Modeling the Population-Level Spread of Dengue Virus and the Impact of Vaccination on Disease Dynamics

Lindsay Keegan, Emily Fagerstrom, Sifat Sharmin, Humaira Haroon

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$$\mathcal{R}_o = \frac{S_o}{N}\left(\frac{\beta_1\delta_1 + \beta_1\mu + \beta_2\delta_1}{\gamma\delta_2 + \gamma\mu + \delta_2\mu + \mu^2}\right)$$

S_o the number of susceptibles in the lowest age class

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- Largest eigenvalue now depends on S, R_1, R_2
- Actually better (smaller $\mathcal{R}_o$) if a few folks with partial recovery

Vaccination

THE HINDU

Health » Medicine

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Dengue vaccine closer to reality, say scientists

PTI

Researchers have inched closer to developing a novel therapy using mutated antibodies to protect people from the dengue virus.

Scientists, from Massachusetts Institute of Technology's Koch Institute of Integrative Cancer Research, said nearly half of the world's population is at risk of infection by the dengue virus, yet there is no specific treatment for the disease.

Threat

Despite the threat the disease posed, developing a vaccine has so far proved challenging, because dengue is not one virus but four different viruses, or serotypes, each of which must be neutralised by the vaccine.

Protecting people from only one or some of the four viruses could cause them to develop the more severe form of dengue if they later become infected with one of the other serotypes, according to Ram Sasisekharan, Professor of Biological Engineering at MIT.

"That was the motivation for carrying out our study, to generate a fully neutralising antibody that works for all four serotypes," he said in a statement.

Efforts to develop a therapeutic antibody for dengue are focused on a part of the virus called the envelope protein. "This is a very critical protein that allows the virus to latch on to the appropriate receptor within the host, to infect them, replicate and spread," said Mr. Sasisekharan.

The team led by Mr. Sasisekharan decided to look for antibodies that target the "A" strand region of the protein.

Such antibodies tend to have much higher potency, but they are unable to neutralise all four serotypes.

They chose as their model an antibody known as 4E11, which has been shown in tests to neutralise dengue 1, 2 and 3, but not dengue 4.

Researchers mined existing antibody-antigen complexes to analyse the physical and chemical features that play an

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Some estimates put $\beta_2 = 10\beta_1$! Eigenvalues of FV^{-1} are then:

$$\{S, S, 10R_1, 10R_2\}\frac{\beta_1}{N}$$

Stochastic Model

Continuous Time Markov Chain

CTMC Summary:

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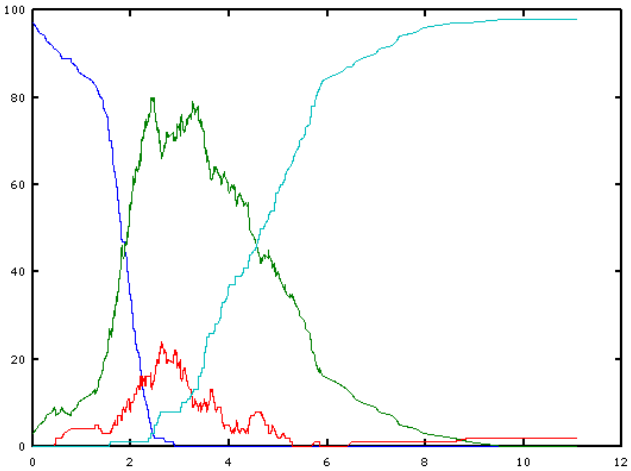
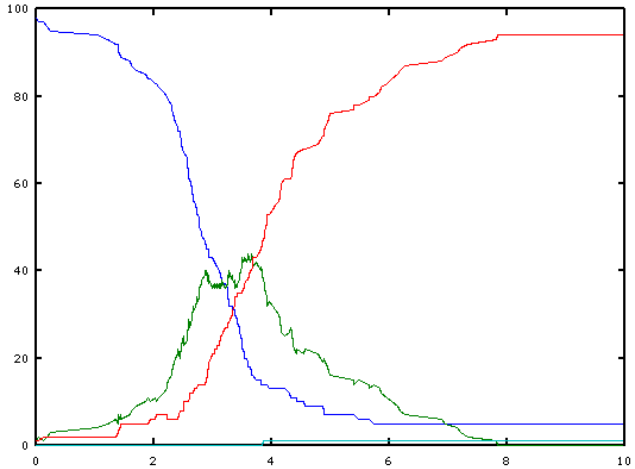
To implement:

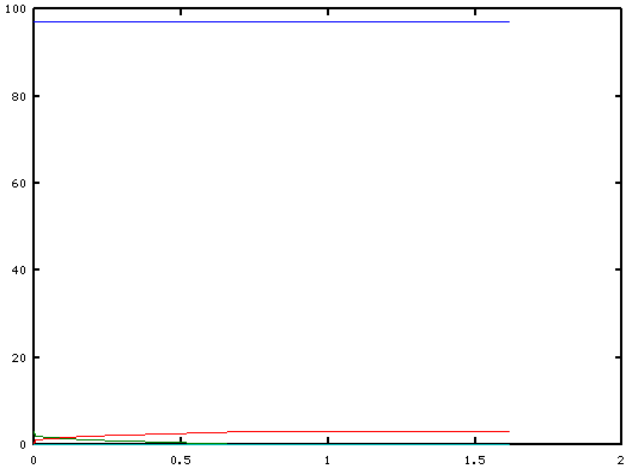
- Pick two random numbers u_1, u_2
- $f(u_1)$ time at which next event occurs
- divide the interval $[0, 1]$ into subintervals of size $P(\text{particular event}|\text{an event occurs})$
- pick which event occurs based on which interval contains u_2

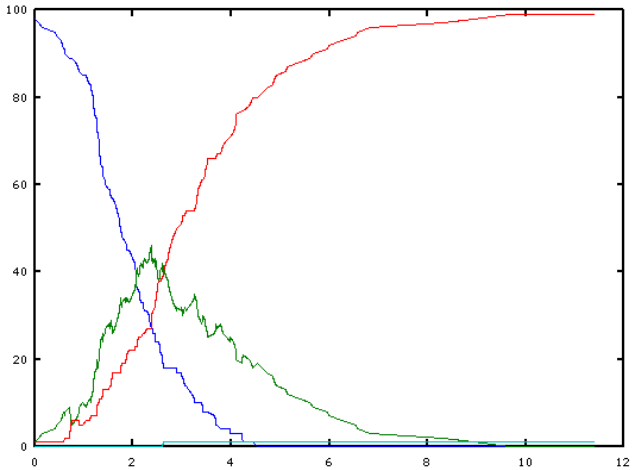
Pictures!

Figure : I_1=1, I_2=1









NIH-developed candidate dengue vaccine shows promise in early-stage trial

National Institute of Allergy and Infectious Diseases (NIAID)

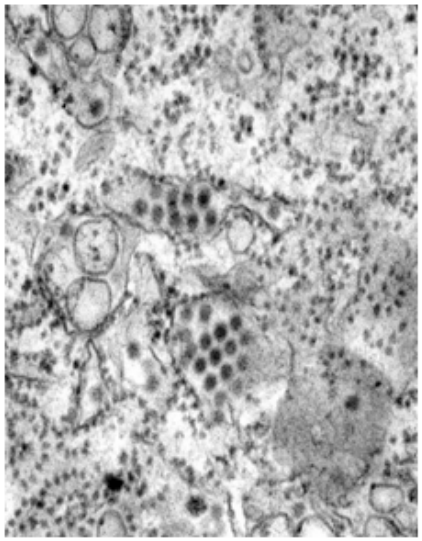
Contact

Nalini Padmanabhan
301-402-1663

A candidate dengue vaccine developed by scientists at the National Institutes of Health has been found to be safe and to stimulate a strong immune response in most vaccine recipients, according to results from an early-stage clinical trial sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the NIH. The trial results appeared in the January 17 issue of the Journal of Infectious Diseases.

Participants were randomized into four groups. In each group, 20 volunteers received a single 0.5-milliliter subcutaneous (under the skin) injection of one of the tetravalent candidate vaccine combinations, and eight others received placebo. All were monitored for immediate adverse reactions for at least 30 minutes after vaccination, and subsequently took their body temperatures three times daily for 16 days to check for possible adverse reactions. Participants also received a physical exam every other day up to Study Day 16, and then again on study days 21, 28, 42 and 180, when blood tests were also performed.

The researchers found that all four candidate vaccine combinations induced antibody responses against each of the dengue viruses. However, one vaccine combination, TV003, appeared to induce the most balanced antibody response against the dengue viruses. A single dose of TV003 resulted in an antibody response to all four dengue viruses in 45 percent of participants and against three of the four viruses in an additional 45 percent. Overall, an immune response to at least three viruses was seen in 90 percent of vaccinees given TV003.



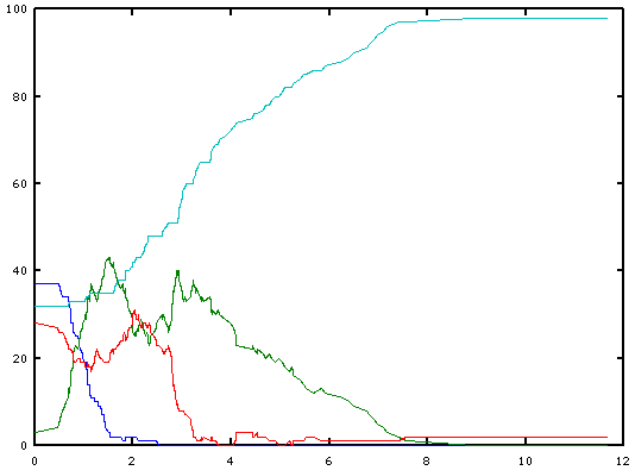
This transmission electron micrograph depicts a number of round, Dengue virus particles that were revealed in this tissue specimen. *(Courtesy CDC)*

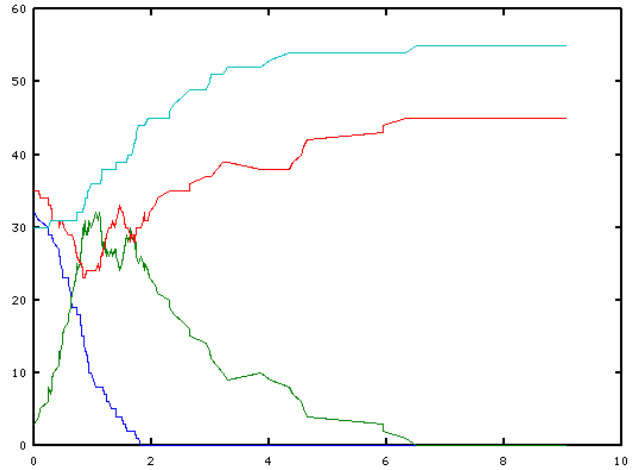
"What is promising about TV003 is that it elicited solid antibody responses after just one dose," explained Stephen Whitehead, Ph.D., of NIAID's Laboratory of Infectious Diseases, who led the development of the vaccine candidates. "Other vaccines in development require two or three injections at higher doses to achieve similar results."

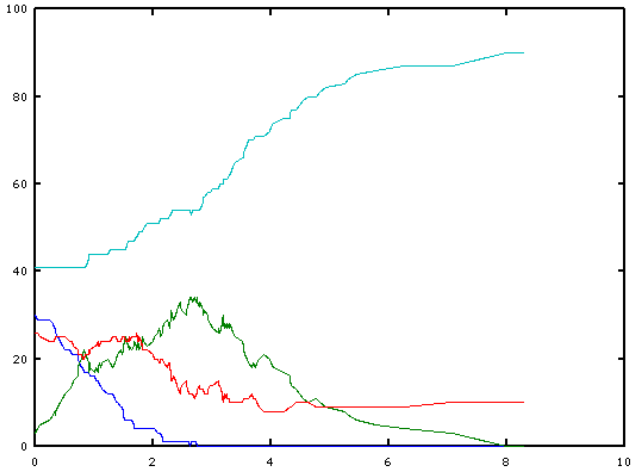
More Pictures!

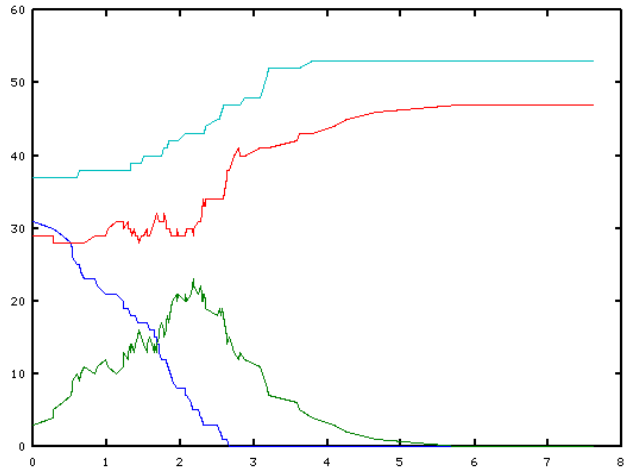
$I_1 = 1$, $I_2 = 1$

80 Vaccinated: 20% immune to 1, 20% to 2, 45% to both

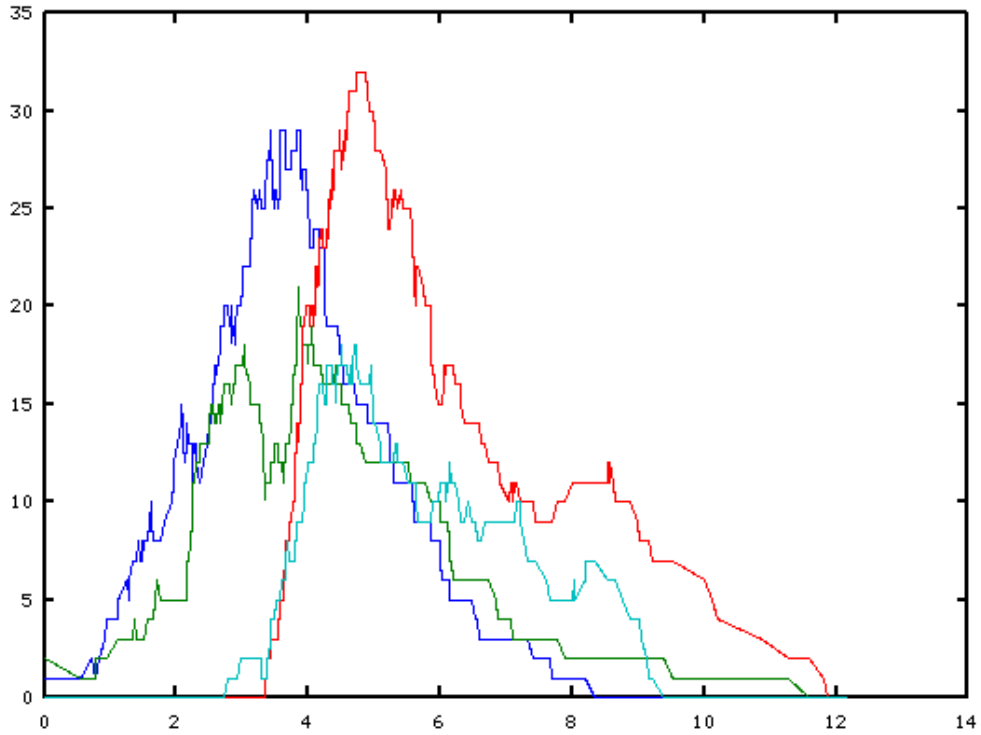








MAYDAY!



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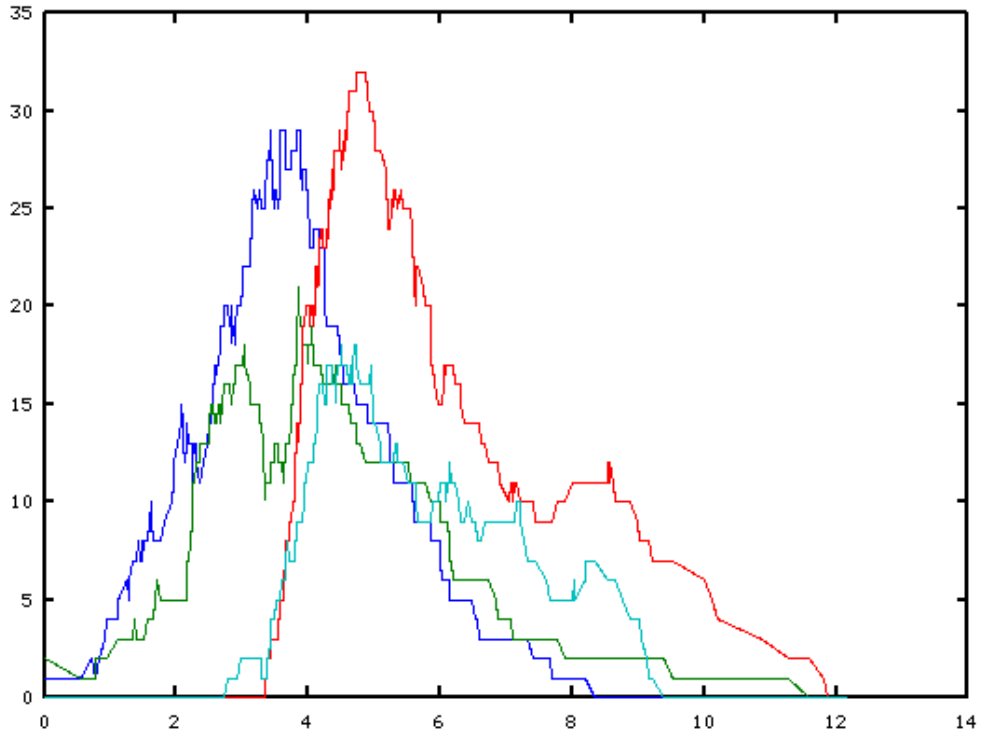

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- Red and teal are second infections

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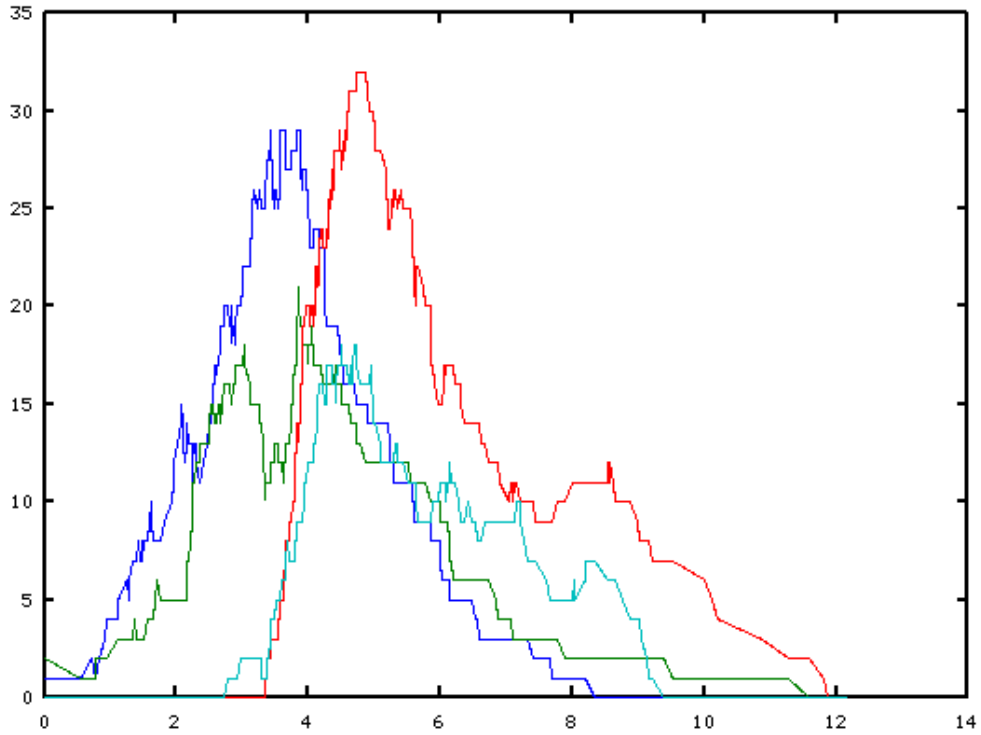

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- Red and teal are second infections
- Time scale is in WEEKS

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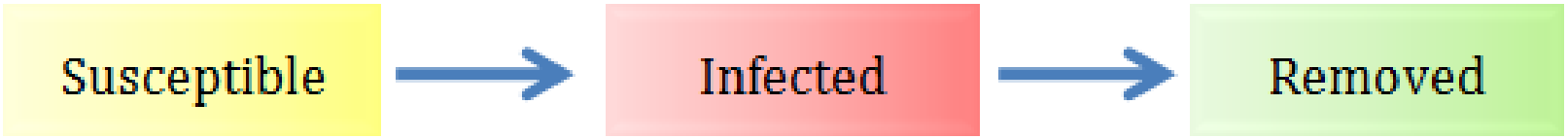
- For any interaction between an infected person and a person in compartment R_j, there is some probability that the person in R_j still has cross-immunity
- Requires knowing average time between infections: probability will be (time of cross-immunity)/(time between infections)

Bayesian estimation of $\mathcal{R}_o$ in stochastic epidemic models

Bayes' Theorem:

$$\pi(p, \beta \,|\, \text{data}) \propto \pi(\text{data} \,|\, p, \beta)\pi(p, \beta)$$



Assumptions:

- Infectious period is exponentially distributed
- $\beta \sim \Gamma(a, b)$
- $\gamma \sim \Gamma(c, d)$

- By Bayes' Theorem, the joint posterior density function of β and γ given i, r is

$$\pi(\beta, \gamma \,|\, i, r) \propto \pi(i, r, \,|\, \beta, \gamma)\, \pi(\beta)\, \pi(\gamma)$$

- Since $\mathcal{R}_o = \beta/\gamma$, we have

$$\pi(\mathcal{R}_o | i, r) \propto F \text{ distribution}$$

- $\mathcal{R}_o$ is only dependent on the infection and removal times
- The posterior density can be explored using MCMC methods

Thank You!