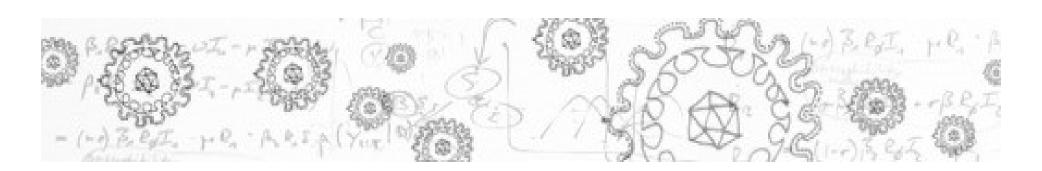
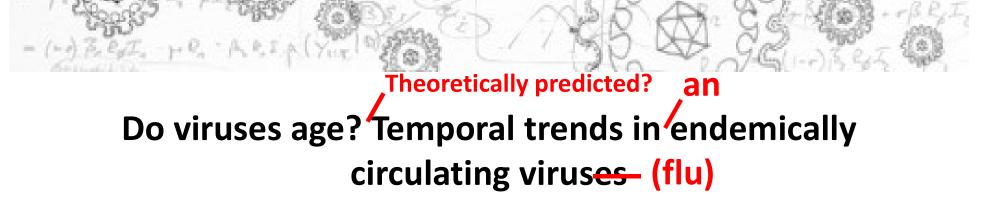


Do viruses age? Temporal trends in endemically circulating viruses

Katia Koelle Department of Biology Emory University

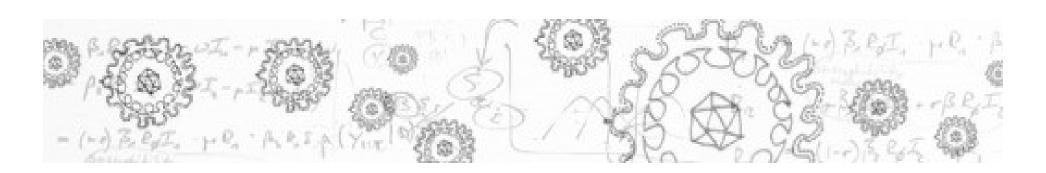
Infectious Disease and Aging July 26-28, 2018 Santa Fe Institute



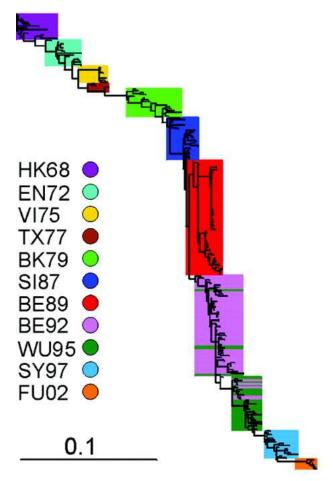


Katia Koelle Department of Biology Emory University

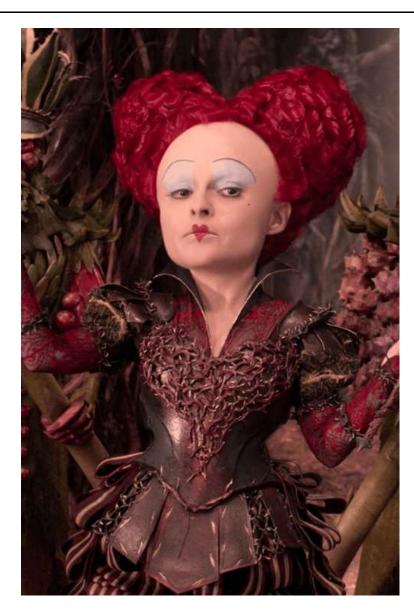
Infectious Disease and Aging July 26-28, 2018 Santa Fe Institute

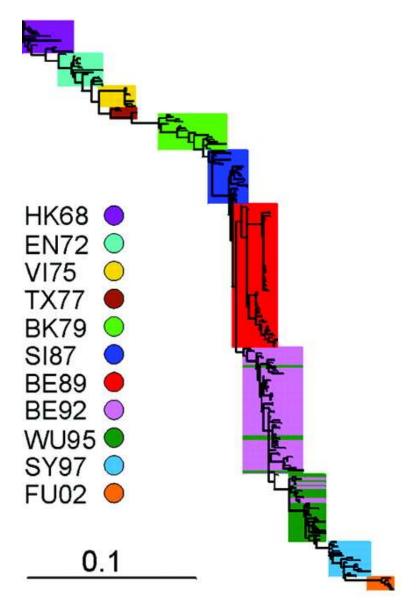


Antigenic evolution and the Red Queen



Smith et al. (2004) Science





(I) Antigenic mutations necessarily occur in a genetic background

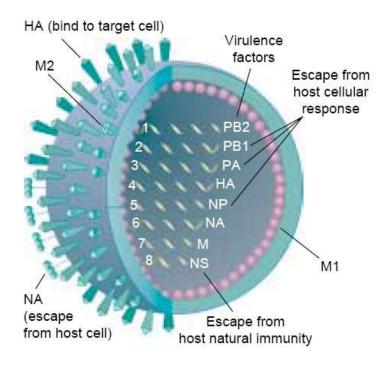
(II) Antigenic mutations may have pleiotropic effects

Smith et al. (2004) Science

Influenza Virus

Seasonal flu in humans caused by:

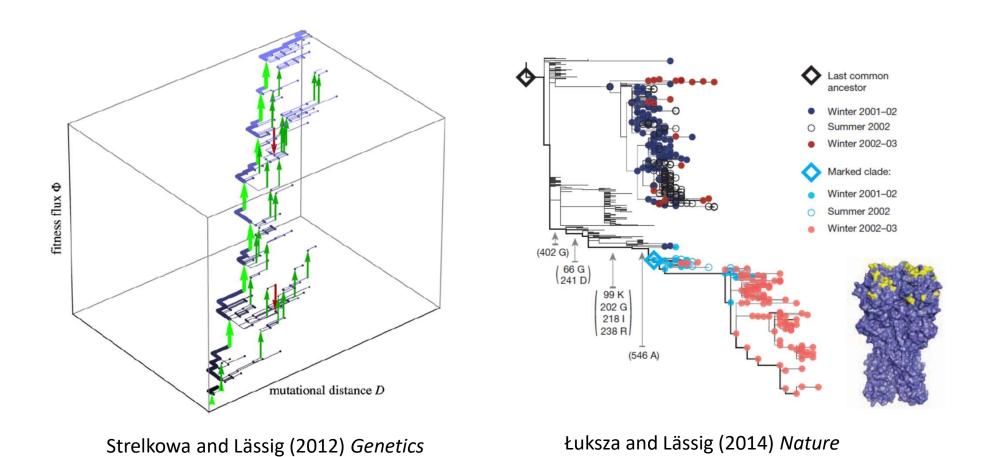
- influenza A/H3N2
- influenza A/H1N1
- influenza B (Yamagata & Victoria)



Influenza A virus

- Segmented RNA virus (8 segments)
- Hemagglutinin HA = 'H' of H3N2
- Importance of HA for adaptive antigenic evolution
- No recombination within gene segments
- Occasional intrasubtypic reassortment

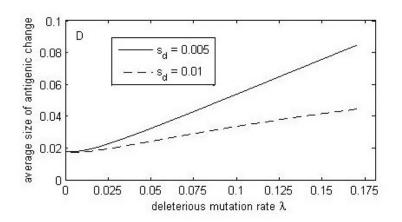
(I) Antigenic mutations necessarily occur in a genetic background



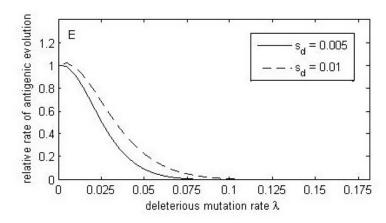
Flu has heritable fitness unrelated to antigenicity

Effect on deleterious mutations on influenza evolution

Expectation of "punctuated" antigenic evolution...



occurring rarely.

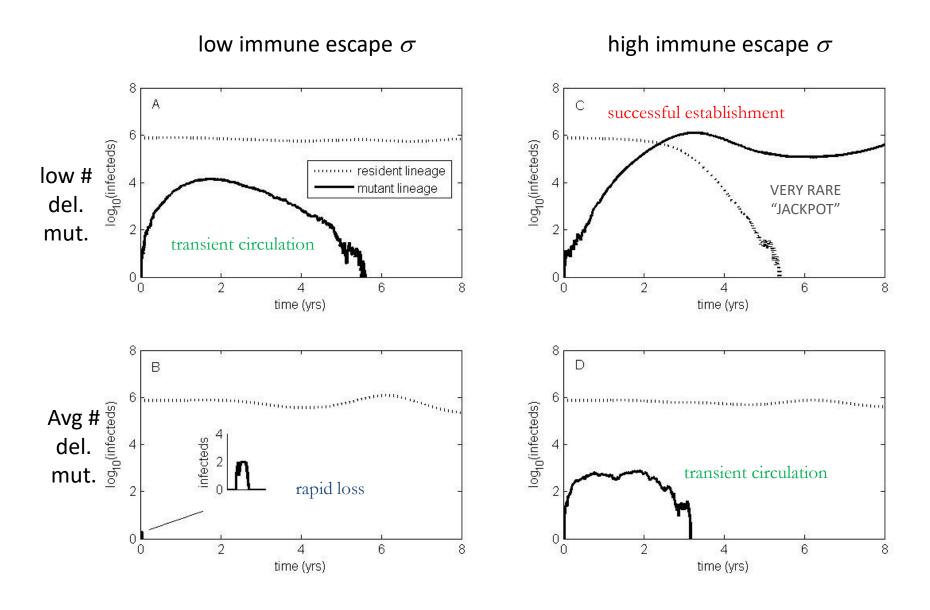


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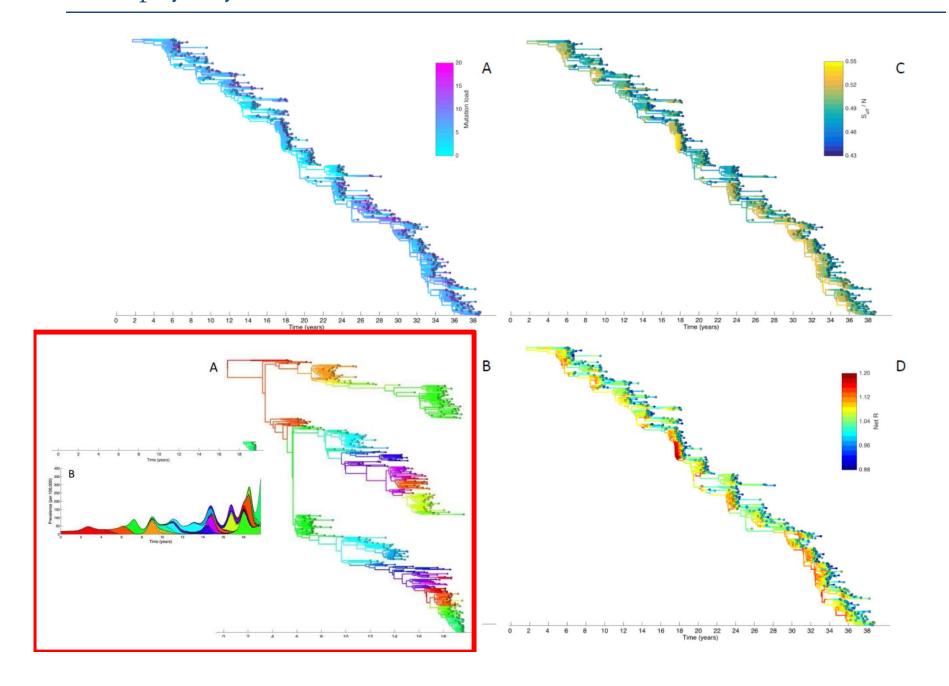
Smith et al. (2004) Science

Koelle and Rasmussen (2015) eLife

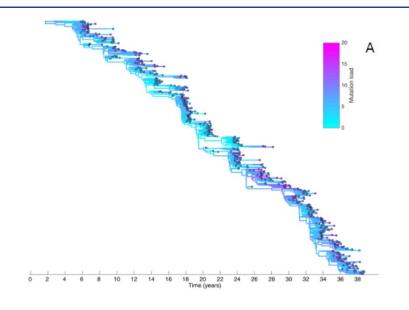
Simple model with explicit epidemiological dynamics



Full 'phylodynamic' simulations of model



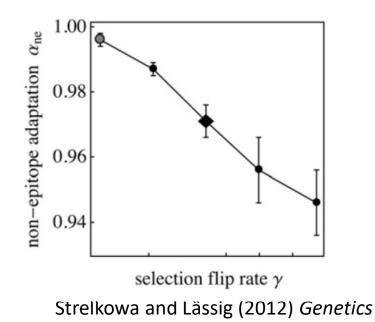
Generation of "adaptive genetic load"? Ultimate mutational meltdown??

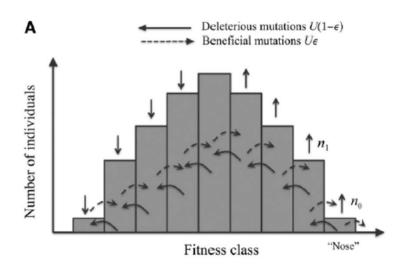


"Clonal interference generates adaptive genetic load on conserved functions encoded in linked sequence."

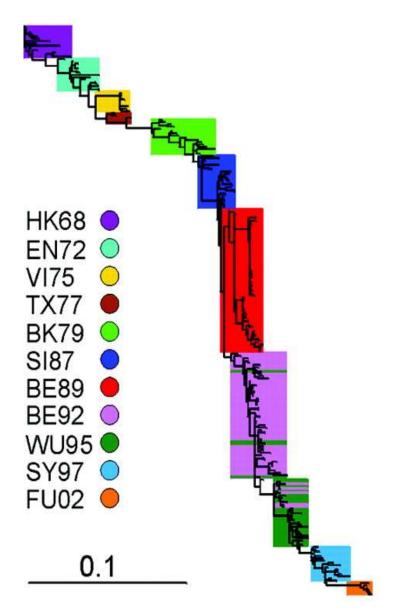
Strelkowa and Lässig (2012) Genetics

Or do beneficial mutations come to the rescue?





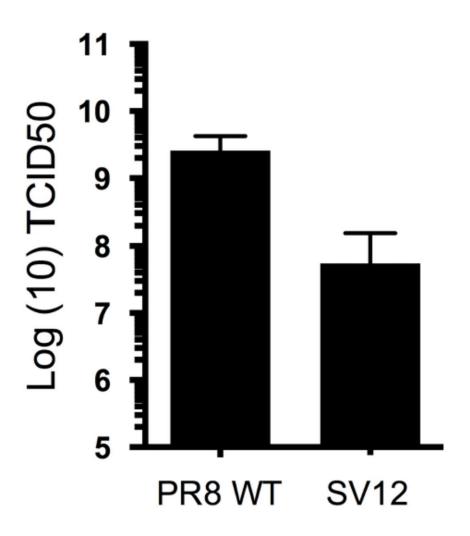
Goyal et al. (2012) Genetics



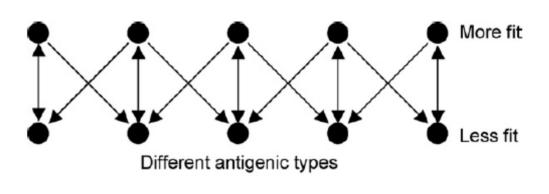
Smith et al. (2004) Science

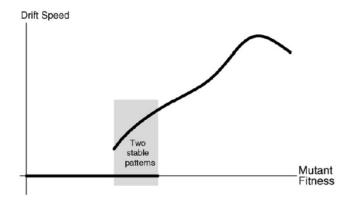
(I) Antigenic mutations necessarily occur in a genetic background

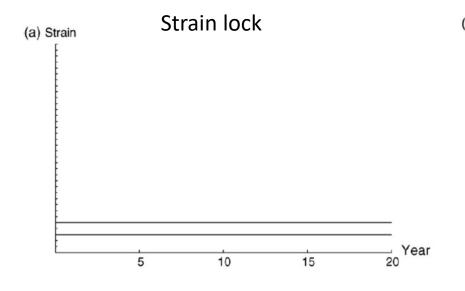
(II) Antigenic mutations may have pleiotropic effects

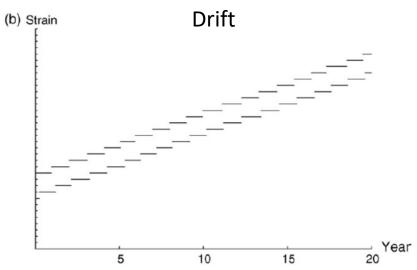


Fitness costs of antigenic mutations



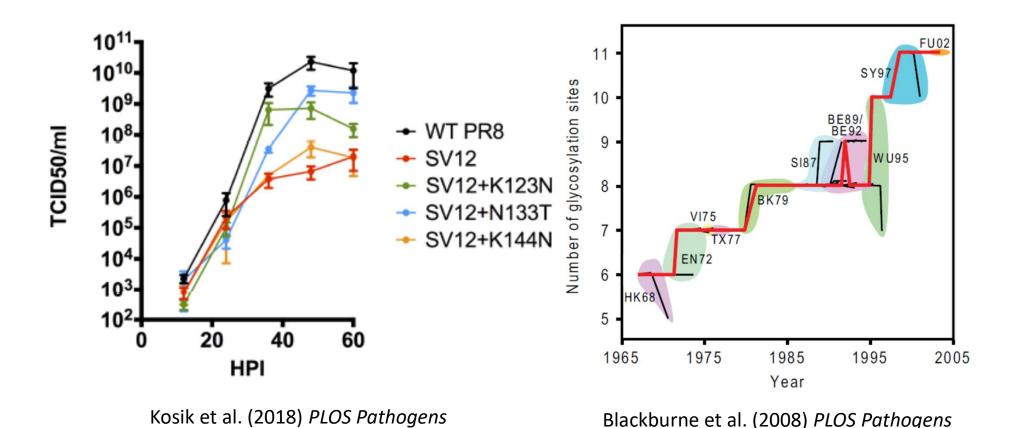






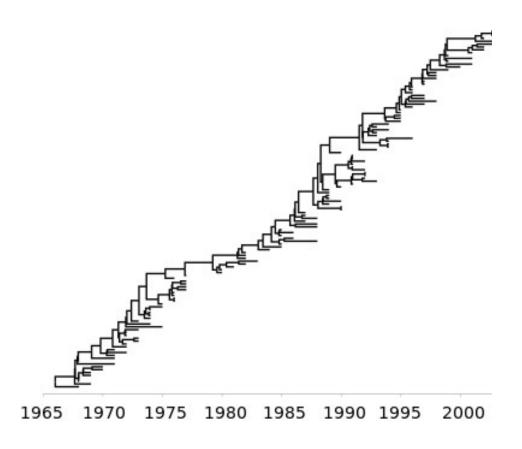
Gog (2008) Vaccine

Evidence for compensatory mutations (glycosylation)



But glycosylation also can have fitness costs...Das et al. (2011) PNAS

Current challenges/questions with potential for transformative breakthroughs



Does influenza virus "aging" occur in avian populations?

How much "adaptive genetic load" is there, and what would viral life be like without it?

Evolution of the receptor binding properties of the influenza A(H3N2) hemagglutinin

Yi Pu Lin^{a,1}, Xiaoli Xiong^{a,b,1}, Stephen A. Wharton^a, Stephen R. Martin^c, Peter J. Coombs^{a,b,2}, Sebastien G. Vachieri^{a,b}, Evangelos Christodoulou^b, Philip A. Walker^b, Junfeng Liu^{a,b,3}, John J. Skehel^a, Steven J. Gamblin^b, Alan J. Hay^a, Rodney S. Daniels^a, and John W. McCauley^{a,4}

Has "adaptive genetic load" been responsible for the genomic architecture of influenza and that of other segmented viruses?

How important are compensatory mutations to the lives of antigenically evolving viruses?

Do flu viruses have a finite lifespan in humans in part because they "age"?