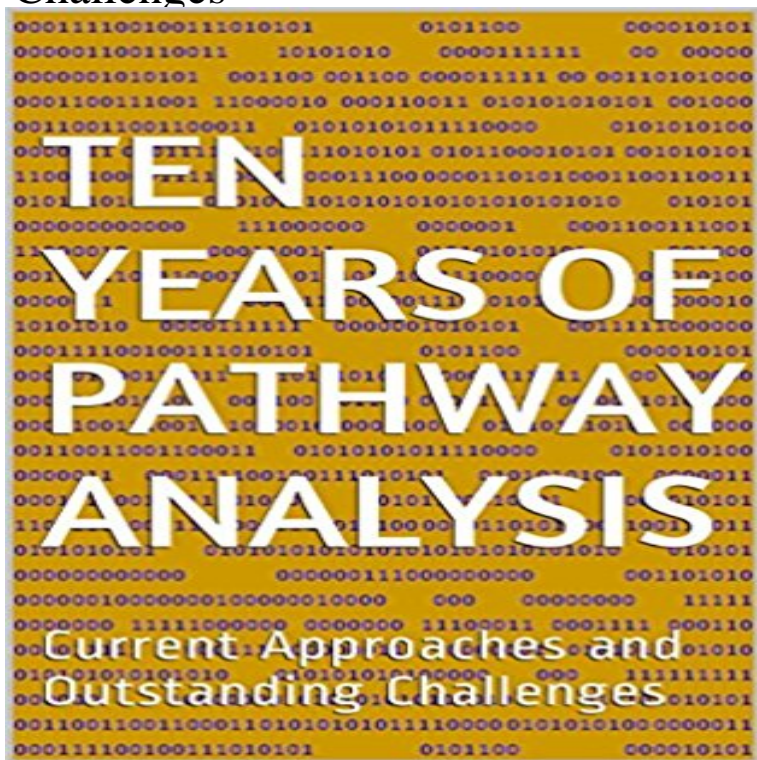


Ten Years of Pathway Analysis: Current Approaches and Outstanding Challenges



Pathway analysis has become the first choice for gaining insight into the underlying biology of differentially expressed genes and proteins, as it reduces complexity and has increased explanatory power. We discuss the evolution of knowledge based driven pathway analysis over its first decade, distinctly divided into three generations. We also discuss the limitations that are specific to each generation, and how they are addressed by successive generations of methods. We identify a number of annotation challenges that must be addressed to enable development of the next generation of pathway analysis methods. Furthermore, we identify a number of methodological challenges that the next generation of methods must tackle to take advantage of the technological advances in genomics and proteomics in order to improve specificity, sensitivity, and relevance of pathway analysis.

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