

United we stand, divided we fall

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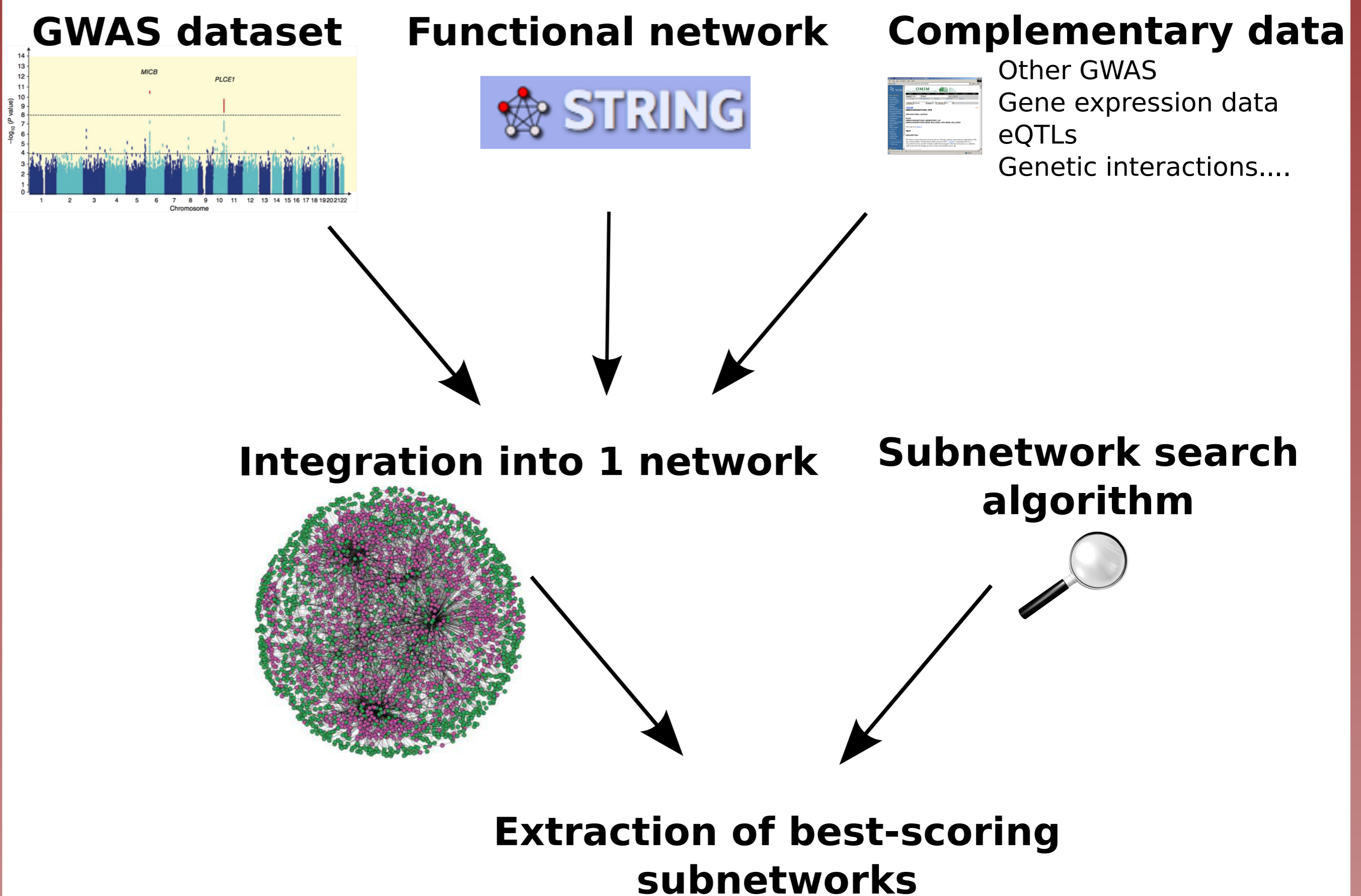
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Introduction

The global incidence of dengue has grown dramatically in recent decades. Severe dengue is a leading cause of serious illness and death among children in some Asian and Latin American countries¹. Genetic predispositions for severe dengue exist. A genome-wide association study (GWAS) has identified 2 statistically associated genes², but the majority of heritable genetic risk factors remain elusive; the phenotype is explained by variations across multiple genes.

Thus, analysing SNPs independently doesn't allow us to uncover the etiology of the disease. We aim to jointly analyze multiple GWAS loci known to functionally interact. We integrate a network of functionally interacting genes with GWAS results. Then we aim to search for subnetworks enriched in significant GWAS results.

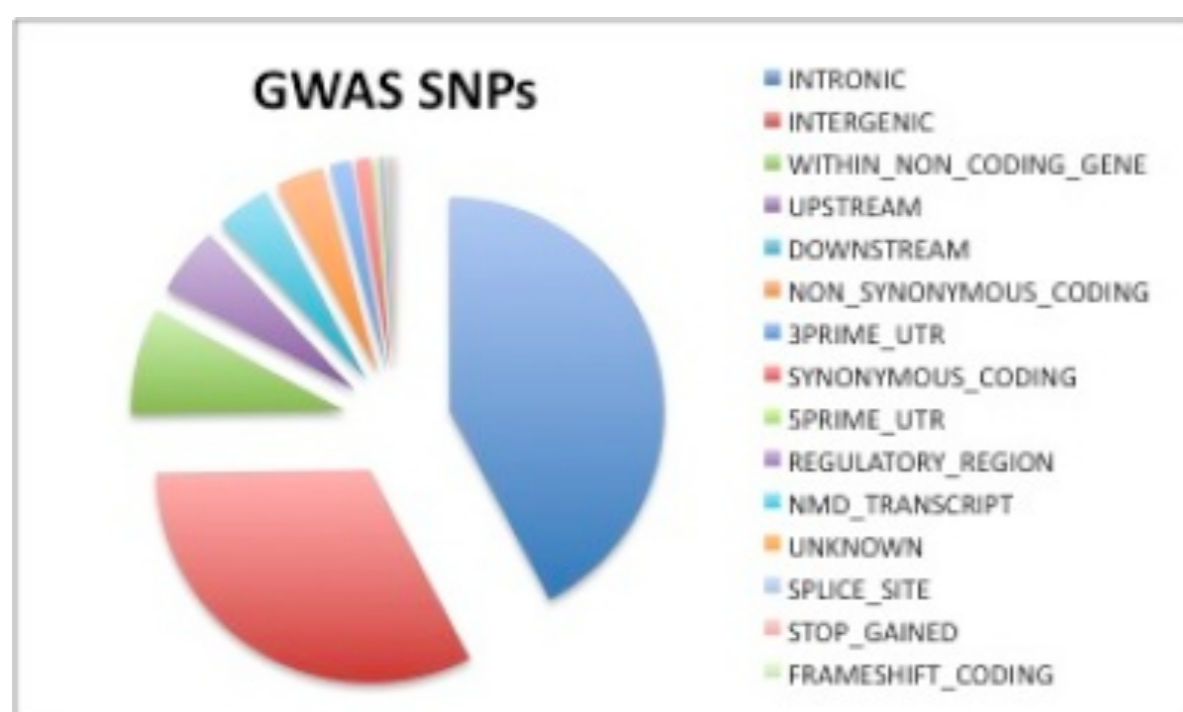
Integrative network analysis of dengue GWAS



Work in progress

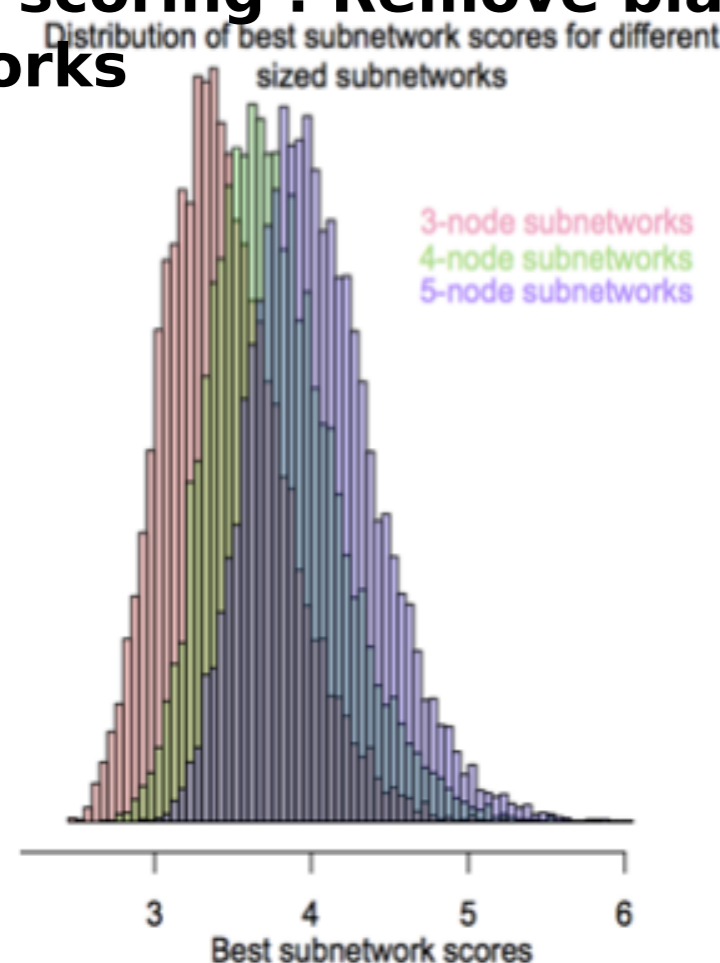
SNP to gene mapping :

Do we map SNPs to genes according to their physical position? Regulatory function? What regulatory data do we use; tissue-specific eQTLs, ENCODE, other?



What type of interactions should we rely on? (Literature curated? Protein interactions? Y2H?)

Subnetwork scoring : Remove bias towards larger networks



Applications

Analysis of available GWAS datasets:

Vietnam² :

- 2009 Dengue shock syndrome pediatric cases
- 2019 Controls

Thailand :

- 609 cases with 3 degrees of severity: Fever, high fever, shock syndrome

Cuba :

- 2 datasets from 2 towns: Havana, Guantanamo
- 2*100 patients, 3 degrees of severity: Asymptomatic, fever, hemorrhagic fever



Literature

[1] Dengue guidelines for diagnosis, treatment, prevention and control, World Health Organisation, 2009

[2] Genome-wide association study identifies susceptibility loci for dengue shock syndrome at MICB and PLCE1, Khor & al., Nat Genet. 2011

[3] STRING v9a.1: protein-protein interaction networks, with increased coverage and integration, Franceschini, A., Szklarczyk, D., Frankild, S., Kuhn, M., Simonovic, M., Roth, A., ... Jensen, L. J. Nucleic Acids Research, 2013