

# Genome architecture of Dengue and Zika viruses

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## **Abstract**

Dengue and Zika are clinically important members of the Flaviviridae family with an 11kb positive strand RNA genome. While structures have been mapped primarily in the UTRs, much remains to be learnt about how the rest of the genome folds to enable function and regulation. Here, we performed structure and interaction mapping on four dengue serotypes and four Zika strains inside their virions and in infected cells. Comparative analysis of SHAPE reactivities across serotypes nominated potentially functional regions that are highly structured, show structure conservation, and low synonymous mutation rates, including a structure associated with ribosome pausing. Pair-wise interaction mapping by SPLASH further reveals new pair-wise interactions, in addition to the circularization sequence. 40% of pair-wise interactions form alternative structures, suggesting extensive structural heterogeneity. Analysis of shared interactions between serotypes revealed a conserved macro-organization whereby interactions can be preserved at their physical locations beyond sequence identities. In addition, structure mapping of virus genomes released in solution- as well as inside host cells- suggested that helicases other than the ribosome play a role in unwinding viral structures inside cells. Compensatory mutations further demonstrate the importance of these new interactions during the virus life-cycle.