Reassortment primes influenza for host group switches

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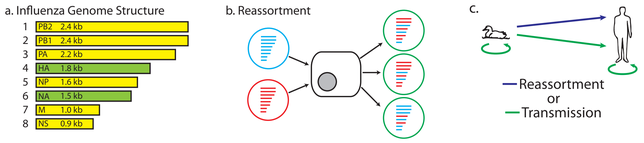
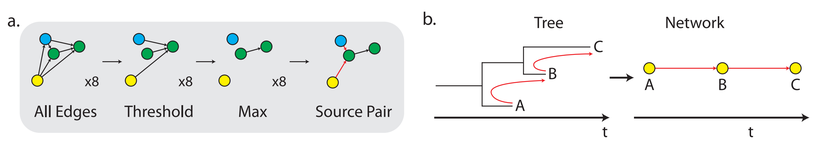
Introduction



- (a) The influenza virus has a segmented genome, which allows it to (b) undergo genomic reassortment.
- Broad host range, including wild birds, other mammals, domestic animals, and humans.
- (c) Dogma: reassortment is important for host switches. Is this true?

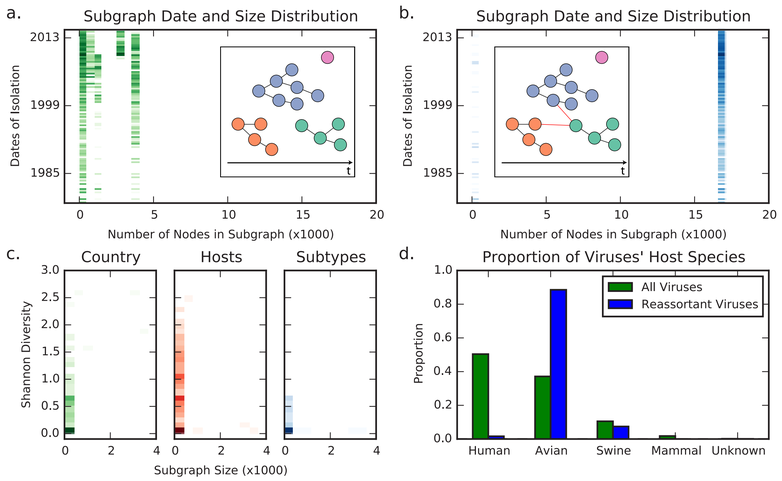
Method



- (a) Schematic of method. The core idea is to look for plausible approximate source-sink relationships across all 8 viral segments. Non-plausible edges are thresholded off.
- (b) The method is a phylogenetic heuristic that is akin to "flattening" a phylogenetic tree. Source-sink inference is often performed on trees by looking at neighboring branches. A network-based representation codifies this intuition.

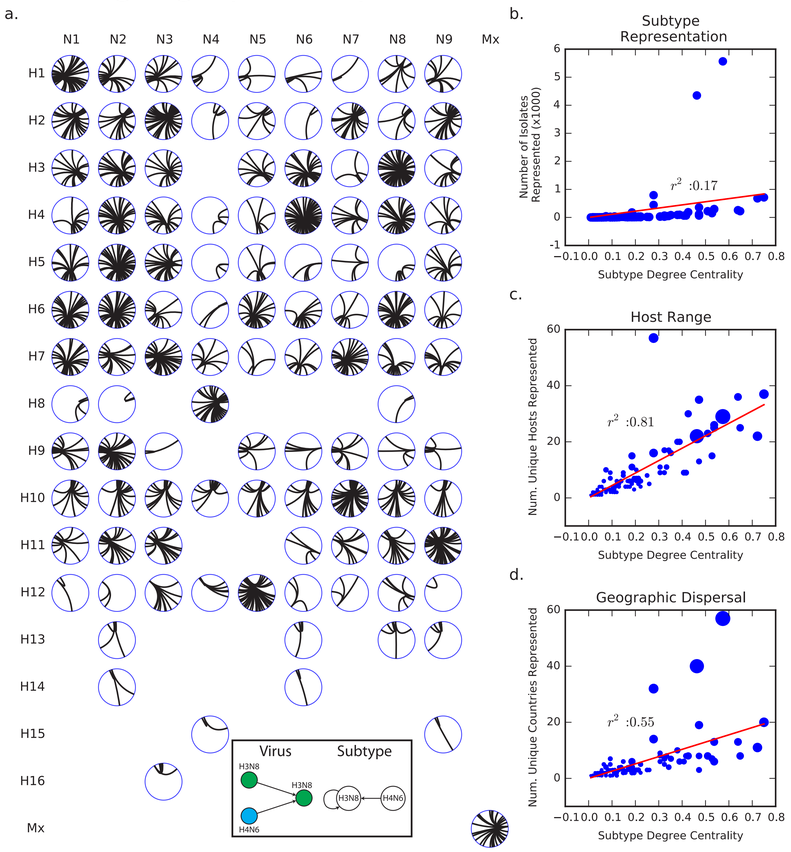
Results

(1) Reassortment links influenza viruses in a global network of gene exchange.



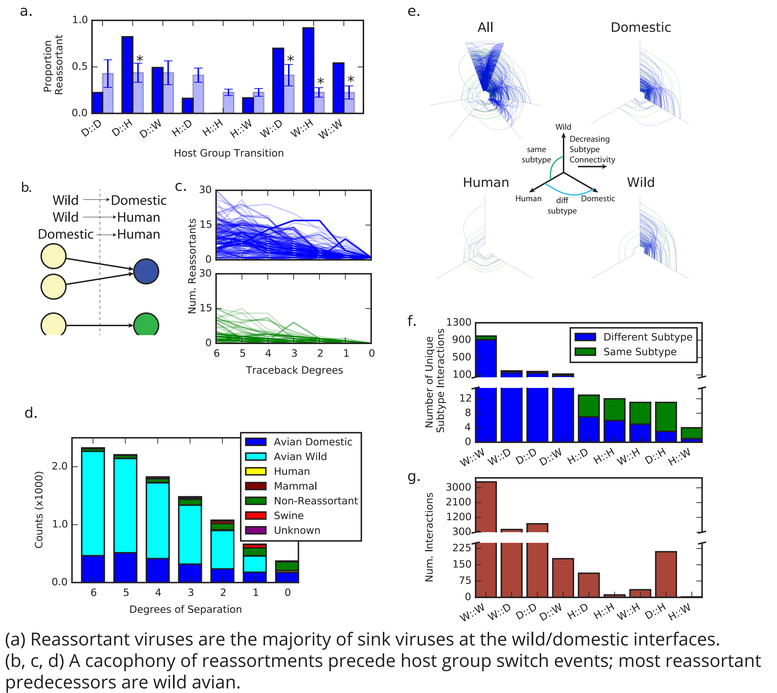
- Subgraph size distribution in network (a) without and (b) with reassortant edges. Toy network illustrations are inset in chart.
- (c) Without reassortant edges added in, subgraphs are homogeneous w.r.t. subtype representation, but not geography and host species.
- (d) As a proportion of all viruses, human and avian-sourced viruses outnumber the rest, but the reassortant viruses were disproportionately avian viruses.
- Known reassortant viruses, including the pH1N1 (2009, global) and H7N9 (2013, China) viruses, were identified in our network.

(2) Hub subtypes have wide host range and broad geographic dispersal.



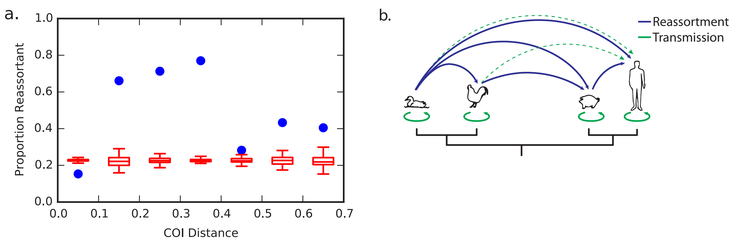
- (a) Circos panel depicting the connectivity of a particular HA & NA subtype combination with other subtypes. Hub subtypes are highly connected to other subtypes.
- Connectivity is best correlated with host range (c) and geographic dispersal (d), but not with sampling effort. Bubble sizes in (c) and (d) are proportional to sampling effort.

(3) Reassortment precedes the switch from wild to domestic animals and humans.



- (a) Reassortant viruses are the majority of sink viruses at the wild/domestic interfaces.
- (b, c, d) A cacophony of reassortments precede host group switch events; most reassortant predecessors are wild avian.
- (e, f, g) Hive plots show the inter-subtype gene exchanges at various wild animal, domestic animal and human interfaces across reassortment events. "All" - all directions considered. "Wild", "Domestic" and "Human" - only subtype interactions donating genes into the respective ecotypes are shown. Nodes are ordered radially according to subtype connectivity.

(4) Reassortment is a favored strategy to cross host phylogenetic barriers.



- (a) Across each edge, host phylogency can be measured by cytochrome oxidase I (COI) distance.
- When binned, the proportion of edges that are reassortant is shown with blue dots.
- Under 100 permutations of COI sequences, the distribution of expected porportions is shown with red box plots.
- Reassortment is favored as a strategy for crossing host barriers
- (b) Favored strategies. Within host species, whole genome transmission is favored (green lines). Between hosts, reassortment is favored (blue lines), though not exclusive.

Further Questions

- Can game theory model the advantages of reassortment in a fluctuating fitness landscape?
- What other ecological factors may drive reassortment?
- Can we sample reassortment events at the source prior to the sink?
- What adpative markers typically come together?
- Are adaptive markers universal?

Acknowledgments:

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