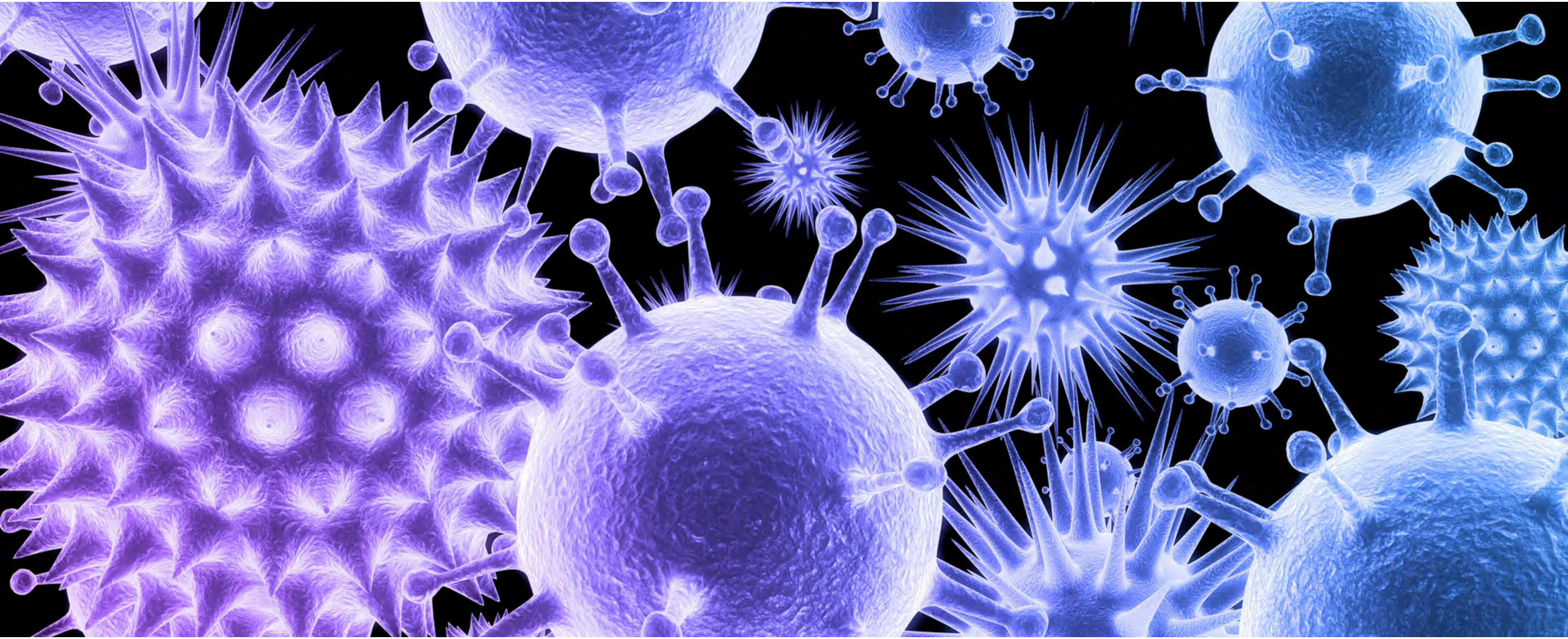
Predicting Evolution of Virus Emergence

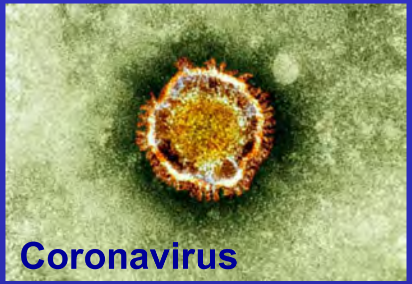


Yale

Paul E. Turner, PhD
Rachel Carson Professor of Ecology & Evolutionary Biology, Yale University
Microbiology Faculty, Yale School of Medicine.

The Yale School of Medicine

- Goal: To more accurately predict emergence potential on new hosts.
- Why are some pathogens successful at infecting new or multiple hosts?
- *What rules govern pathogen evolution, adaptation, constraint and extinction?*


Coronavirus


SARS CoV-2

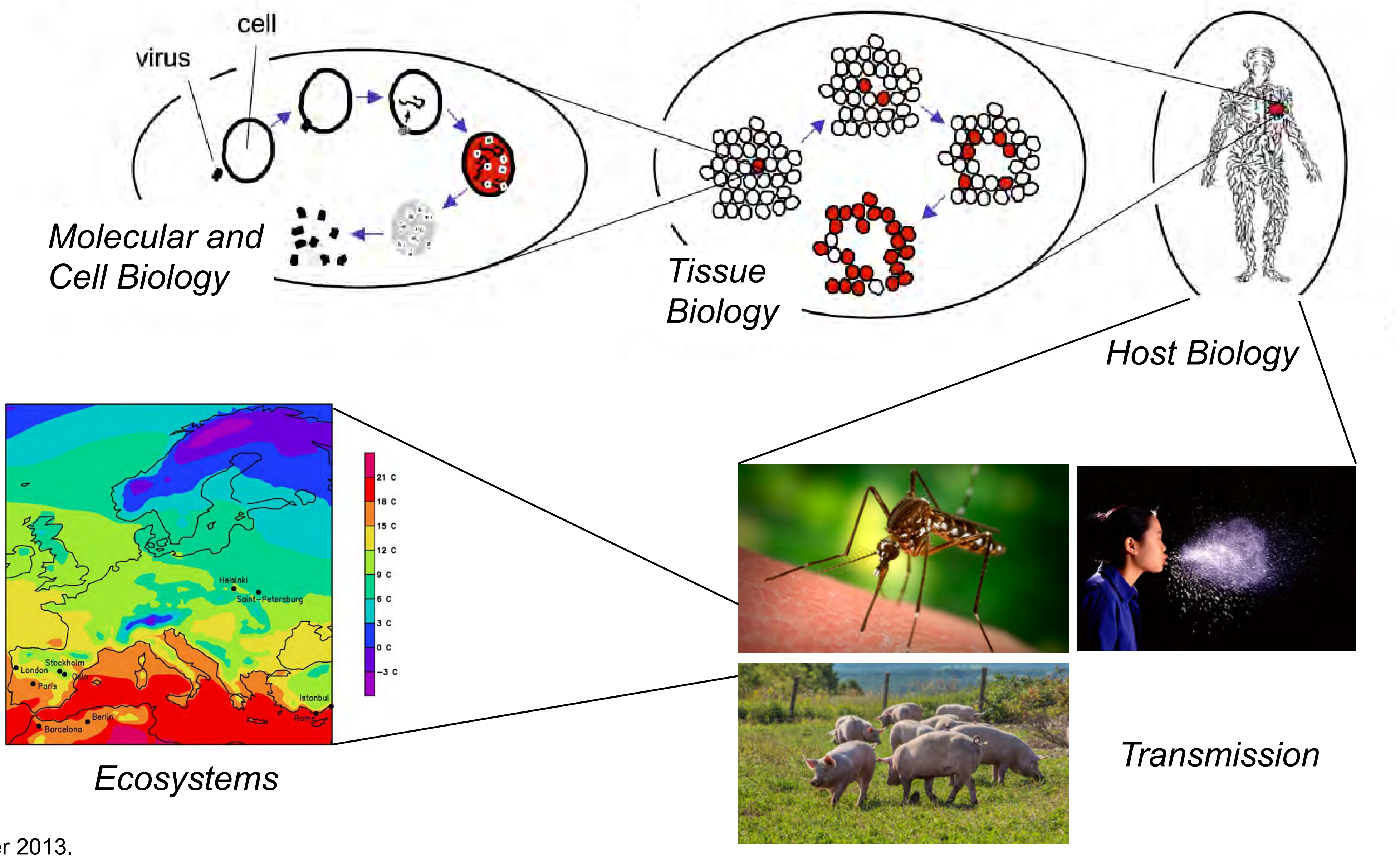

MERS


SARS CoV-1


HIV


Influenza virus

Levels of Selection in Virus Emergence



see Wasik & Turner 2013.
Annual Review of Microbiology

Levels of Selection in Pathogen Emergence

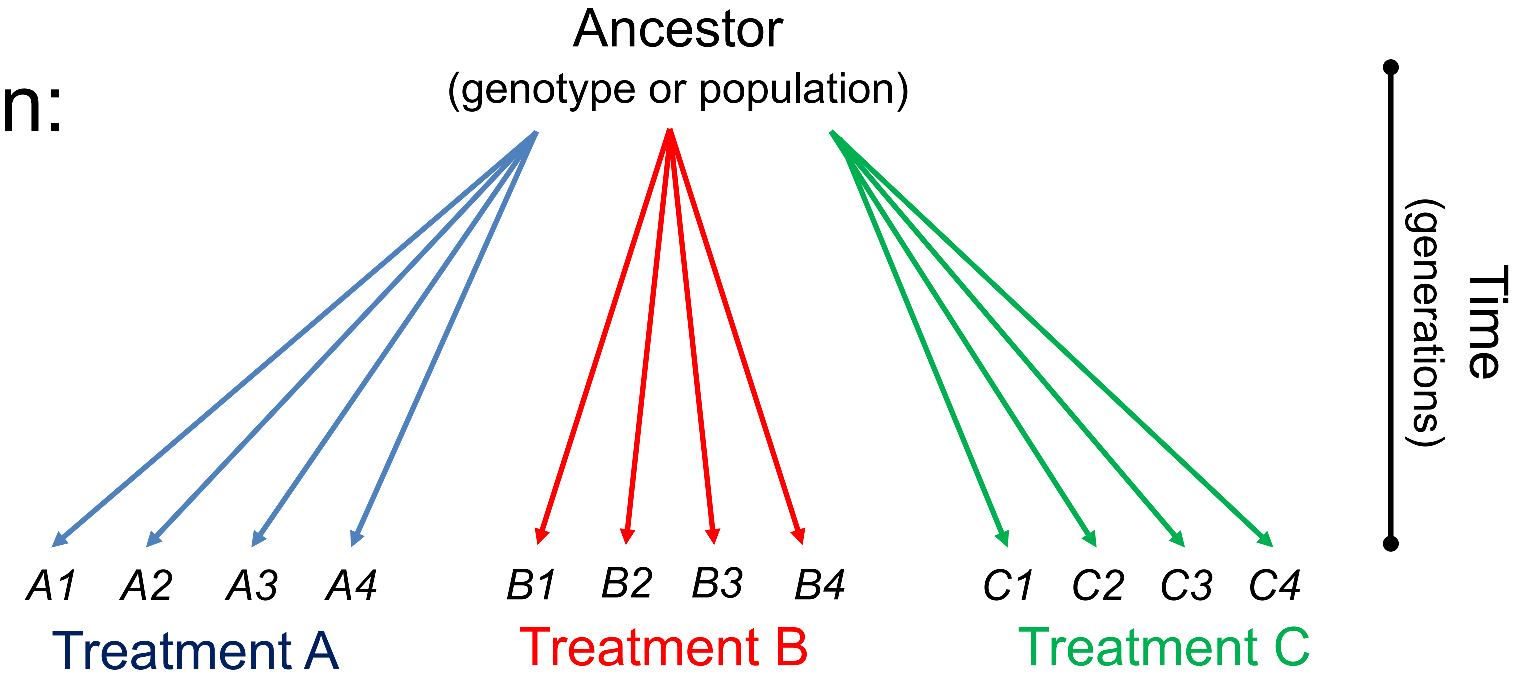
Themes, emphasizing role of evolutionary prediction:

- EVOLVABILITY – how does variation arise and is it maintained?
- ADAPTABILITY – which traits foster pathogen-emergence success?
- CONSTRAINT – what prevents pathogens from exploiting new hosts?
- EXTINCTION – why can (cannot) pathogens persist through time?

Experimental Evolution

Studies of 'evolution-in-action'

Typical design:



Experimental Evolution

Studies of ‘evolution-in-action’ can reveal:

- Molecular and phenotypic variation
- Tempo and mode of adaptation
- Plausible vs. implausible genetic solutions
- Extinction probabilities

Case example: Role of novel-host encounters in emergence

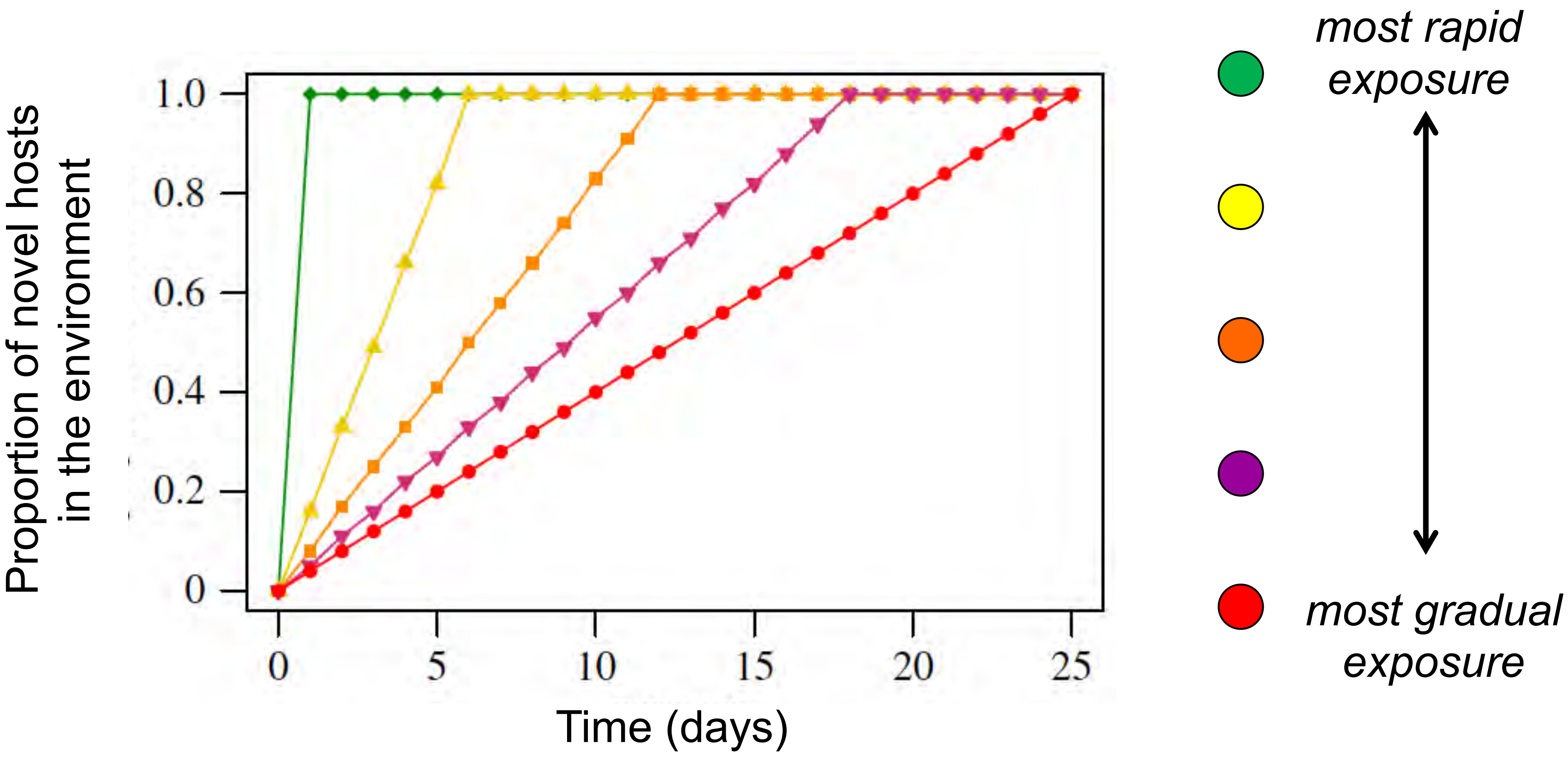
Does sudden vs. gradual exposure to novel host species affect virus emergence potential?

Emergence can occur quickly versus slowly

Does sudden vs. gradual exposure to novel host species affect virus emergence potential?

Valerie Morley, PhD
(Penn State U)

Sandra Mendiola
(Emory U)



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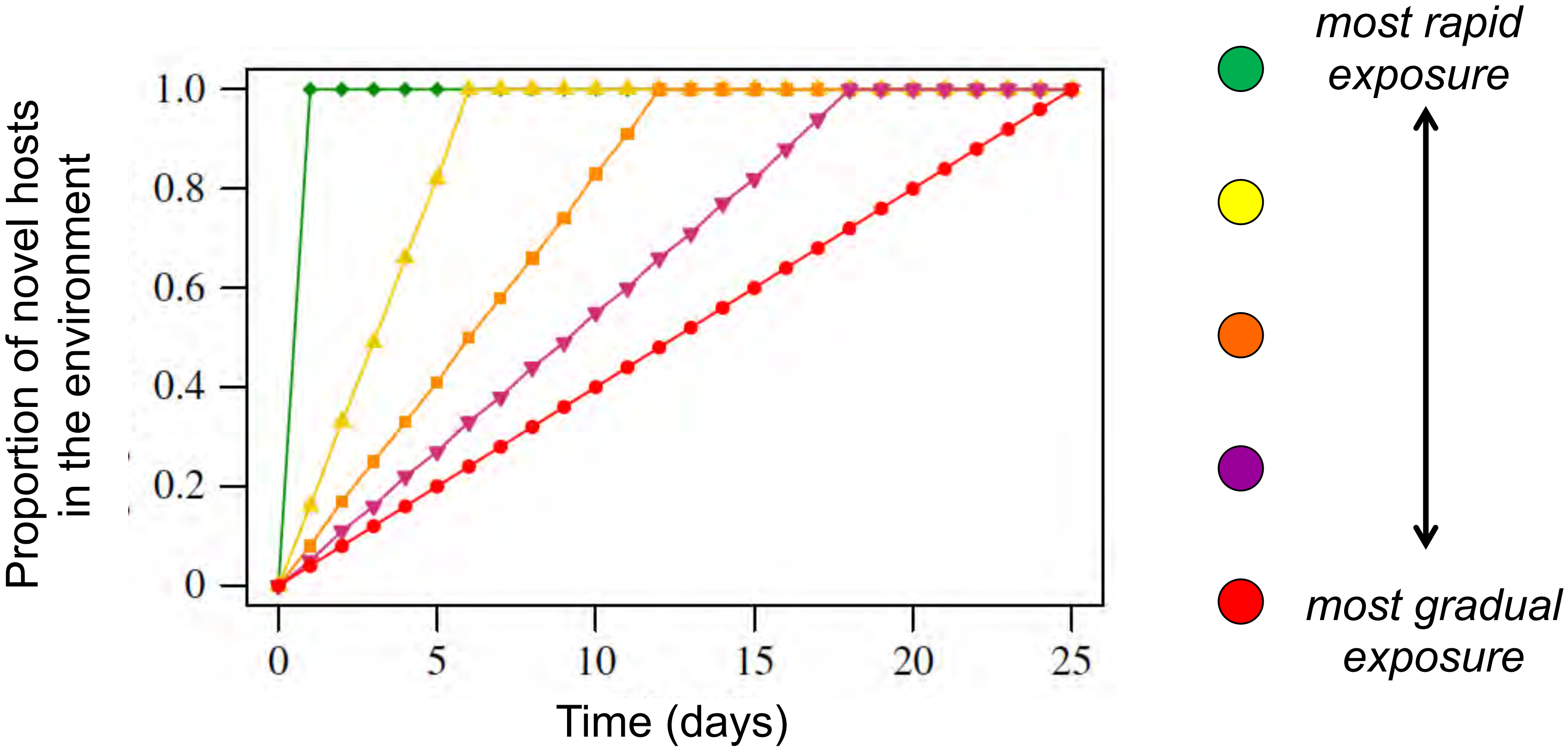
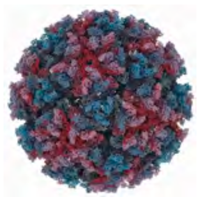
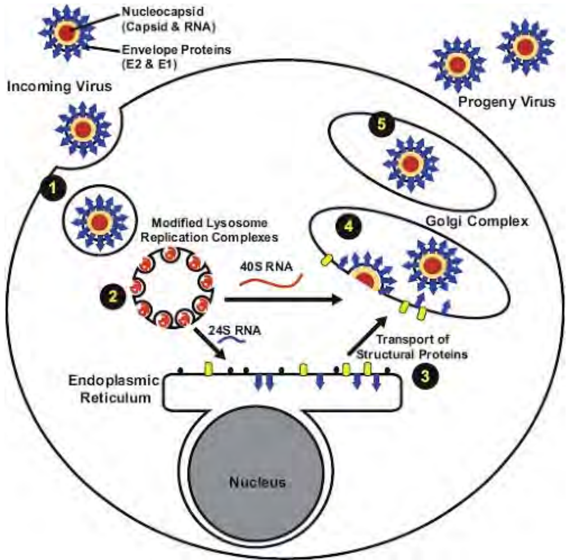




- Sindbis virus
- model (+)RNA virus
- *Togaviridae* family
  - rubella
  - West Nile fever
- 144 test lineages



Emergence can occur quickly versus slowly

Does sudden vs. gradual exposure to novel host species affect virus emergence potential? – <u>YES!</u>

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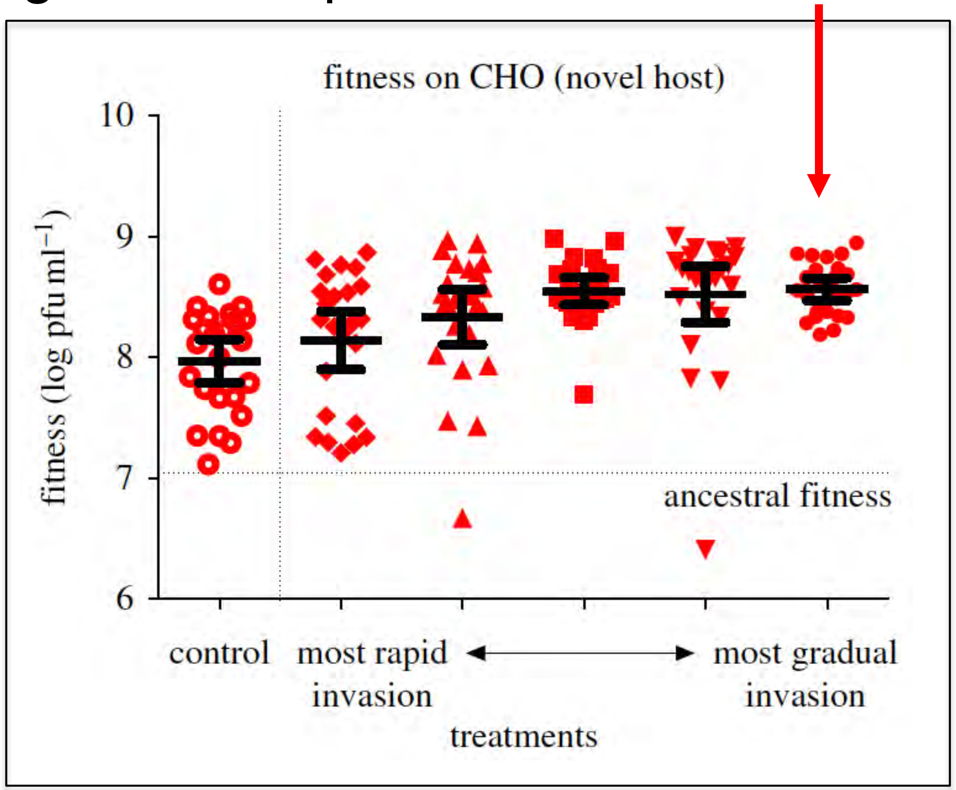
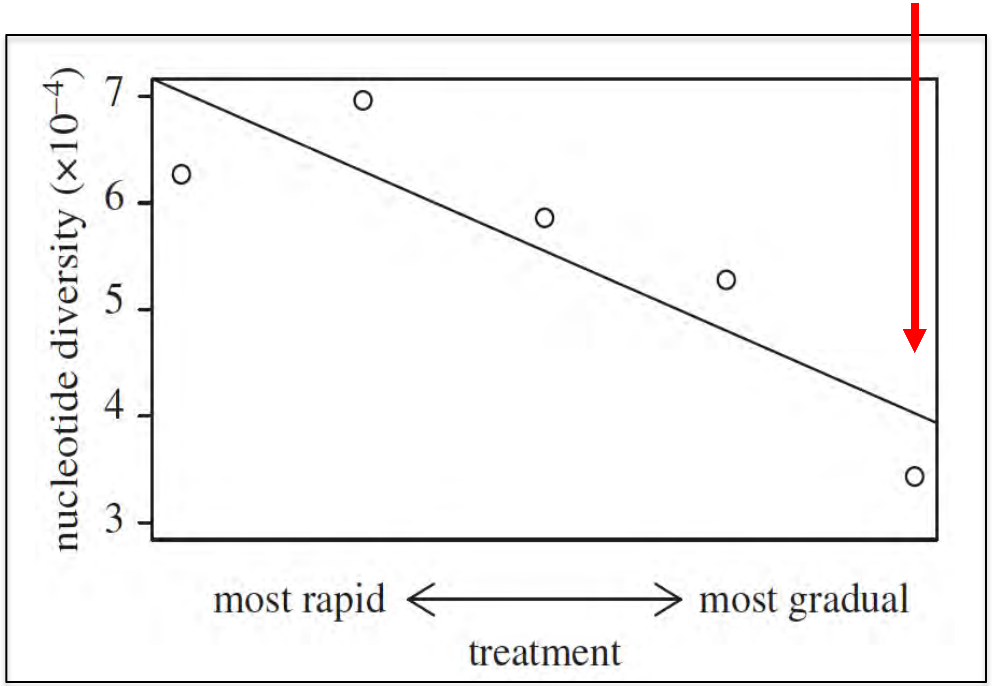
Gradual host invasions caused:

Lesser phenotypic variation and greater adaptation on novel hosts.



Lesser genetic variation among evolved lineages (less variable genomes).



Morley, Mendiola & Turner 2015, *Proceedings B*

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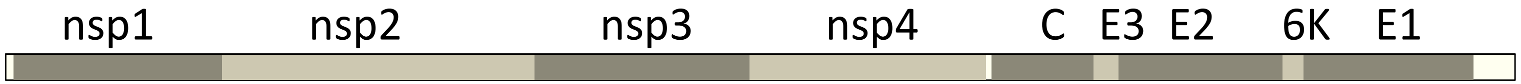
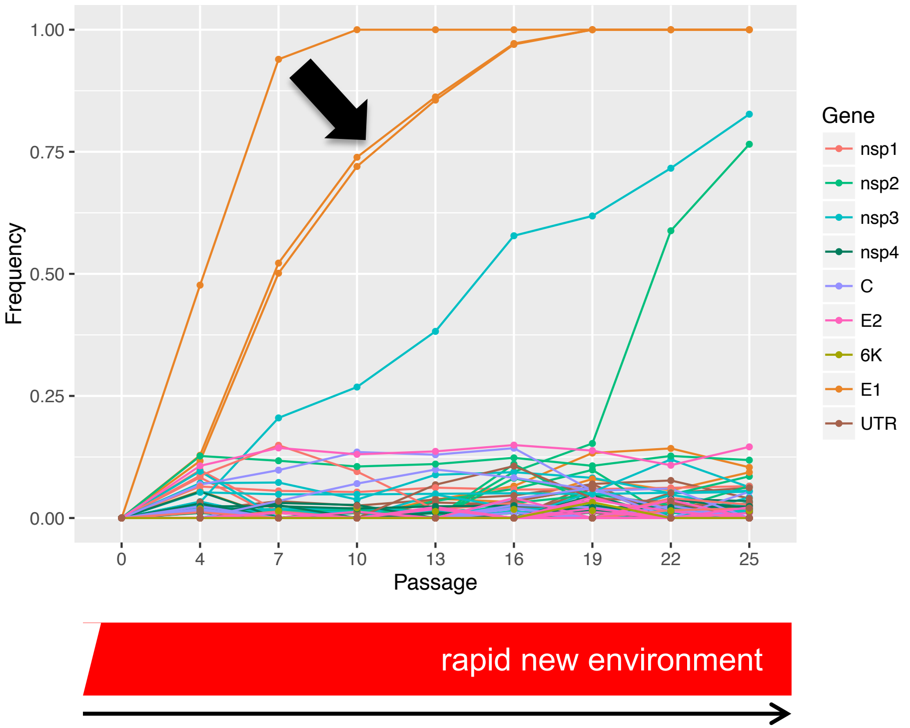
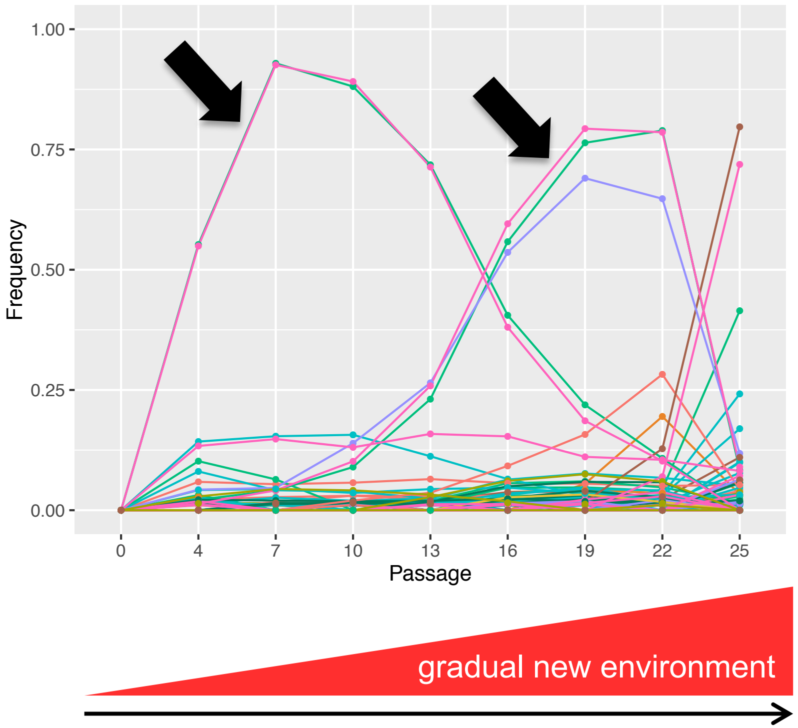
Sindbis virus (+)ssRNA genome:



Dynamics of virus molecular evolution constrained by sudden vs. gradual host exposure:





Morley & Turner 2017, *Evolution*

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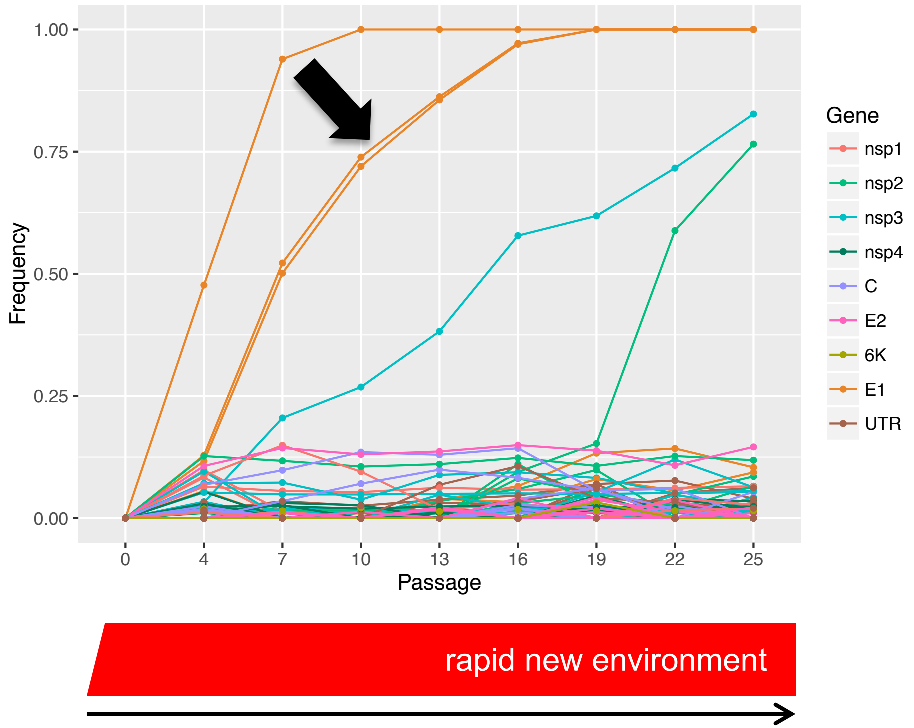

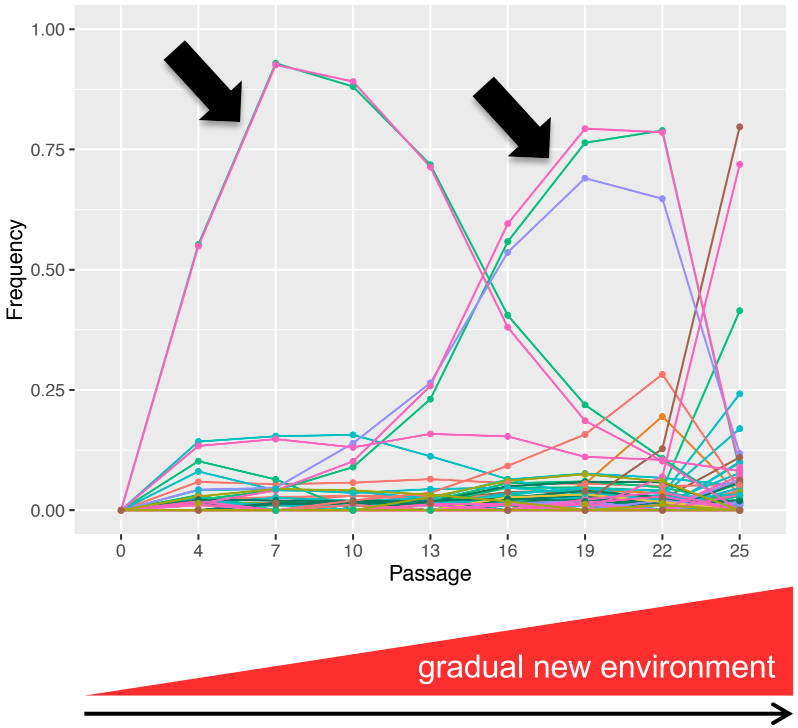

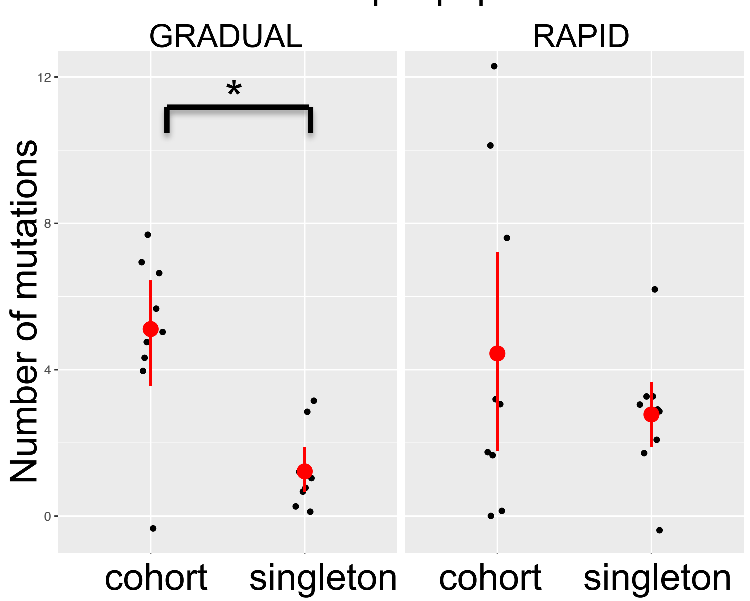

Morley & Turner 2017, *Evolution*

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Dynamics of molecular evolution in RNA virus populations depend on sudden versus gradual environmental change

Valerie J. Morley[1] and Paul E. Turner[1,2,3]

[1]Department of Ecology and Evolutionary Biology, Yale University, P. O. Box 208106, New Haven, Connecticut 06520

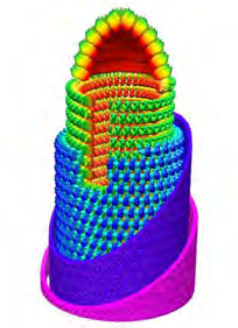
[2]Graduate Program in Microbiology, Yale School of Medicine, New Haven, Connecticut 06520

Supported by: NSF Graduate Research Fellowship to V. Morley
NSF Beacon Center for Study of Evolution-in-Action

Winner of 2017 R.A Fisher Prize for most outstanding thesis paper in *Evolution*

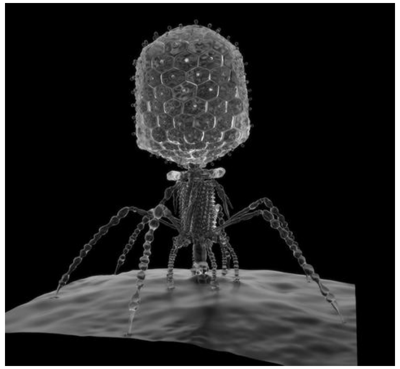
What other approaches could be used in studying emergence?

Model and Non-Model Systems



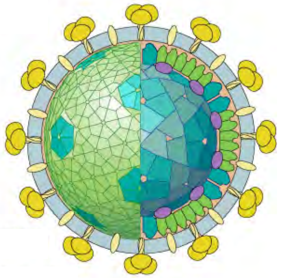
vesicular stomatitis virus

(-)ssRNA



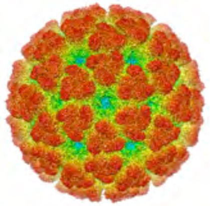
phage T4

dsDNA

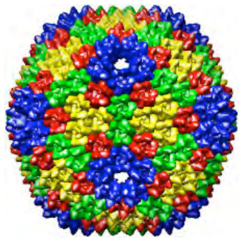


phage phi-6

segmented dsRNA

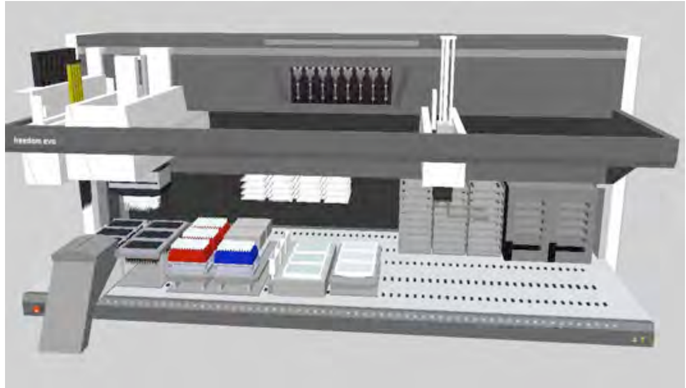


chikungunya virus



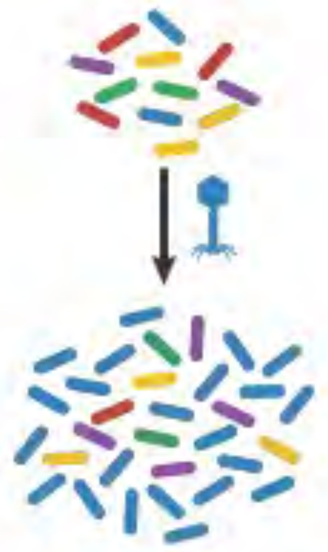
dengue virus

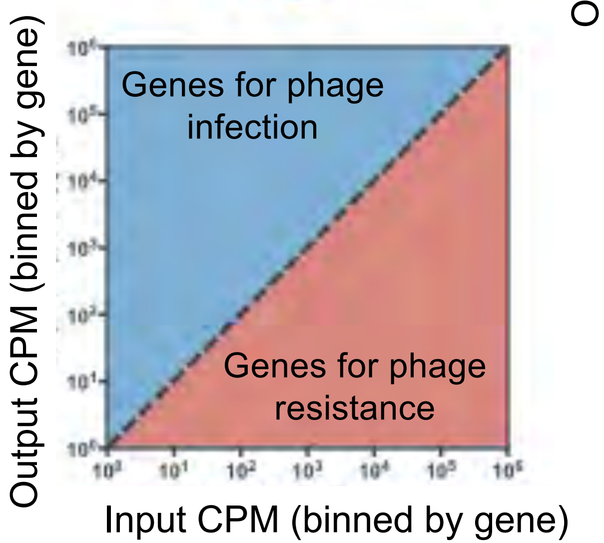
(+)ssRNA

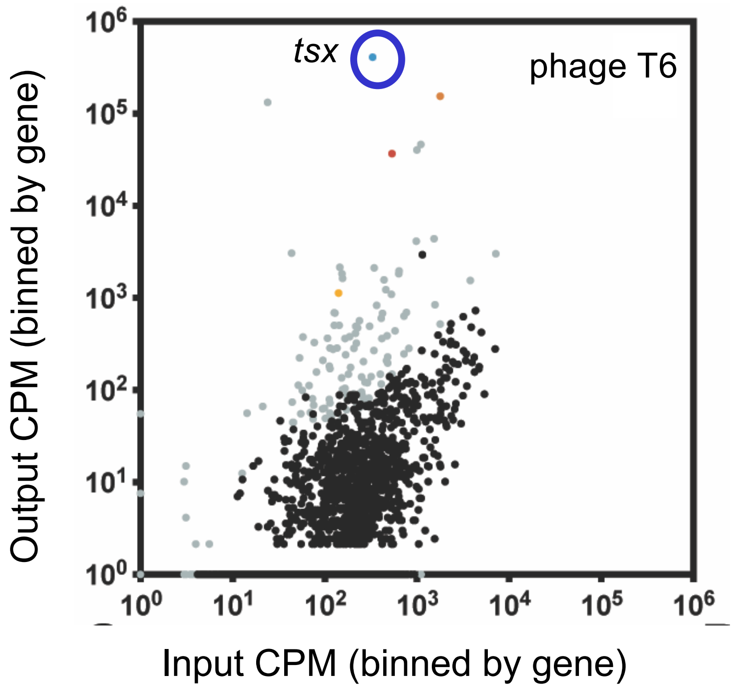


High-Throughput Phenotyping

Discovering cell-receptor(s) used by a virus:







Kortright, Chan & Turner. 2020
PNAS USA

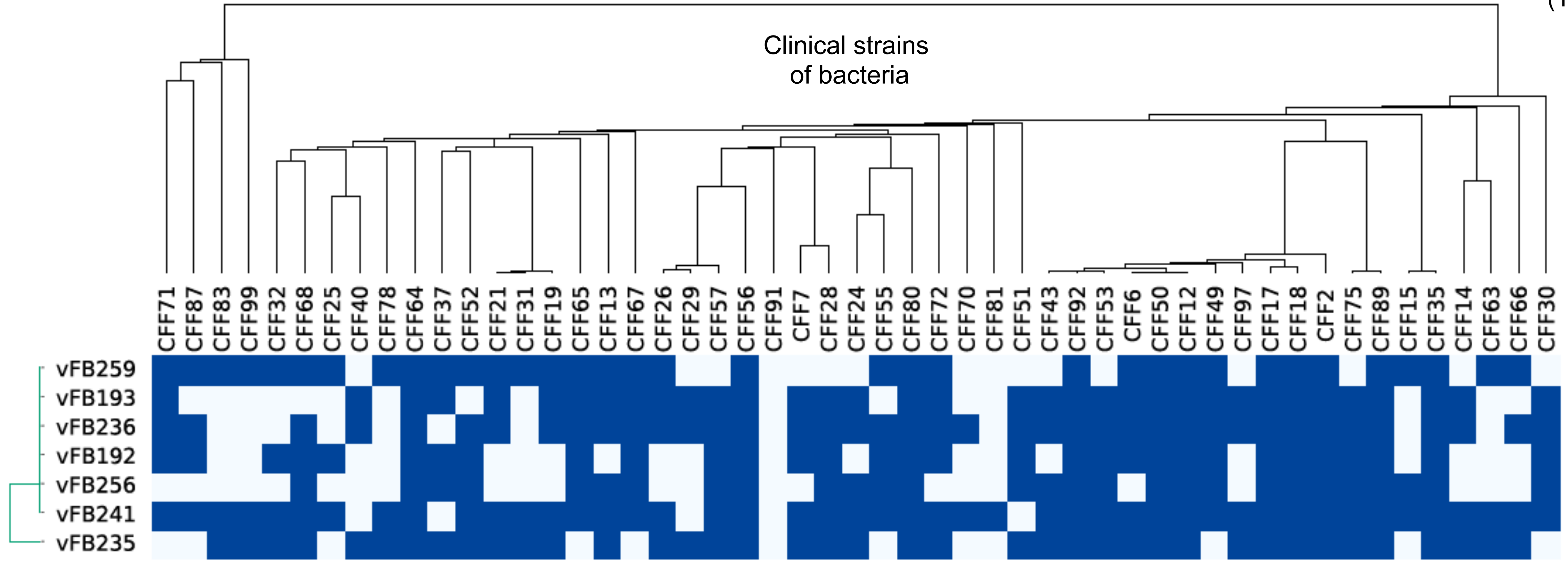
How do emerging pathogens interact with:

- Microbiomes
- Viromes
- Host cells
- Other pathogens

Computer and Data Science

Ben Chan, PhD
(Yale U)

Measuring phenotypic and molecular ‘rules’ of virus host-breadth:

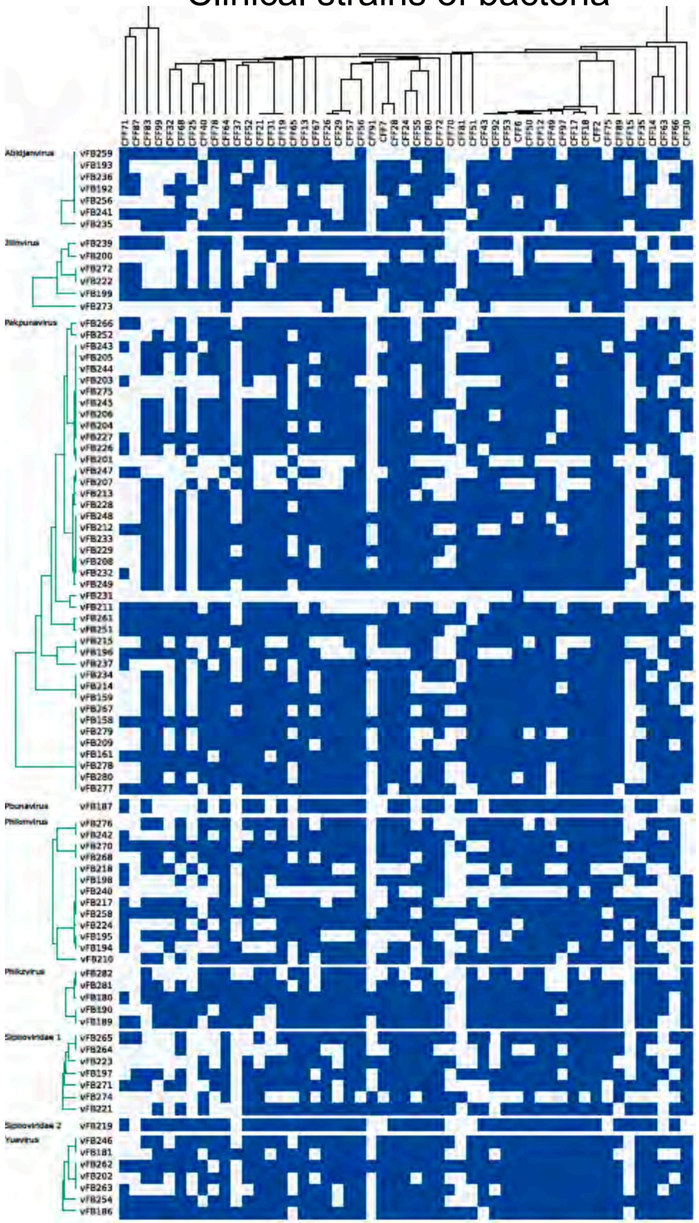


Candidate viruses
for phage therapy

Chan et al. (unpublished)

Computer and Data Science

Clinical strains of bacteria



Candidate phages

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Can machine learning sort through such datasets to accurately predict virus infection potential?

Chan et al. (unpublished)

Computer and Data Science

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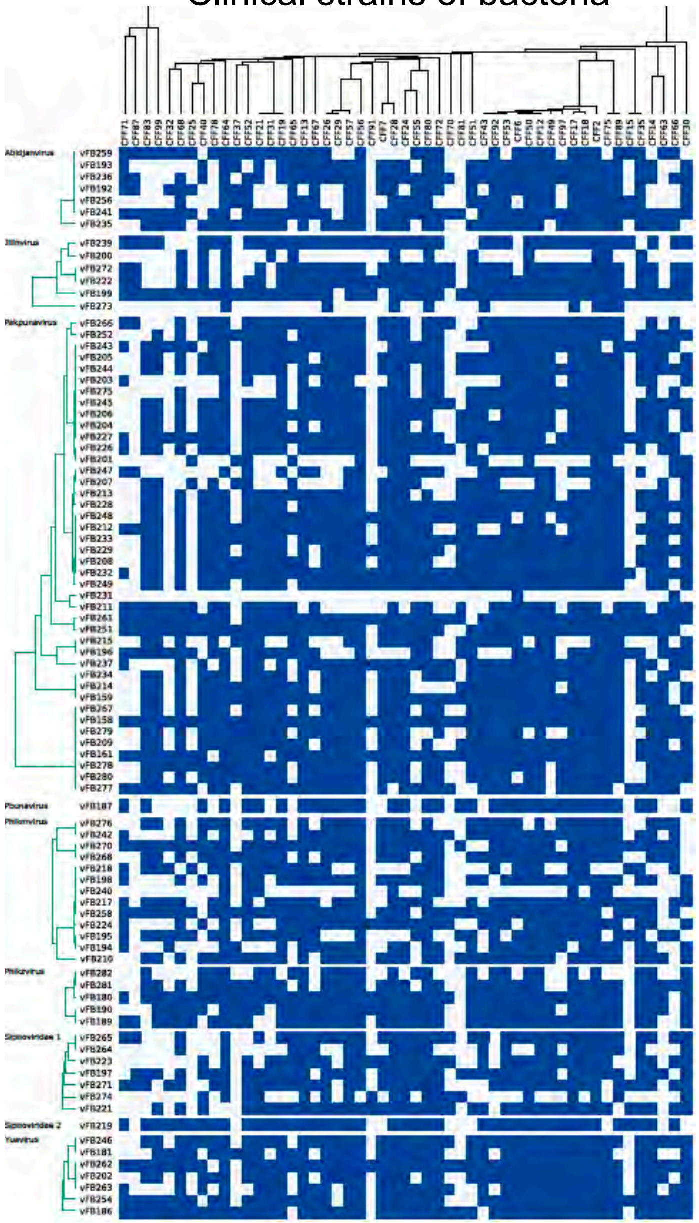

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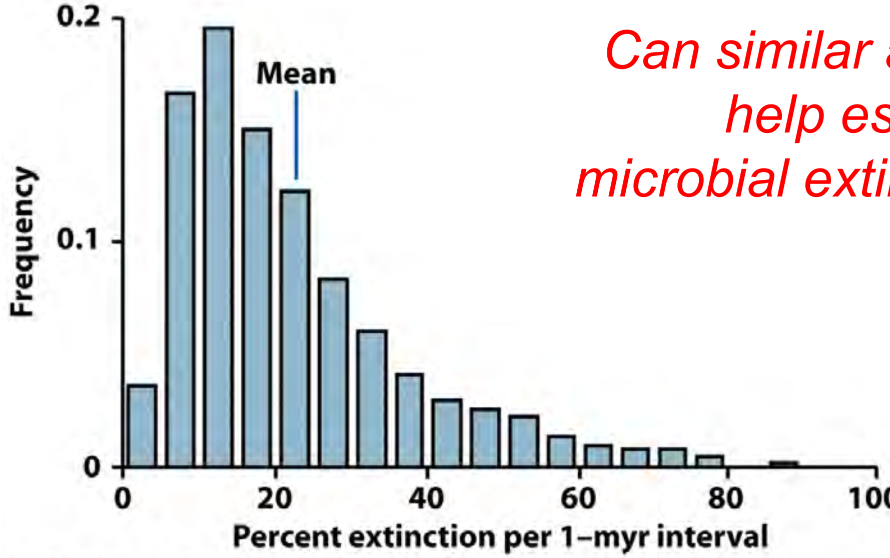

Can similar approaches help estimate microbial extinction rates?

Rates of 'background extinction' estimated for macro-organisms.
(Raup 1994 *PNAS USA*).

Ensuring Diverse Approaches <u>and</u> Participants