it. The identification of states as clusters relies on standard clustering algorithms that ignore conformational energy and instead use similarity over low-dimensional representations (a process referred to as featurization in current MSM analysis) of conformations. In this work, we propose to leverage the fact that the conformations sampled in simulation populate an unknown energy landscape. The neighborhood structure of the landscape can be extracted via spatial statistical analysis that does not ignore energy but instead uses it to identify basins and basin-separating saddles in the landscape. We utilize this information to identify states and show that such a definition of states is more robust than that obtained via clustering. We proceed to analyze in this manner various MD trajectories and summarize the conformational dynamics in a comparative manner, showing that a landscape-based identification of conformational states is promising for detecting and summarizing conformational dynamics.

1438-Pos

Genetic Mutation Classification using Machine Learning

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DNA-Sequencing of tumor cells has revealed thousands of genetic mutations but cancer is caused by some of them. The challenge is to identify the mutations that contribute to tumor growth which is currently being done manually. A clinical pathologist manually reviews and classifies each genetic mutation based on evidence from clinical literature. This process is very cumbersome and expensive in terms of money and time. We have used different Machine Learning (ML) classifiers (Random Forest, k-Nearest Neighbors, Naive Bayes, Support Vector Machine and Gradient Boosting etc) for multiclass classification of cancer mutations. We used OncoKB dataset which has three features (Gene, Mutation/Variation, Clinical literature). Gene and Variation were encoded to numerical features from categorical features using one-hot encoding. Clinical literature was converted to numerical vectors of fixed length using tf-idf, word2vec and doc2vec and then fed into ML models. We achieved 0.9 logloss and 68% accuracy by XGBClassifier, while the random model gives 2.68 logloss and 12% accuracy. Our model performs significantly better than random model (3x on logloss and 5.67 times on accuracy). This work will assist the pathologist in classifying the genetic mutation in less time and save the patient's life and time by reducing the misdiagnosis rate. Moreover accurate treatment will reduce toxicity in cancer patients.

1439-Pos

Characterization of Spectral Feature Upon Cellular Morphodynamics and its Application

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Cellular morphodynamics is a phenotypic outcome of numerous cellular processes, including migration, proliferation, and differentiation. It is commonly utilized as an indicator of physiological and pathological state of cells. Therefore, quantitative characterization on morphodynamic feature of cells is essential for evaluating cell state and understanding the effect of underlying molecular pathway that governing the morphogenetic process. By employing Hilbert-Huang transform (HHT) based spectral decomposition method, we decomposed the convoluted cell edge movement time series into several analyzable functions with instantaneous frequency and magnitude characterized at each location, and formed the frequency spectra to represent the signaling topology of individual cell. We then applied the frequency spectra of cell migration to evaluate the performance of several FRET based biosensors expressing GTPases RhoA, Rac1 and Cdc42. The intrinsic and inter-group variation of the spectral features among control, wildtype and mutated biosensors were compared, and the dependence of morphodynamic variation on the expression level of biosensors were quantitatively estimated. We discovered consistent frequency spectra with considerable heterogeneity upon amplitude spectra within each biosensor condition, while evidently distinguishable spectral patterns between different conditions. One type of mutated biosensor (TQ10) is found to present much more stable performance with less adverse perturbation of cells over a range of expression levels compared to the control cells tagged with membrane marker CAAX. The proposed spectral profiling method, with high sensitivity, consistency and efficiency, could have promising application prospect in biosensor development, and provide incisive information upon the correlation between cellular morphogenesis and underlying molecular regulation pathways.

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1440-Pos

Soft Material Programming through the Spatiotemporal Release of Oligonucleotides

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The programmable spatiotemporal release of molecular outputs is a prerequisite for creating new classes of stimuli responsive biomaterials capable of executing sensing and computational programs. Here we demonstrate the ability to fabricate heterogeneous micromaterials that implement sequentially activated molecular cascades with programmed timescales of activation and release from a hydrogel. These materials use enzyme-free DNA-based strand-displacement to direct the sequential release of short oligonucleotides from spatial domains. Maskless photolithography enables the spatial sequestration of acrylate-modified short oligonucleotides within hydrogels at sizes of tens of microns. To control temporal release, a DNA reaction-cascade that relies on toehold mediated strand displacement was implemented, allowing for the controlled release of oligonucleotides at 8-hour intervals. The tuning of reactant concentrations and toehold sizes allows for the temporal control of DNA release. The programmed release of DNA oligonucleotides from hydrogel substrates enables the scalable development of DNA-based reaction-diffusion systems that regulate the availability of oligonucleotides at different points in space and time.

1441-Pos

Detection and Mapping of dsDNA Breaks using Graphene Nanopore Transistor

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Single-strand DNA (ssDNA) breaks that are often converted into DNA double-strand (dsDNA) breaks make up a vast majority of lesions a normal human cell undergoes everyday. If the repair mechanism fails, the dsDNA break can cause chromosomal instability leading to tumorigenesis. Additionally, a single break in a critical gene can cause the cell to undergo apoptosis. Existing genome sequencing techniques are not suitable for detecting such changes directly. As an alternative methodology, we propose to employ graphene-Quantum Point Contact nanopore transistor to detect and map defects in the DNA backbone, as miniscule as ssDNA breaks, efficiently using electronic sheet currents obtained across the transistor membrane. For this purpose, we use large-scale comprehensive all-atom molecular dynamics simulation techniques accompanied with electronic transport calculations, data denoising and signal detection. In all our simulations, we observe the molecule sticking in the pore at the nicked site due to strong hydrophobic attraction between the graphene membrane and the damaged-backbone. While the ionic currents calculated for the translocation of 20 base-pair dsDNA strand with a break in the backbone does not show any distinct signature from the nicked-site in the signal, a clear dip is seen in the transverse sheet current signal corresponding to the location of the breakage, thereby enabling us to detect and map these damages, electronically. We validated our methodology by detecting other sequence specific dsDNA breaks along randomly sequenced strands. We strongly believe such a detection mechanism enables the development of versatile semiconductor electronics for early cancer detection caused by structural modification of the genome.

1442-Pos

Autochemophoretic DNA Motors Generate 100+ Piconewton Forces

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DNA walkers, which ''walk'' along linear or planar tracks via burnt-bridge hybridization interactions, are promising synthetic analogs of motor proteins such as kinesin, myosin, and dynein. DNA walkers can precisely transport nanoscale cargo but cannot generate piconewton-scale force. This primary function of motor proteins is necessary for countless processes including muscle contraction, clotting, immunosensing, embryogenesis, and mechanosensation. We present progress towards the design of force-generating nanomachines by showing that highly polyvalent DNA motors (HPDMs) generate 100+ piconewtons of force via a novel mechanism that we term autochemophoresis. HPDMs are DNA-coated microparticles that connect to planar RNA-functionalized surfaces via DNA-RNA hybridization (Yehl &