Integro-differential–Equation Models for Infectious Disease

Jan Medlock
Yale University
Epidemiology and Public Health
jan.medlock@yale.edu

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Introduction

- Many ecological and epidemiological systems are better modeled in continuous time instead of discrete time.
- There are many continuous-time frameworks: reaction–diffusion integral equations, integro-differential equations.
- Diffusion is a local operator, $i.e.$, individuals can only influence their immediate neighbors and may also present some difficulty in matching with experimental data
- Integrals have been used instead to model non-local spatial processes giving rise to integral and integro-differential equations.
- These models have all the advantages of the discrete-time integrodifference equations: more flexibility in using dispersal data, predicting faster wave speeds, and the possibility for accelerating waves.

Spatial epidemic models

- Reaction–diffusion: Noble (1974); Bailey (1975); Murray, Staley, & Brown (1986)

$$\begin{aligned} \partial_t S &= -\beta(I + \alpha\nabla^2 I)S + D_S\nabla^2 S, \\ \partial_t I &= \beta(I + \alpha\nabla^2 I)S - \gamma I + D_I\nabla^2 I, \\ \partial_t R &= \gamma I + D_R\nabla^2 R \end{aligned}$$

- Integral equations: Thieme (1977, 1979); Diekmann (1978, 1979); Rass & Radcliffe (1984, 1986, 2003)

$$\begin{aligned} \dot{S} &= -\lambda S, \\ i(t,0,x) &= \lambda S, \\ i(t,\tau,x) &= i(t-\tau,0,x), \\ \lambda(t,x) &= \int_0^\infty \int_\Omega i(t,\tau,\xi)A(\tau,x,\xi)\ \mathrm{d}\xi\mathrm{d}\tau \end{aligned}$$

- Integro-differential equations: Kendall (1957, 1965) and Mollison (1972); Medlock & Kot (2003)

- Integrodifference equations: Allen & Ernest (2002)

$$
\begin{aligned}
S_{t+1} &= \int_{\Omega} \left[S_t(y) + (\mu + \gamma) I_t(y) - \beta I_t(y) S_t(y) \right] k(x - y) \mathrm{d}y, \\
I_{t+1} &= \int_{\Omega} \left[(1 - \mu - \gamma) I_t(y) + \beta I_t(y) S_t(y) \right] k(x - y) \mathrm{d}y
\end{aligned}
$$

Outline

- Two integro-differential–equation models from epidemiology
  - The SI model: Brief review
  - Distributed Contacts model
  - Distributed Infectives model
  - The movement process: Linear integro-differential equations
  - Wave speed
  - Wave shape
- Conclusions

SI model: Brief review

- We divide the population into two groups:
  - Susceptible individuals, $S(t)$
  - Infective individuals, $I(t)$

$$\boxed{S} \xrightarrow{\lambda S} \boxed{I}$$

- Assumptions
  - Population size is large and constant, $S(t) + I(t) = K$
  - No birth, death, immigration, or emigration
  - No recovery or latency
  - Homogeneous mixing
  - Infection rate is proportional to the number of infectives, *i.e.*, $\lambda = \beta I$

$$\boxed{S} \xrightarrow{\beta I S} \boxed{I}$$

- A pair of ordinary differential equations describes this model (Ross, 1911):

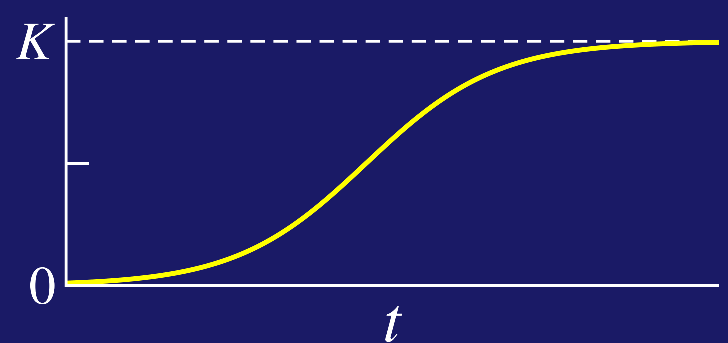
$$\begin{aligned} S'(t) &= -\beta I(t)S(t), \\ I'(t) &= \beta I(t)S(t). \end{aligned}$$

- With constant population size, $K = S(t) + I(t)$, this reduces to

$$I'(t) = \beta I(t)(K - I(t)).$$

- The solution is the logistic curve,

$$I(t) = \frac{I(0)K}{I(0) + (K - I(0))\mathrm{e}^{-\beta K t}}.$$



Spatial spread: Two different non-local mechanisms

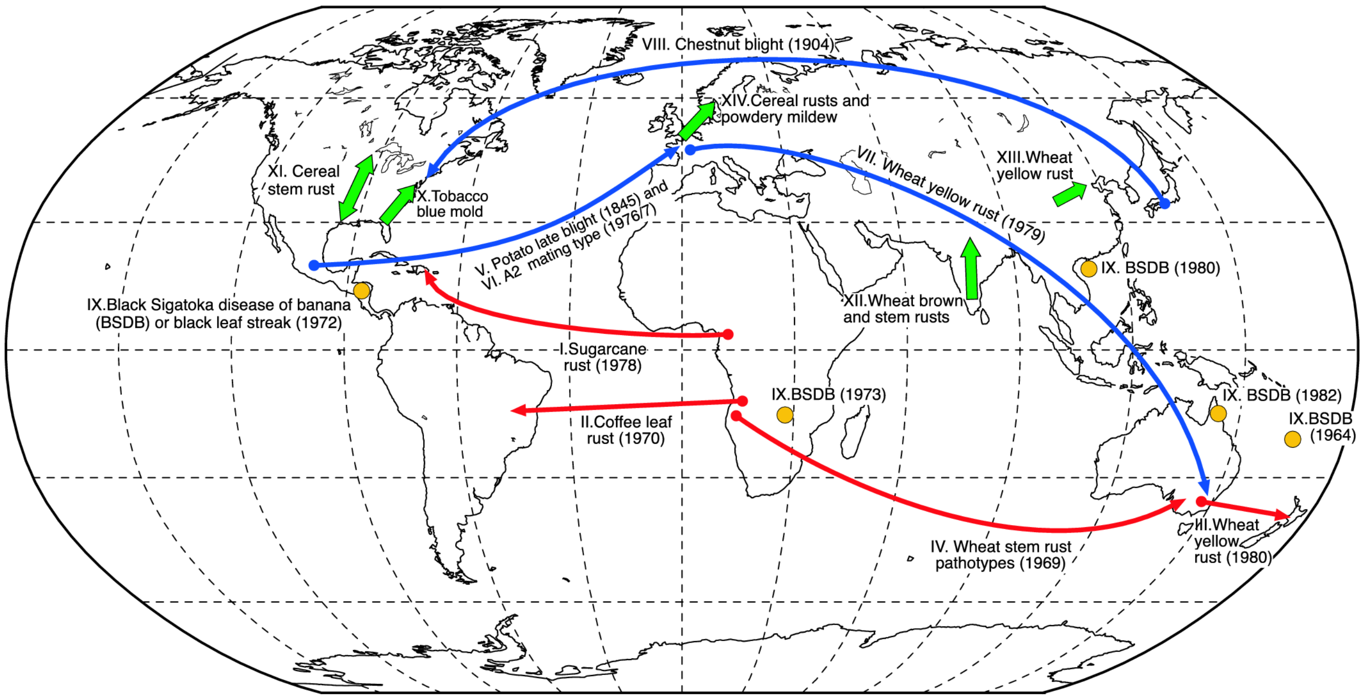


Fig. 1. Selected dispersal events of fungal pathogens. Red and blue arrows indicate invasions of new territories (first year recorded in brackets). Red arrows indicate dispersal that probably occurred by direct movement of airborne spores [I (*12*), II (*11*), III (*23*), and IV (*52*)]. Blue arrows indicate pathogens that were probably transported to the new territory in infected plant material or by people and spread thereafter as airborne spores [V (*9*), VI (*21*), VII (*22*), and VIII (*10*)]. Orange circles indicate the worldwide spread of black Sigatoka disease of banana; the first outbreak recorded on each continent is marked [IX (*19*)]. Green arrows indicate periodic migrations of airborne spores in extinction-recolonization cycles [X (*32*), XI (*33*), XII (*34*), XIII (*35–38*), and XIV (*41*)]. [Background world map © C. Lukinbeal, Southern Connecticut State University, New Haven, Connecticut]

From Brown, J.K.M. & Hovmøller, M.S., *Science*, **297** 537.

From http://www.hort.uconn.edu/ipm/veg/htms/potblpic.htm.

Distributed Contacts (DC)

- The governing equations (Kendall, 1957, 1965; Mollison, 1972):

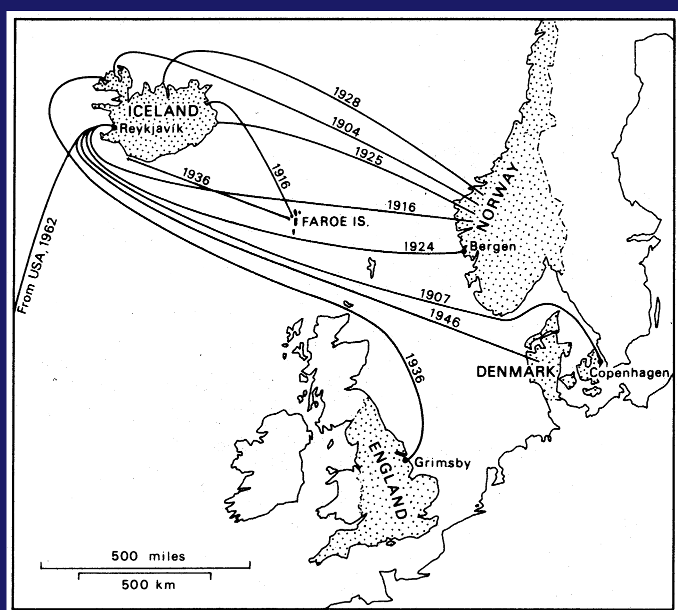
$$\begin{aligned} \partial_t S &= -\beta \left(\int_\Omega k(x-y) I(y,t)\ \mathrm{d}y \right) S, \\ \partial_t I &= \beta \left(\int_\Omega k(x-y) I(y,t)\ \mathrm{d}y \right) S. \end{aligned}$$

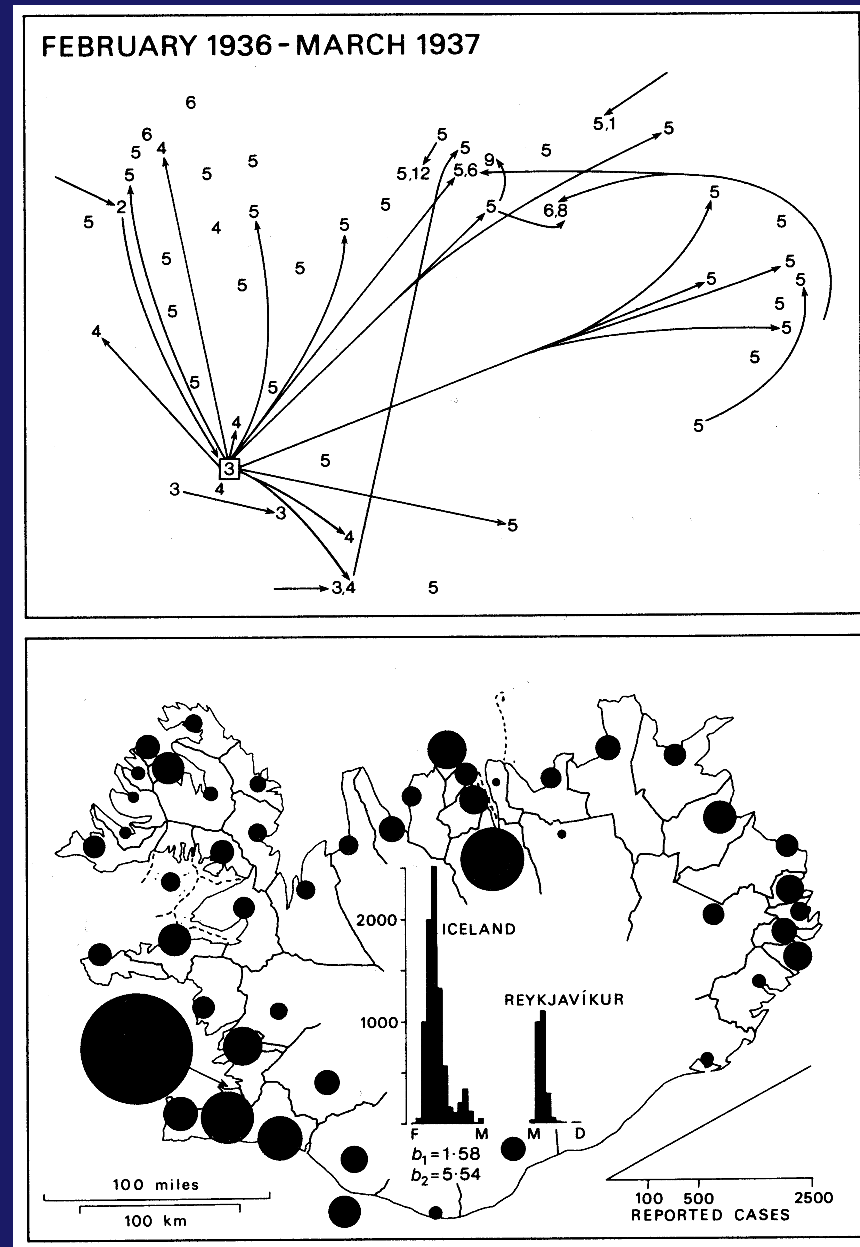
  - β is the infection rate
  - $k(u)$, the kernel, is the contact distribution

- Assumptions: $K = S + I$ is constant and $\Omega = \mathbb{R}$, give

$$\partial_t I = \beta \left(\int_\mathbb{R} k(x-y) I(y,t)\ \mathrm{d}y \right) (K - I).$$

From http://www.phls.wales.nhs.uk/measlgen.htm.





From Cliff, A.D., Haggett, P., Ord, J.K. & Versey, G.R., *Spatial Diffusion*, 1981.

Distributed Infectives (DI)

- The governing equations (Fedotov, 2000; Medlock & Kot, 2003; Lutscher *et al.*, 2004):

$$\begin{aligned} \partial_t S &= -\beta I S - D S + D \int_\Omega k(x-y) S(y,t)\,\mathrm{d}y, \\ \partial_t I &= \beta I S - D I + D \int_\Omega k(x-y) I(y,t)\,\mathrm{d}y. \end{aligned}$$

  - β is the infection rate
  - D is the dispersal rate
  - $k(u)$, the kernel, is the dispersal distribution

- Assumptions: $K = S + I$ is constant and $\Omega = \mathbb{R}$, give

$$\partial_t I = \beta I (K - I) - D I + D \int_\mathbb{R} k(x-y) I(y,t)\,\mathrm{d}y.$$

The movement process: Linear integro-differential equations

- $N(x,t)$ is the density of a population at position x and time t
- At rate D, individuals move to a new location instantaneously
- $k(x-y)$ is the proportion of individuals moving from y to x

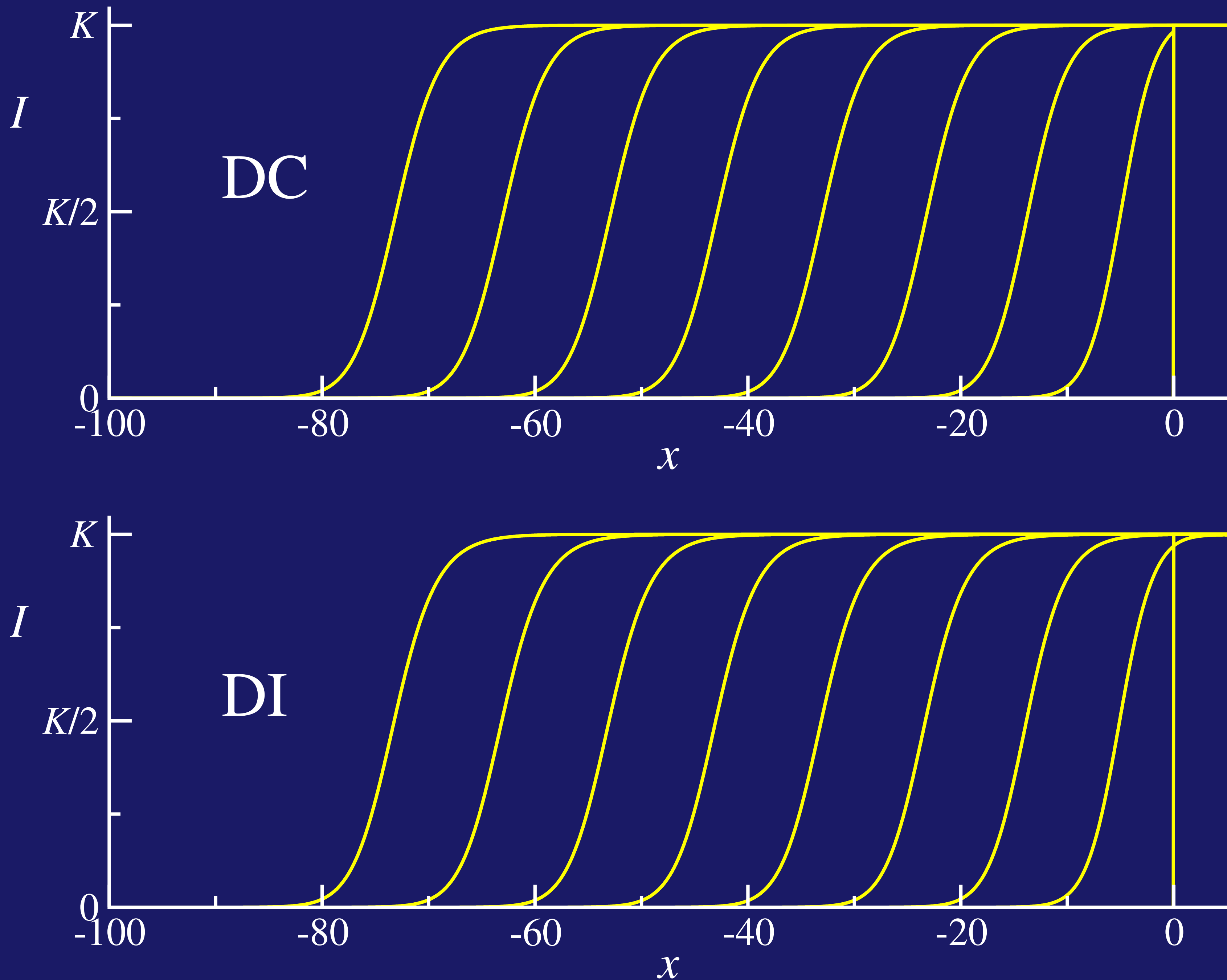
$$\partial_t N = D \int_{\mathbb{R}} k(x-y) N(y,t)\,\mathrm{d}y - DN$$

Position jump process or kangaroo process (Othmer *et al.*, 1988)

- An individual starts at $x = 0$ at $t = 0$
- He waits an exponentially-distributed time (with parameter D)...
- ...and then jumps to a new position y that is governed by the distribution $k(x - y)$

$$\partial_t N = D \int_{\mathbb{R}} k(x - y) N(y, t) \, \mathrm{d}y - DN$$

Both models have traveling wave solutions



Wave speed

- Distributed Contacts

$$\partial_t I = \beta \left(\int_{\mathbb{R}} k(x-y) I(y,t)\ \mathrm{d}y \right) (K - I)$$

Using the traveling-wave coordinate, $z = x + ct$,

$$cI' = \beta \left(\int_{\mathbb{R}} k(z-y) I(y)\ \mathrm{d}y \right) (K - I).$$

Linearizing about $I = 0$,

$$cI' = \beta K \left(\int_{\mathbb{R}} k(z-y) I(y)\ \mathrm{d}y \right).$$

Assuming $I = A\mathrm{e}^{-\theta z}$,

$$c\theta = -\beta K M(\theta),$$

where

$$M(\theta) = \int_{\mathbb{R}} k(u)\mathrm{e}^{\theta u}\,\mathrm{d}u.$$

For a constant speed traveling wave, $k(x) \le A\mathrm{e}^{-\gamma|x|}$, which implies $M(\theta)$ exists for $|\theta| < \gamma$.

The critical speeds are

$$c_R = -\beta K \sup_{\theta>0} \frac{M(\theta)}{\theta}, \quad c_L = -\beta K \inf_{\theta<0} \frac{M(\theta)}{\theta}.$$

Parametrically,

$$\begin{aligned} c^* &= -\beta K M'(\theta^*), \\ M(\theta^*) &= \theta^* M'(\theta^*). \end{aligned}$$

Aronson (1977) showed this is the asymptotic speed.

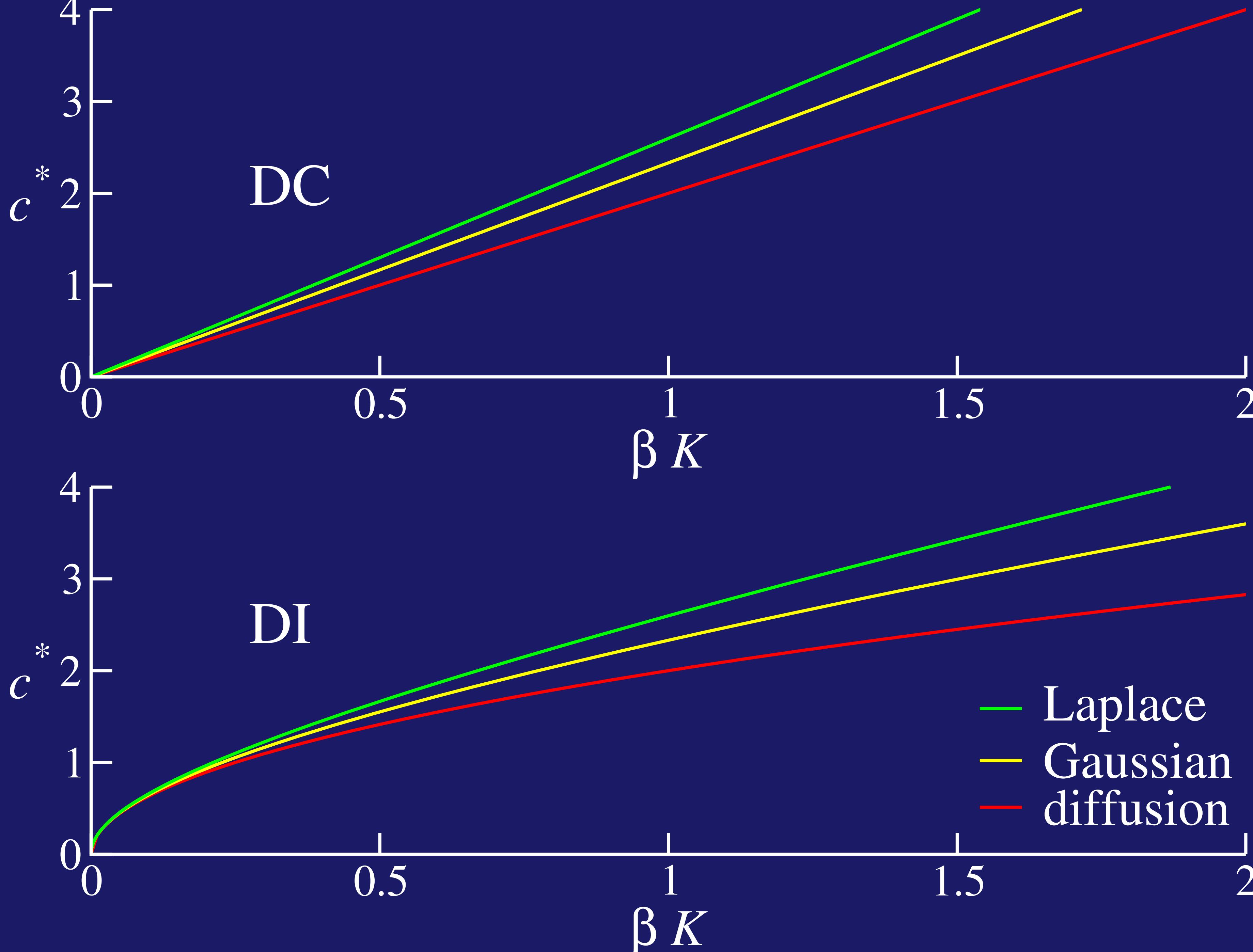
- Distributed Infectives

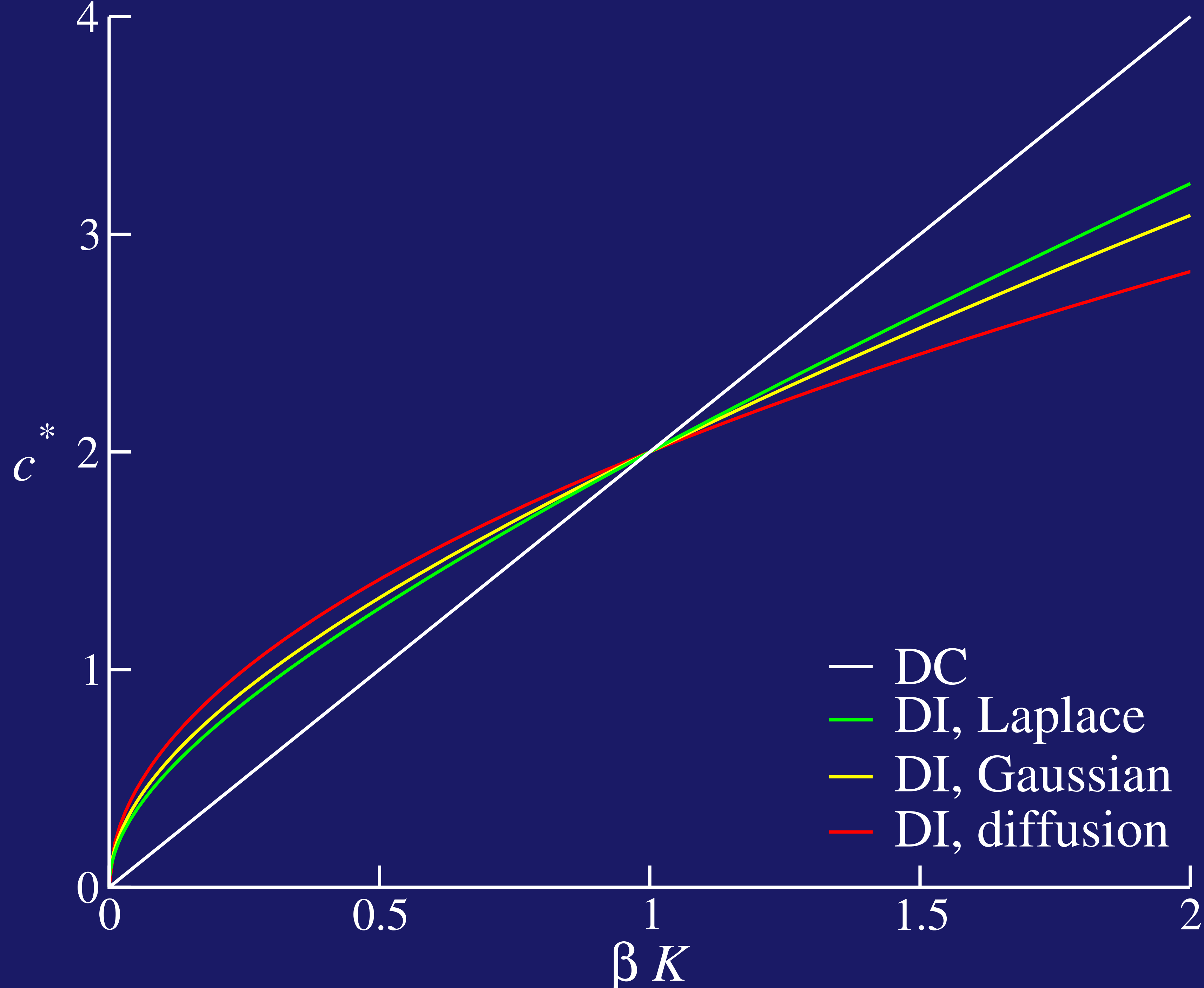
$$\partial_t I = \beta I(K - I) - DI + D \int_{\mathbb{R}} k(x-y) I(y,t) \, \mathrm{d}y$$

The same procedure gives

$$\begin{aligned} c^* &= -DM'(\theta^*), \\ \beta K &= D\left[1 - M(\theta^*) + \theta^* M'(\theta^*)\right]. \end{aligned}$$

Lutscher *et al.* (2004) showed this is the asymptotic speed.


DC
DI
c^*
βK
0
0.5
1
1.5
2
0
1
2
3
4
Laplace
Gaussian
diffusion


4
3
2
1
0
c^*
0
0.5
1
1.5
2
βK
DC
DI, Laplace
DI, Gaussian
DI, diffusion

A perturbation scheme for the wave shape

The key to the perturbation scheme is expanding the convolution

$$k * I = \int_{\mathbb{R}} k(y) I(z-y)\ \mathrm{d}z$$

for large c.

Let $\xi = z/c$ and $h(\xi) = I(z)$. Then

$$\begin{aligned} k * I &= \int_{\mathbb{R}} k(y) I(z-y) \mathrm{d}y \\ &= \int_{\mathbb{R}} k(y) h\left(\xi - \frac{y}{c}\right) \mathrm{d}y \\ &= \int_{\mathbb{R}} k(y) \left[h(\xi) - \frac{y}{c} h'(\xi) + \mathrm{O}\left(\frac{1}{c^2}\right)\right] \mathrm{d}y \\ &= h(\xi) - \frac{M'(0)}{c} h'(\xi) + \mathrm{O}\left(\frac{1}{c^2}\right). \end{aligned}$$

Distributed Infectives

$$cI' = \beta I(K - I) - DI + D \int_{\mathbb{R}} k(y) I(z-y)\, \mathrm{d}y$$

with $I(-\infty) = 0$, $I(+\infty) = K$, $I(0) = K/2$.

Letting $\xi = z/c$ and $h(\xi) = I(z)$ gives

$$h' = \beta h(K - h) - D\left[\frac{M'(0)}{c} h' + \mathrm{O}\left(\frac{1}{c^2}\right)\right].$$

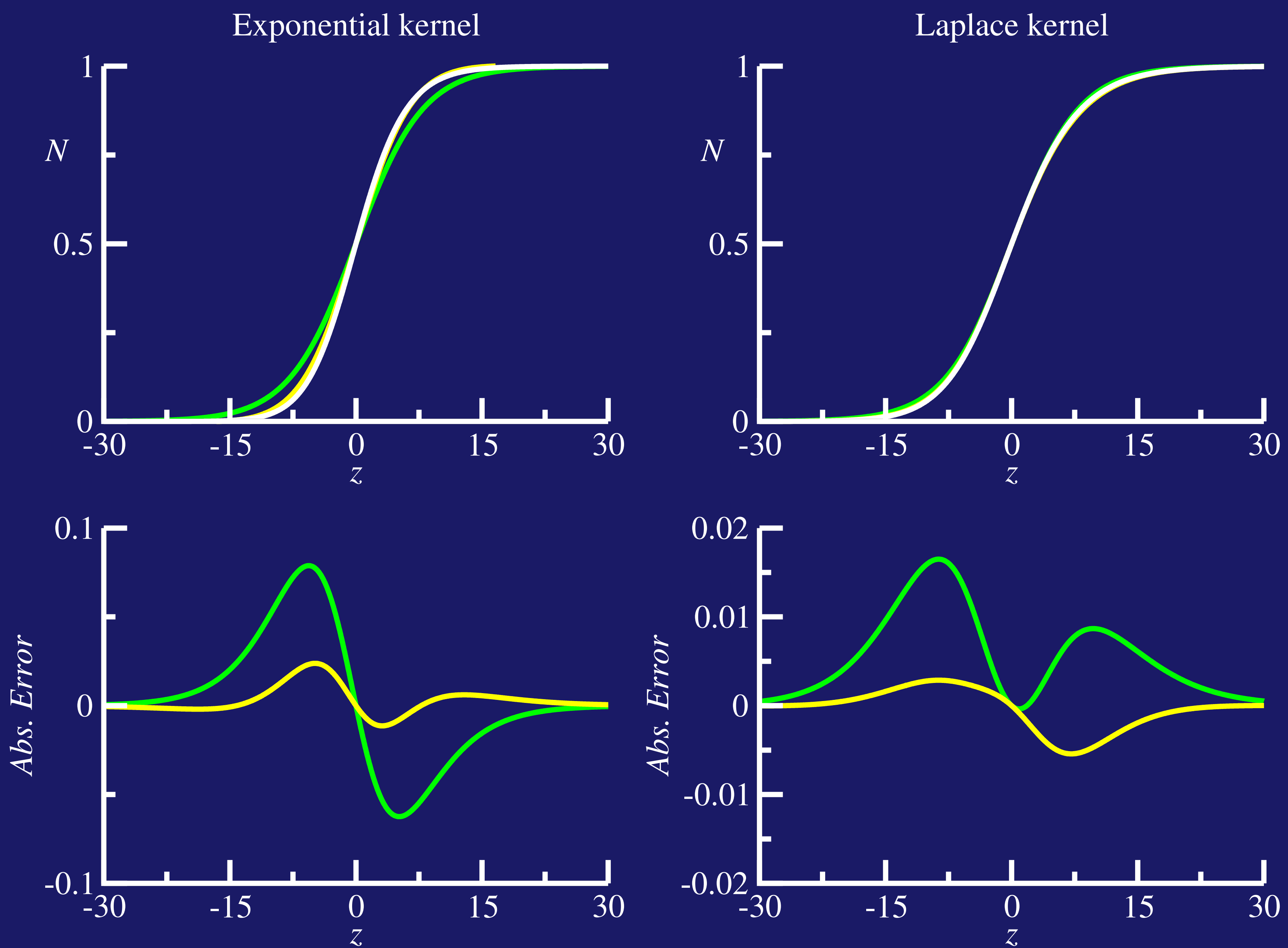
Expanding $h = h_0 + \frac{1}{c}h_1 + \mathrm{O}\left(\frac{1}{c^2}\right)$,

$$\begin{aligned} h_0' &= \beta h_0(K - h_0), \\ h_1' &= \beta h_1(K - 2h_0) - DM'(0)h_0', \end{aligned}$$

with $h_0(-\infty) = 0$, $h_0(+\infty) = K$, $h_0(0) = K/2$,
and $h_1(-\infty) = h_1(+\infty) = h_1(0) = 0$.

Then

$$\begin{aligned} h_0(\xi) &= \frac{K\mathrm{e}^{\beta K\xi}}{1 + \mathrm{e}^{\beta K\xi}}, \\ h_1(\xi) &= D\beta K^2 M'(0)\frac{\xi\mathrm{e}^{\beta K\xi}}{\left(1 + \mathrm{e}^{\beta K\xi}\right)^2}. \end{aligned}$$


Exponential kernel
Laplace kernel
N
1
0.5
0
-30
-15
0
15
30
z
Abs. Error
0.1
-0.1
0.02
0.01
-0.01
-0.02

Asymptotic speed

For an accelerating invasion $k(x) > A\mathrm{e}^{-\gamma|x|}$, we can compute the wave asymptotically.

- Starting with the linearized DC equation

$$\partial_t I = \beta K \int_{\mathbb{R}} k(x-y) I(y,t) \mathrm{d}y, \quad I(x,0) = I_0 \delta(x),$$

taking the Fourier transform

$$\partial_t \hat{I} = \beta K \hat{k}(\omega) \hat{I}, \quad \hat{I}(\omega) = I_0,$$

gives

$$\hat{I}(\omega, t) = I_0 \mathrm{e}^{\beta K \hat{k}(\omega) t}.$$

Inverting gives

$$I(x,t) = \frac{I_0}{2\pi}\int_{\mathbb{R}} \mathrm{e}^{-\imath\omega x}\mathrm{e}^{\beta K\hat{k}(\omega)t}\mathrm{d}\omega \approx I_0\mathrm{e}^{\beta K t}k(x) \quad \text{as} \quad |x| \to \infty,$$

subject to some technical conditions.

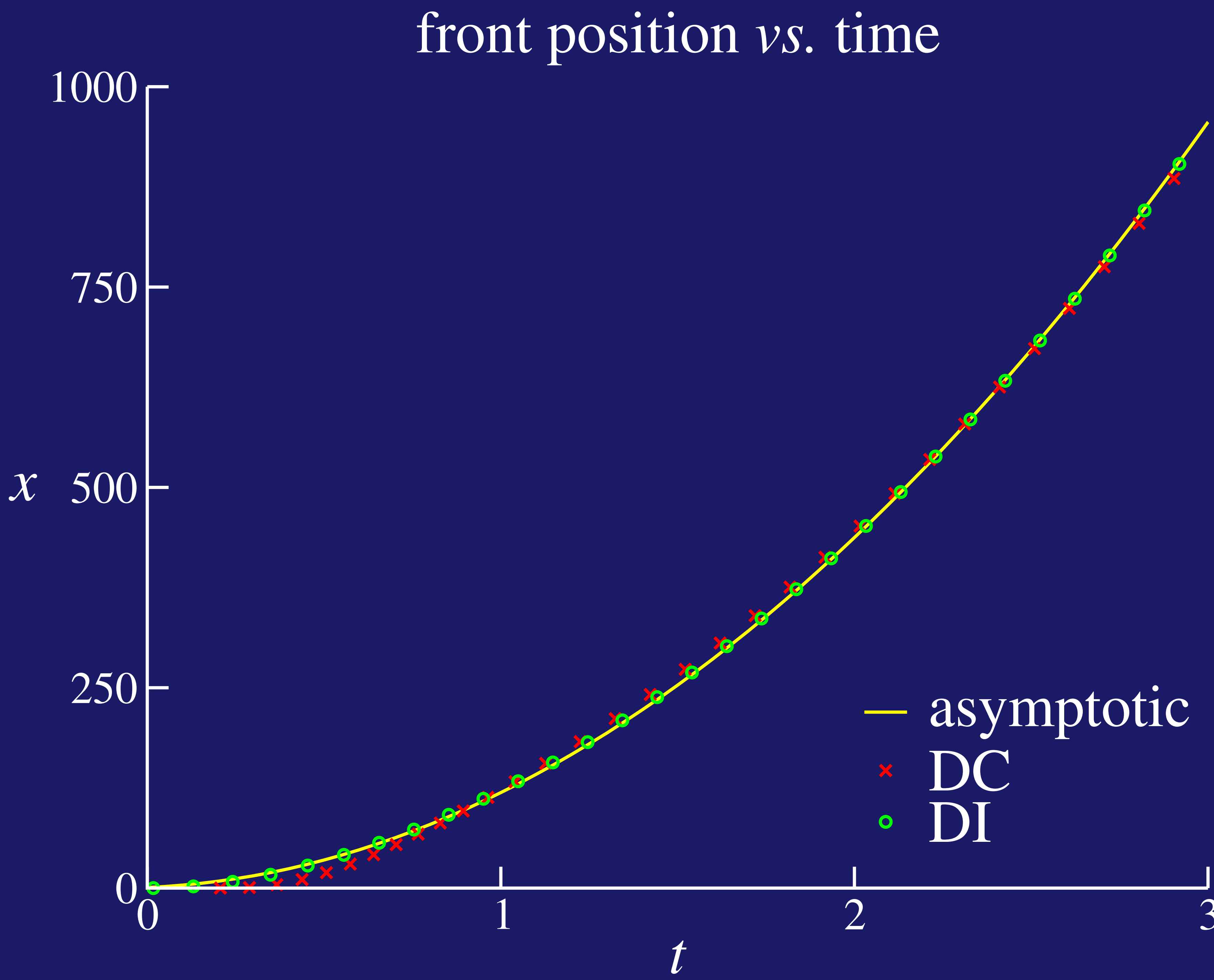
- Likewise for the DI model

$$I(x,t) \approx I_0\mathrm{e}^{\beta K t}k(x) \quad \text{as} \quad |x| \to \infty.$$

Setting some threshold value, $\tilde{I}$, gives

$$x \approx k^{-1}\left(\frac{\tilde{I}}{I_0}\mathrm{e}^{-\beta K t}\right),$$

the position of the threshold as a function of time.


front position vs. time
1000
750
500
250
0
x
0
1
2
3
t
asymptotic
DC
DI

Time-periodic coefficients

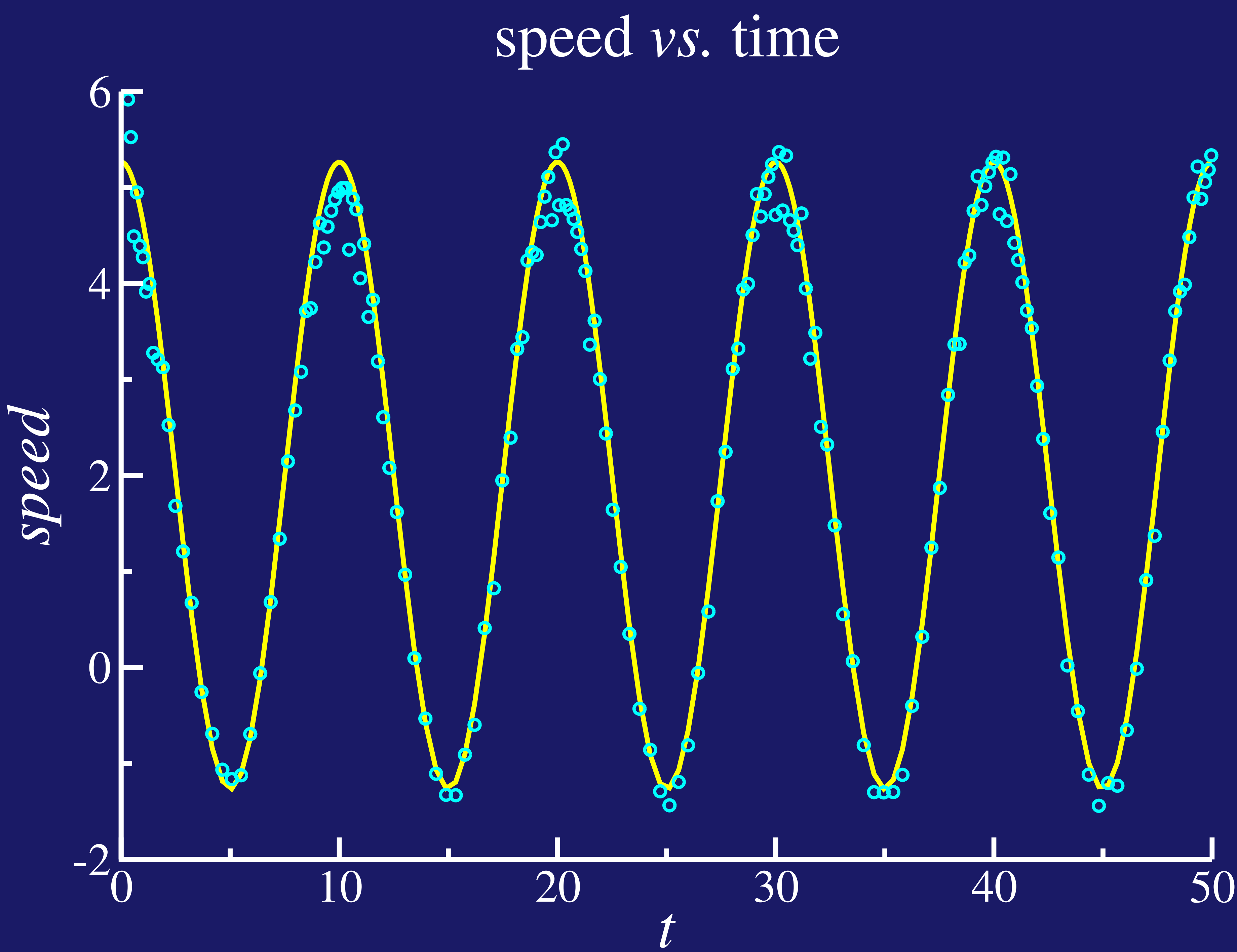
$$\partial_t I = \beta(t) I(K(t) - I) - D(t) I + D(t) \int_{\mathbb{R}} k(x-y,t) I(y,t)\ \mathrm{d}y$$

Using the same linearization procedure, the speed is given by

$$\begin{aligned} \overline{\beta K} &= \overline{D} - \overline{DM}(\theta) + \theta \overline{D\partial_\theta M}(\theta), \\ \bar{c} &= -\overline{D\partial_\theta M}(\theta), \end{aligned}$$

where

$$\overline{f} = \frac{1}{T} \int_0^T f(t)\ \mathrm{d}t.$$


speed vs. time
6
4
2
0
-2
speed
0
10
20
30
40
50
t

Numerics: IDEs are better than PDEs!

- Integral dispersal is much more stable than diffusion, which allows much larger time steps
- In general,

$$\partial_t \begin{bmatrix} u_1 \\ \vdots \\ u_n \end{bmatrix} = f\left(\begin{bmatrix} u_1 \\ \vdots \\ u_n \end{bmatrix}, \begin{bmatrix} k_1 * u_1 & \dots & k_m * u_1 \\ \vdots & & \vdots \\ k_1 * u_n & \dots & k_m * u_n \end{bmatrix} \right).$$

- Trapezoid rule and Simpson's rule are $\mathrm{O}\left(N^2\right)$.
- FFT is $\mathrm{O}\left(N \log N\right)$ (Andersen, 1991)

$$\mathcal{F}(k_i * u_j) = \mathcal{F}(k_i)\mathcal{F}(u_j).$$

- Algorithm
  - Compute $\mathcal{F}(k_i)$ at the beginning.
  - Each time step, compute $\mathcal{F}(u_j)$ and $\mathcal{F}^{-1}\left[\mathcal{F}(k_i)\mathcal{F}(u_j)\right]$.
  - Step in time with Runge–Kutta scheme.

Conclusions

- There are more flexible frameworks than reaction–diffusion for continuous-time models.
- Integro-differential equations can be used with empirical dispersal data, give faster speeds than r–d, and can give accelerating waves.
- Traveling wave speed is sensitive to the form of the model; care should be used.
- Perturbation techniques can be used to compute approximate solutions to the IDEs.

Problems

- Instead of space, x represents some other characteristic.
- Estimating kernels from dispersal data.
- The inverse problem: Given a traveling wave, what is the kernel?