, 2023, 10.1038/ng.3648