Detecting recurrent gene mutation in interaction network context using multi-scale graph diffusion

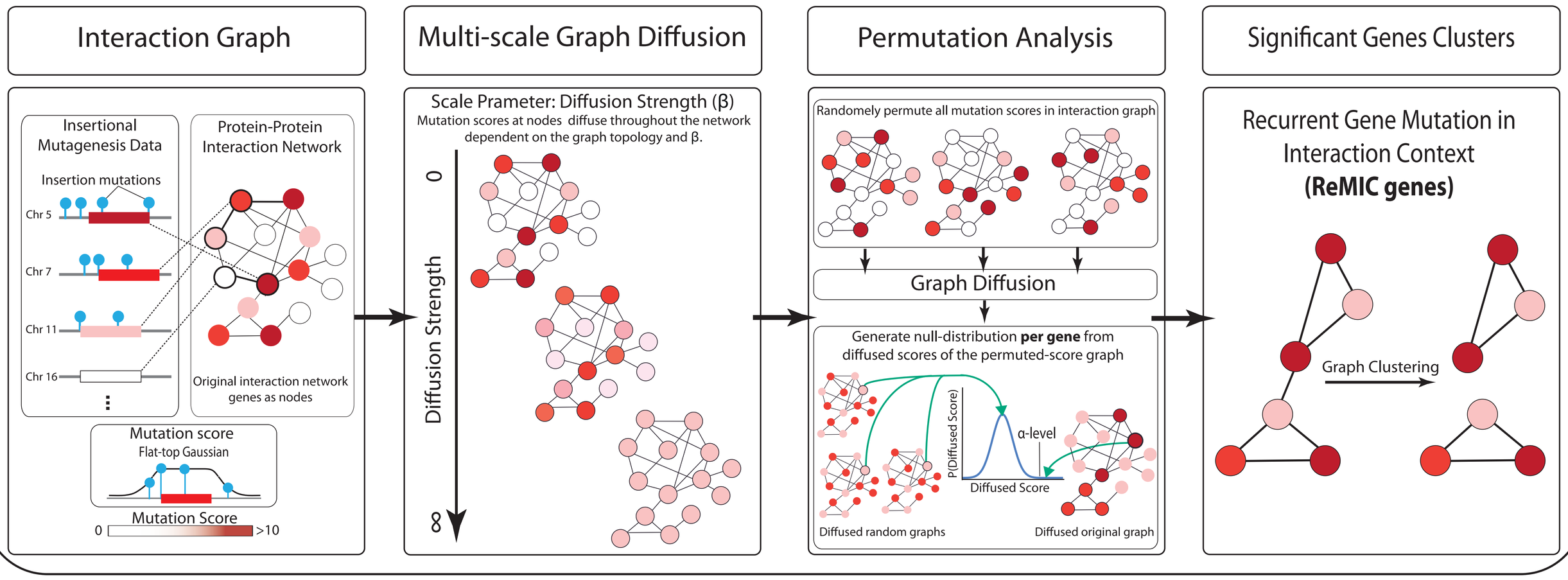
Sepideh Babaei[1,2], Marc Hulsman[1], Marcel Reinders[1,2], Jeroen de Ridder[1,2]

[1]Delft Bioinformatics Lab, Delft University of Technology, [2]Netherlands Bioinformatics Center.

Summary

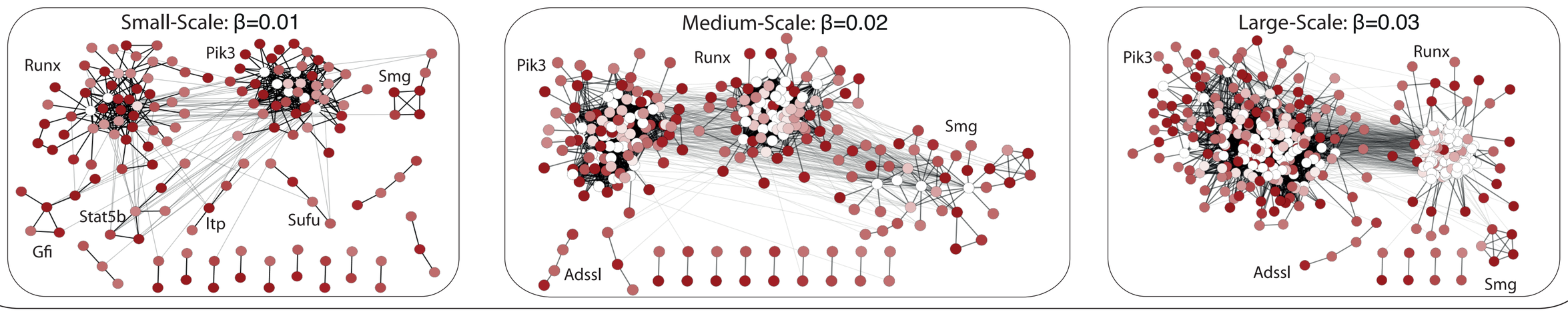
We introduce a multi-scale kernel diffusion framework and apply it to a large collection of murine retroviral insertional mutagenesis data. The diffusion strength plays the role of scale parameter. As a result, in addition to detecting genes with frequent mutations in their **genomic vicinity** (red nodes in the interaction graph) we can also find genes that harbor frequent mutations in their **interaction network context** (white and pink nodes).

Methods



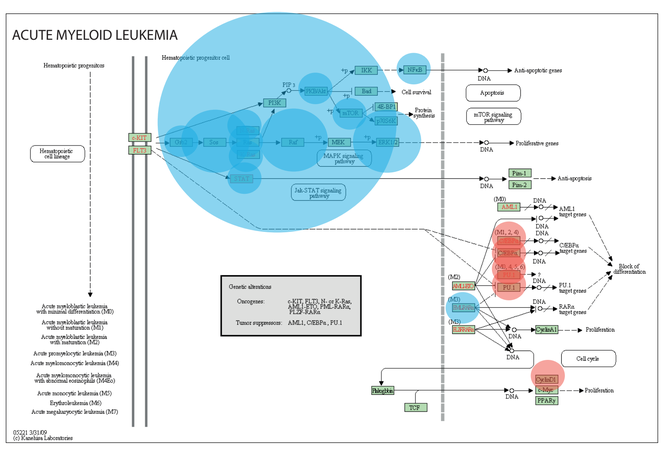
Results

ReMIC genes clusters in 3 diffusion scale-levels



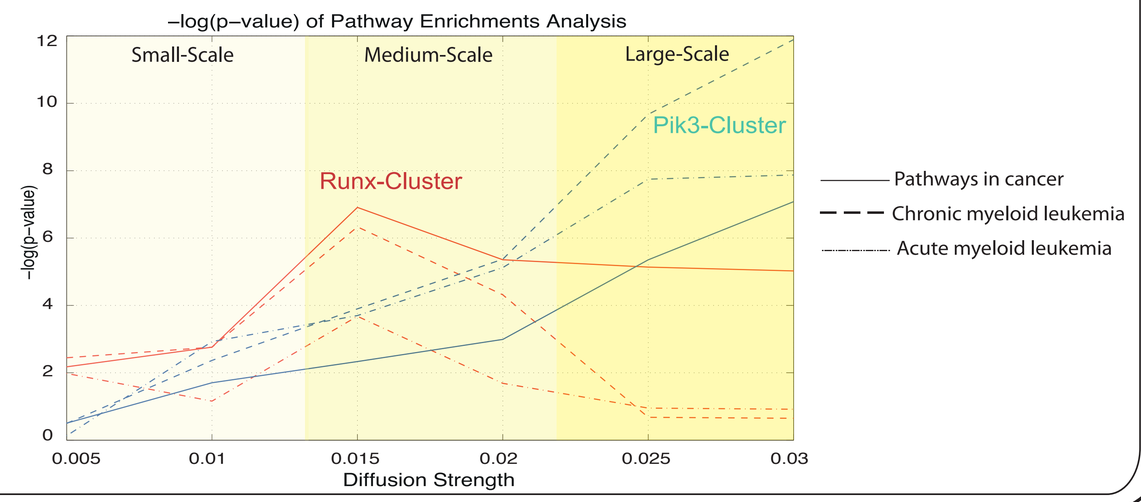
White and Pink ReMIC genes are co-localized in Leukemia Pathway

Significant white and pink ReMIC genes in Pik3-cluster



Significant white and pink ReMIC genes in Runx-cluster

ReMIC clusters are enriched for cancer related pathways



Conclusion

We identify densely connected components of known and novel cancer genes. They are strongly enriched for cancer related pathways across the diffusion scales. The mutations in the clusters exhibit a **significant pattern of mutual exclusion**.The results demonstrate the importance of defining recurrent mutations in the **interaction network context** at **multiple scales**.

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Netherlands Bioinformatics Centre

Delft University of Technology