{% extends "layout.html" %} {% block title %}PiTP{% endblock %} {% block header2 %}

{% endblock %} {% block content %}

Prospects in Theoretical Physics 2019: Great Problems in Biology for Physicists

PiTP 2019 is titled '*Great Problems in Biology for Physicists*,' and will cover topics ranging from virology, cancer, and immunology to machine learning and neural networks. Recent technologies have generated enormous amounts of hitherto unseen biological/genetic data. The tools of modern physics have enabled novel approaches to exploration and interrogation of such data, allowing physicists to draw conclusions that will result in leaps of the fundamental understanding of evolution and basic biological processes. Because physicists are now reaching out to explore problems in biology, PiTP 2019 will focus on some of the great questions in biology that are being explored.

Some quantitative problems in the evolution and heterogeneity of human cancers

In this lecture we will study how genomics has enabled the characterization of the genetic lesions that are associated with the initiation and development of human cancers. We will focus on four different open questions where quantitative approaches are needed:

- What are the genes that are responsible for the development of human cancers?
- Can we reconstruct the mutational history of human cancers?
- Can we infer the mutational processes leading to cancer?
- What is the role of tumor heterogeneity and the surrounding cells in the progression of cancers?

Below students can find some references and datasets associated with this lecture series.

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(1) Identifying driver genes in cross-sectional cancer studies

Papers

- **Mutational heterogeneity in cancer and the search for new cancer-associated genes**
  Michael S. Lawrence, Petar Stojanov et al.
  Nature. 2013 Jul 11; 499(7457): 214â€“218.
- **The integrated landscape of driver genomic alterations in glioblastoma**
  Frattini V. et al.
  Nature Genetics 2013 Aug 05. doi:10.1038/ng.2734.

Datasets

- TCGA_Somatic_Mutations

(2) Reconstructing the evolutionary history of tumors in longitudinal cancer genomic studies

Papers

- **Clonal evolution mechanisms in NT5C2 mutant-relapsed acute lymphoblastic leukaemia**
  Gannie Tzoneva et al.
  Nature. Volume 553 (25 January 2018) doi:10.1038/nature25186.
- **Immune and genomic correlates of response to anti-PD-1 immunotherapy in glioblastoma**
  Junfei Zhao et al.
  Nat Med. 2019 Feb 11. doi: 10.1038/s41591-019-0349-y.
- **Clonal evolution of glioblastoma under therapy**
  Jiguang Wang et al.
  Nature Genetics volume 48, pages 768â€“776 (2016).

Datasets

- Glioblastoma variants

(3) Archeology of human cancers: mutational signatures

Papers

- **Signatures of mutational processes in human cancer**
  Ludmil B Alexandrov et al.
  Nature volume 500, pages 415â€“421 (22 August 2013).
- **The Repertoire of Mutational Signatures in Human Cancer**
  Ludmil B Alexandrov et al.
  doi: https://doi.org/10.1101/322859.
- **Characterizing Mutational Signatures in Human Cancer Cell Lines Reveals Episodic APOBEC Mutagenesis**
  Petljak M et al.
  Cell, 2019; 176 (6): 1282.
- **Landscape of somatic mutations in 560 breast cancer whole-genome sequences**
  Serena Nik-Zainal et al.
  Nature. 2016 May 2; 534(7605): 47â€“54.
- **Passenger hotspot mutations in cancer driven by APOBEC3A and mesoscale genomic features**
  RÃ©mi Buisson et al.
  Science 28 Jun 2019: Vol. 364, Issue 6447, eaaw2872 doi: 10.1126/science.aaw2872.
- **A Compendium of Mutational Signatures of Environmental Agents**
  Jill Kucab et al.
  Kucab et al., 2019, Cell 177, 821â€“836

Datasets

- Mutations from 560 WGS breast cancer samples

(4) Studying cancer and stromal heterogeneity using single cell data

Papers

- **Single-cell topological RNA-seq analysis reveals insights into cellular differentiation and development**
  Abbas H Rizvi et al.
  Nat Biotechnol. 2017 Jun; 35(6): 551â€“560.
- **Quasi-universality in single-cell sequencing data**
  Luis Aparicio et al.
  arXiv preprint arXiv:1810.03602 (2018).
- **Single-Cell RNA-Seq Analysis of Infiltrating Neoplastic Cells at the Migrating Front of Human Glioblastoma**
  Darmanis S. et al.
  Cell Rep. 2017 Oct 31;21(5):1399-1410. doi: 10.1016/j.celrep.2017.10.030.

Tools

- **Randomly** (background | manual | Github)

Datasets

- PBMC
- GBM

Other References

- **Geometry and topology of genomic data**
  A.J. Blumberg and R. Rabadan.
  Chapter 64 in J.E. Goodman, J. O'Rourke, and C.D. Toth, editors.
  Handbook of Discrete and Computational Geometry, 2nd edition,Â CRC Press, Boca Raton, FL, 2017, pp. 1735-1773.

- **Spatiotemporal genomic architecture informs precision oncology in glioblastoma**
  Lee JK, Wang J, et al.
  Nat Genet. 2017 Apr. doi: 10.1038/ng.3806.

- **Topological Data Analysis for Genomics and Evolution: Topology in Biology**
  Raul Rabadan and Andrew J. Blumberg.
  Cambridge University Press. 2019. ISBN-13: 978-1107159549.

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