Other stuff by students of CSSS 2003
Comparison of deterministic and stochastic model output

Buckee et al. ‘04
Metrics for the measurement of ‘diversity and discordance’

Diversity: entropy measure based on Shannon-Weaver diversity index

\[
D = \frac{\sum_{i=1}^{Ns} p_i \log(1/p_i)}{\log(N_s)}
\]

Discordance: hamming distance measure based on Warwick & Clark ‘95

\[
H = \frac{1}{n} \left( \frac{\sum \sum_{i<j} w_{ij} p_i p_j}{\sum \sum_{i<j} p_i p_j} \right)
\]
Local clustering between hosts increases pathogen diversity

\[ \rho : \text{Regular} \rightarrow \text{Small world} \rightarrow \text{Random} \]
The effects of community structure on antigenic profiles?

Buckee, Danon, & Gupta 2007
‘Homogenization’ of pathogen population versus differentiation of the host populations

Rapid transition to same dominant strains in both host communities
Non-overlapping structure in real life: *Neisseria meningitidis*

- Causal agent of bacterial meningitis and septicaemia
- Lives in the nasopharynx, transmitted by air droplet
- High rates of recombination - very diverse
- Generally commensal, but causes 170,000 deaths annually
Neisseria meningitidis

Capsular polysaccharide (serogroup)

Subcapsular antigens

FetA

PorA

Hypervariable regions

VR1

VR2

Subcapsular antigens
PorA variable regions show non-overlapping structure consistent with the model.
How do stable genetic lineages interact with stable antigenic combinations?
Meningococcal strains defined by antigens and housekeeping genes: dynamic association facilitated by recombination
Low cross-immunity

High cross-immunity
Weak cross-immunity:
Strong cross-immunity: competitive interactions between lineages drive dynamics with antigenic islands.

- a) One ST per antigenic variant
- b) Oscillations
- c) Competitive exclusion
Dengue virus: 50-100 million infections, 200-500,000 DHF cases

Epidemic dengue
Vector: Aedes aegypti
Seasonal waves of transmission across Thailand

Cummings et al., 2004
Antibody-dependent enhancement and original antigenic sin

Whitehead et al., 2007
What are the dynamical implications of ADE?

\[
\frac{dX(t)}{dt} = \mu - X(t) \left[ \sum_i \beta \left( Y_i(t) + \phi_i \sum_{j \neq i} Y_{ji}(t) \right) \right] - \mu X(t), \quad [1]
\]

\[
\frac{dY_i(t)}{dt} = X(t) \left[ \beta \left( Y_i(t) + \phi_i \sum_{j \neq i} Y_{ji}(t) \right) \right] - \sigma Y_i(t) - \mu Y_i(t), \quad [2]
\]

\[
\frac{dZ_i(t)}{dt} = \sigma Y_i(t) - Z_i(t) \sum_{j \neq i} \left[ \beta \left( Y_j(t) + \phi_j \sum_{k \neq j} Y_{kj}(t) \right) \right] - \mu Z_i(t), \quad [3]
\]

\[
\frac{dY_{ij}(t)}{dt} = Z_i(t) \left[ \beta \left( Y_j(t) + \phi_j \sum_{k \neq j} Y_{kj}(t) \right) \right] - \sigma Y_{ij}(t) - \mu Y_{ij}(t), \quad [4]
\]

\[
\frac{dZ_{**}(t)}{dt} = \sum_{i,j,i \neq j} \left[ \sigma Y_{ij}(t) \right] - \mu Z_{**}(t). \quad [5]
\]

Ferguson et al., 1999, Cummings et al., 2005
Ferguson et al., 1999
Trade-off between short-term enhancement and amplitude of osc.

Cummings et al., 2005
The effects of clinical immunity and non-stationary transmissibility

1. Clinical immunity can also produce oscillatory behavior.
2. Non-stationary R0 leads to an increase in periodicity
Challenges associated with antigenically variable pathogens

- Effects of vaccination often unpredictable, vaccine design complicated

- High rates of recombination prevent the application of standard phylogenetic techniques

- Drugs often short-lived (particularly wrt malaria) because of capacity for rapid evolution

- As usual, greatest impact in developing world…
Thanks

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