Which question is worth answering? "what appears to happen" or "what has happened" in a biological system

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Nowadays, undertaking enrichment analysis on biological annotations is common in making claims about the potentially implicated biological pathways in disease. Specifically, upon identifying differentially expressed genes, molecular mechanistic insights are proposed based on statistically enriched biological processes for disease etiology and drug discovery. In other words, differentially expressed genes are used as a clue of cellular perturbation in general while analyzing the effects of altered expression on the activity of signaling pathways is often ignored. In this talk, I want to introduce the concept of coherency or sign consistency among gene pairs relationships. This concept is based on data extracted from four commonly used and comprehensive databases. I want to re-consider whether significant changes in gene expression necessarily lead to dysregulated signaling pathways. I will provide the pieces of evidence to highlight the ignored challenge of reliability or sufficiency of expression profile to infer biological relationships among genes and, in turn, describe cellular behavior.