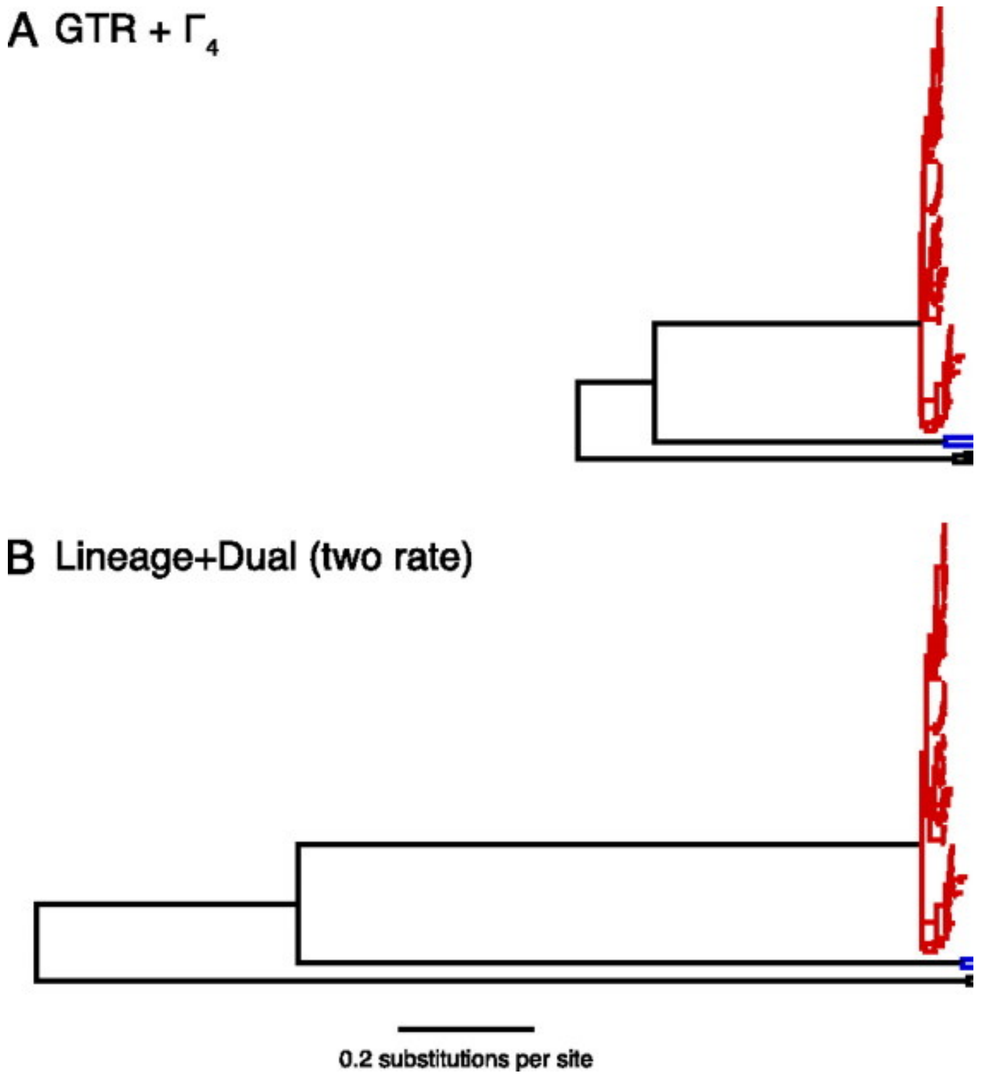
- Using models that do not vary selection pressure across lineages yields a patently false “*too young*” estimate for the origin of **measles** (about 600 years ago)

- This estimate is refuted by clear historical records which suggest that measles is at least 1,500-5,000 years old
  - *This includes a treatise by a Persian physician Rhazes about **differential diagnosis of measles and smallpox** published circa 600 AD.*
- Same patterns found for corona-viruses, ebola, avian influenza and herpesvirus



Wertheim and Pond (2011) Mol Biol Evol. 28(12):3355-65

Interpreting dN/dS for intra-host and intra-species pathogen

- **dN/dS** can be estimated for all sorts of sequence data (e.g., it has been done for cancer SNP data)
- Traditional interpretation of dN/dS is based on the assumption that **substitution ~ fixation**
- Not the same for intra-species / intra-host pathogens
  - Much of variation is due to polymorphism, or even dead-end mutations
- This is because selection has not had a chance to “filter” mutations (except for patently deleterious ones)
- This often manifests as differences in selective “regimes” between tips and internal branches