

BIAS-AWARE CONSENSUS PERTURBATION PATHWAY ANALYSIS

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Abstract:

Motivation: Pathway analysis techniques have been widely used to understand the molecular mechanisms under certain conditions, especially with complex diseases. Recently, an abundance of genomic data under microgravity environment has been generated. Pathway analysis has been proving as a useful technique to investigate the effects of spaceflight on living organisms. More than 70 pathway analysis methods have been developed to determine significantly impacted pathways when comparing genomic data collected under different conditions. However, most of these methods are sensitive to the noisy nature of genomic data and are bias toward certain pathways.

Method: We developed a powerful pathway analysis technique, Bias-Aware Consensus Perturbation Analysis (BACPA), that (i) is robust against noise by repeatedly perturbing the input data, (ii) performs consensus statistical significance test by combining three different statistical hypothesis tests, and (iii) is non-bias by correcting the results using empirical null distributions of p-values generated from only control samples.

Results: We validated the method on 22 datasets containing 4 diseases (Acute myeloid leukemia, Prostate cancer, Parkinson's, and Alzheimer's disease) with a total of 1,713 samples (742 control samples, 971 disease samples). The results show that BACPA produces the best rankings for target pathways compared with results produced by main-stream pathway analysis methods.

Future directions: We will continue to test the method using data from diseases with known target pathways, e.g., Huntington's disease, Colorectal Cancer, Pancreatic Cancer, and Thyroid Cancer. We will finally apply the method to investigate the effects of microgravity on living organisms using genomic data from NASA GeneLab.