Type: New
Title: "Computational Physical Genomics: Exploring Potential Novel Cancer Therapies"

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Scientific Discipline: Biological Sciences: Biophysics

INCITE Allocation:
Site: Argonne National Laboratory
Machine (Allocation): Cray XC40 (1,000,000 node-hours)

Research Summary: With the ultimate aim of exploring novel therapies potentially applicable to a broad spectrum of human cancers, this project combines high-performance computing with laboratory experiments and preclinical studies to model and study physical genomics. "Physical genomics" refers to the functional structure of interphase DNA and how it is affected by ambient conditions within a cell's nucleus, inside which DNA is compacted into chromatin. Understanding chromatin folding and how it is affected by physico-chemical factors is important both for early-stage cancer detection and the rational design of new cancer treatments.

Partial wave spectroscopic (PWS) microscopy as an optical imaging technique has revealed mass-fractal-like heterogeneous chromatin packing with a global impact on gene expression. To explain such heterogeneous chromatin packing, the researchers have developed a mathematical model called a self-returning random walk (SRRW), which provides a new theoretical framework to understand chromatin folding. Related findings suggest the potential of macrogenomic engineering for cancer treatment—i.e., using physico-chemical strategies to regulate chomatin packing for whole-scale transcriptional engineering that constrains the adaptive potential of neoplastic cells. Achieving this goal requires a more detailed molecular description of chromatin folding beyond the SRRW model.

To this end, this work will build a high-fidelity computational model of chromatin to investigate the interplay between different folding mechanisms and to decipher the effects of genetic and epigenetic codes on the self-organization of the human genome. It will also extend the current static model into a dynamic one that leverages the dynamic PWS imaging technique developed in a previous INCITE allocation. This research could yield significantly improved understanding of chromatin folding and the cause of cancer, while also providing new insights and strategies to develop genetic therapeutics that target specific domains and networks of our genome.