A blending hybrid model for representing reaction-diffusion equations

OVERVIEW

Main Idea:

- To implement the hybrid blending method using a pure compartment-based algorithm in one part of the domain, a pure molecular-based in another and an overlap region that uses both.

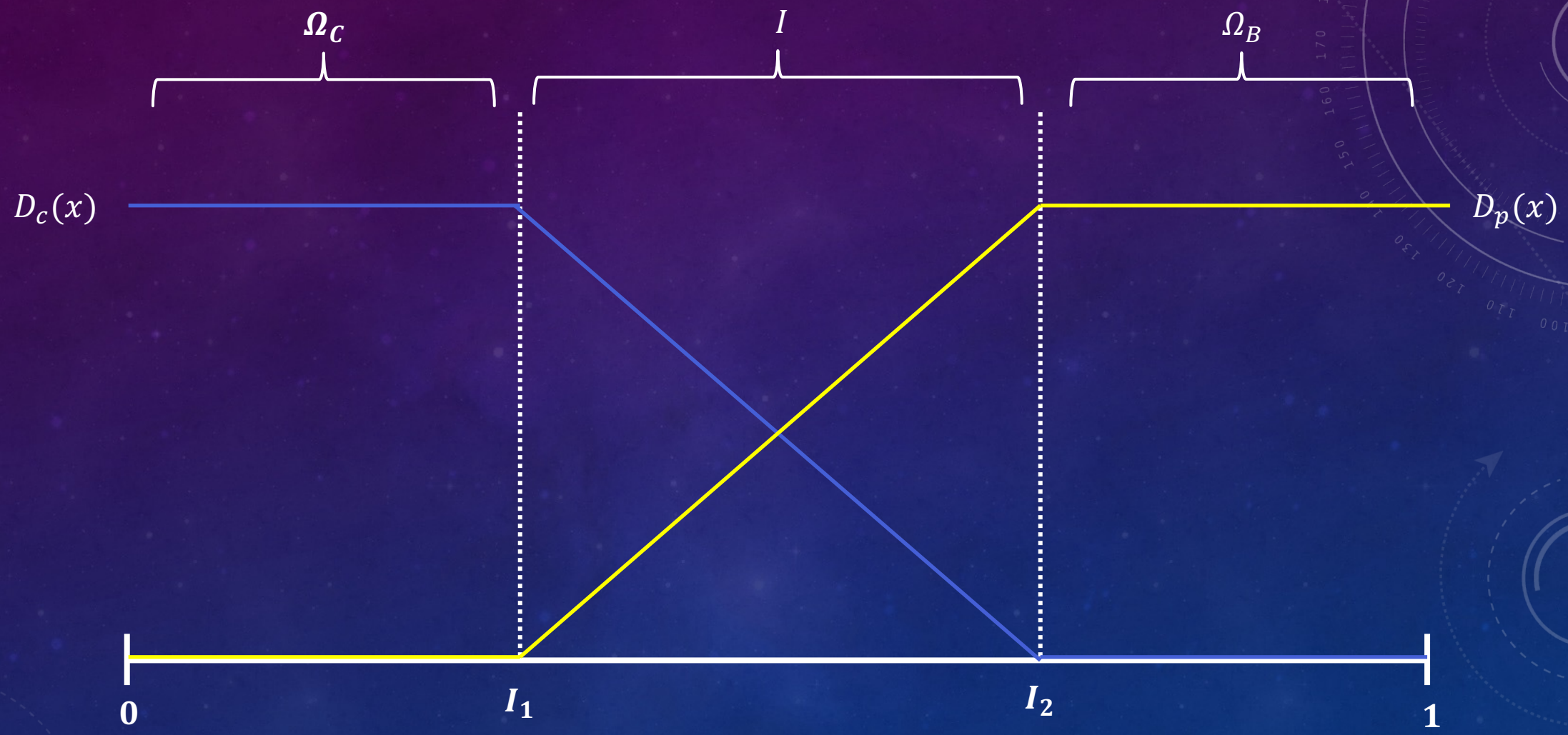
Why Important?:

- More efficient exploration of biological systems.
- Reduces the need for highly computational simulations of particles across entire domain.
- Therefore allowing faster computation in areas where less detail required.

How is it answered?:

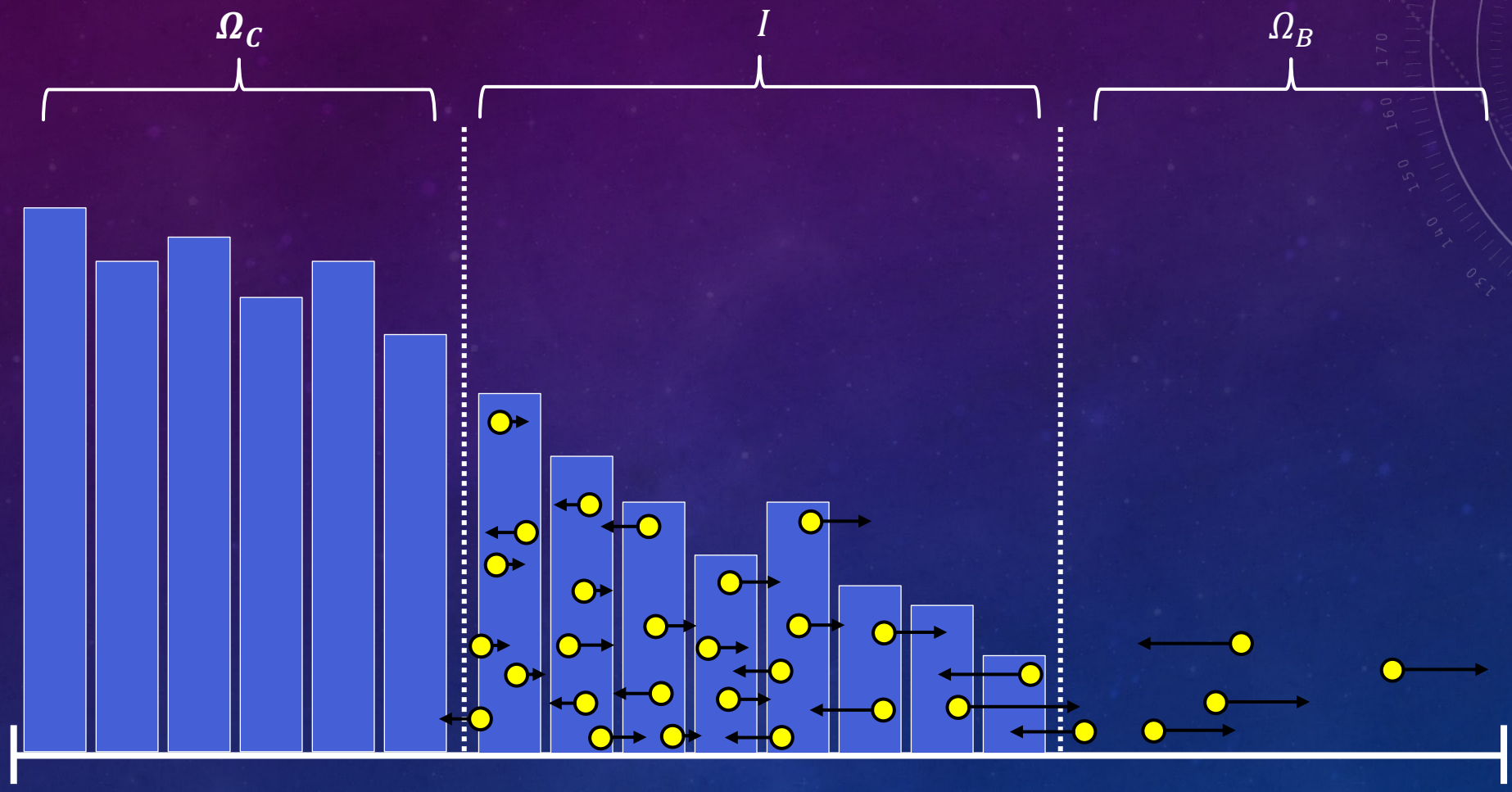
Two examples are given, one diffusion problem and one morphogen gradient problem where simulations are plotted against analytical solutions to check for accuracy and relative error plots are provided as well.

THE BLENDING METHOD



We can use any blending functions, as long as long as the following holds: $D_c(x) + D_p(x) = D \; \forall x \in [0,1]$.

THE DOMAIN



Ω_C: Particles jump (diffuse) between compartments

I: Particles jump/move in a blended manner (either by compartment or Brownian motion)

Ω_B: Particles move (diffuse) freely according to Brownian motion.

COMPARTMENT REGION

- We run the standard Gillespie algorithm to simulate diffusion in the pure-compartment/blending region.
- Split region into k compartments each of length h where diffusive jumps occur at rate $\frac{D_C(x)}{h^2}$.
- We evaluate $D_C(x_j)$ at the midpoint of each compartment x_j for j= $1 \dots k$.
- So then we know that:

$$\alpha_j(t)dt = \mathbb{P}\left(Jump\ occurs\ in\ the\ j^{th}\ compartment\ in\ [t, t+dt]\right)$$

where

$$\alpha_j(t) = \frac{D_C(x_j)}{h^2} N_j(t).$$

where $N_j(t)$ is the number of particles in the jth compartment at time t.

- Then we run the Gillespie algorithm as usual.

BROWNIAN REGION

- We store and evolve all positions of particles in the blending/pure Brownian region using the standard Brownian motion formula:

$$\boldsymbol{x}_i(t + \Delta t) = \boldsymbol{x}_i(t) + \sqrt{2D_P(x_i)\Delta t}\boldsymbol{\xi} \quad \text{where } \boldsymbol{\xi} \sim \mathrm{N}(0,1).$$

- Here we remember that $D_P(x_i)$ is a function of space and so we evaluate this at each time-step for each particle in the blending/Brownian region.
- We also prescribe zero flux boundary conditions at the right hand end of the domain (not across interfaces).

THE BLENDING METHOD

I. First initialise all the molecules in their compartments or at positions in the Brownian regime (initial conditions).

II. Now set Δt for molecules in Ω_B and determine τ for all diffusive jumps in Ω_C, then set $t_M = \Delta t$ and $t_C = \tau$.

III. If $t_C \leq t_M$ then a compartment-based event (C-event) occurs:

- Update the time $t = t_C$.
- If a particle leaves I for Ω_C, update compartment numbers and delete a Brownian particle in that compartment at random.
- If a particle leaves Ω_C for I, update compartment numbers and initialise its distance from interface I_1 using a uniform random number r such that $x_i = I_1 + rh$.
- If a particle jumps in I, update the compartments and select a Brownian particle in that compartment at random and shift its positon by $\pm h$ depending on the jump direction.
- If a particle leaves I for Ω_B, remove a particle from the last compartment and select a Brownian particle in that compartment at random and shift its positon by $+h$.
- Else update the compartment numbers in Ω_C.

THE BLENDING METHOD CONT.

IV. If $t_M \leq t_C$ then a molecular-based event (M-event) occurs:

- Update the time $t = t_M$.

- Update the positions of all particles in Ω_B and I according to our Brownian motion equation.
- Enforce boundary condition at RHS of domain.
- If particles move over I_1 from Ω_B the delete those particles and add the number of them into the nearest compartment to I_1 in Ω_C.

- Bin the particles according to their position in I for recording.

- Set $t_M = t_M + \Delta t$ and $t_C = \tau$ (where the propensities have been updated).

V. Repeat until desired end of simulation.

DIFFUSION EXAMPLE

Working over $\Omega = [0,1]$ with interfaces located at $I_1 = 0.25$, $I_1 = 0.75$ and $D = 1$ the following deterministic equation governs the system:

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2}$$

where $u(x,0) = 4H(0.25 - x)$ and $u_x(0,t) = u_x(1,t) = 0$.

Plotting the deterministic solution below against simulations gives a very good fit (next steps would be to plot total compartment probability as shown in next slide):

$$u(x,t) = 1 + \frac{8}{\pi}\sum_{i=1}^{\infty}\frac{1}{n}\sin\left(\frac{n\pi}{4}\right)\cos(n\pi x)e^{-(n\pi)^2 t}$$

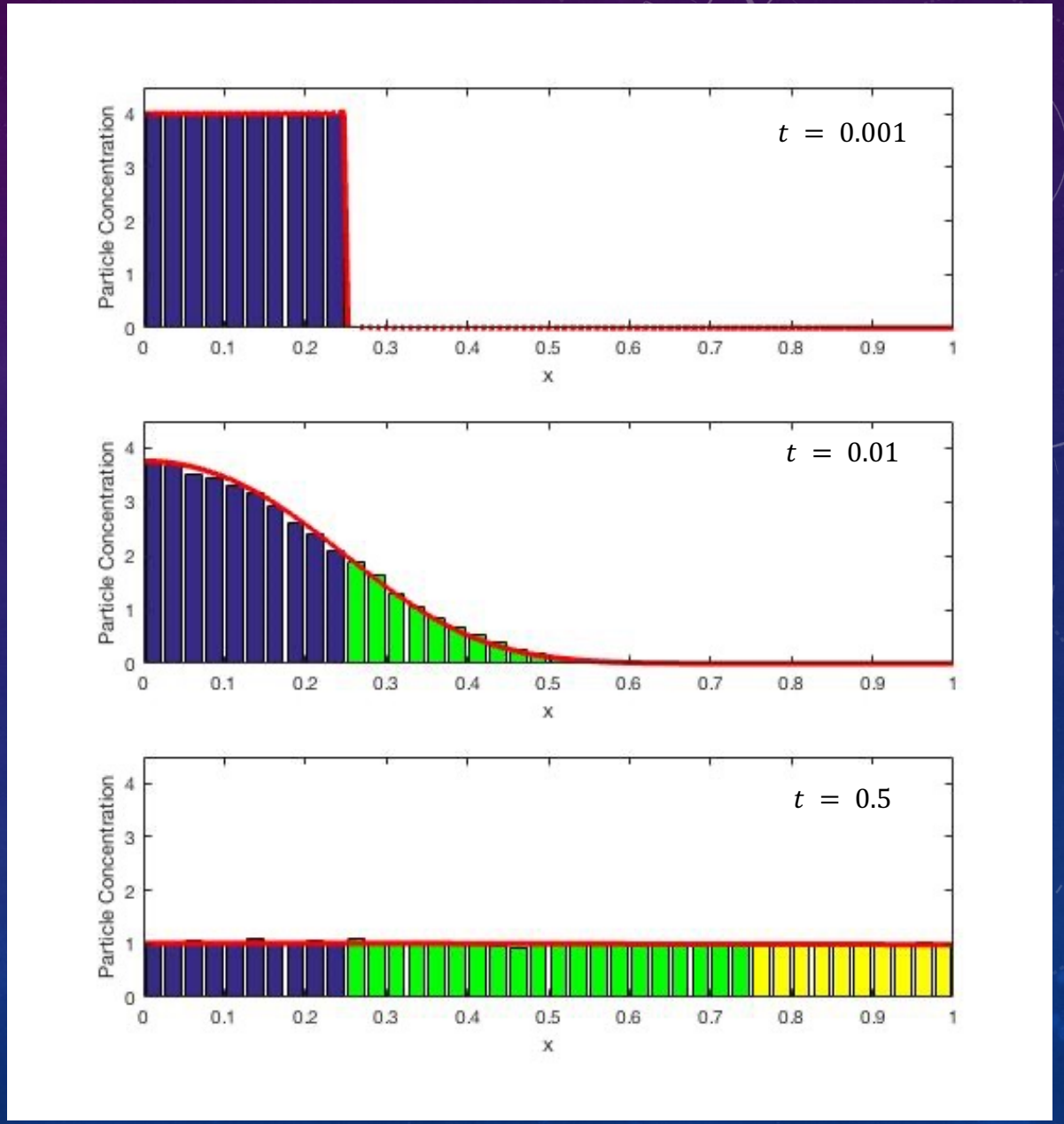
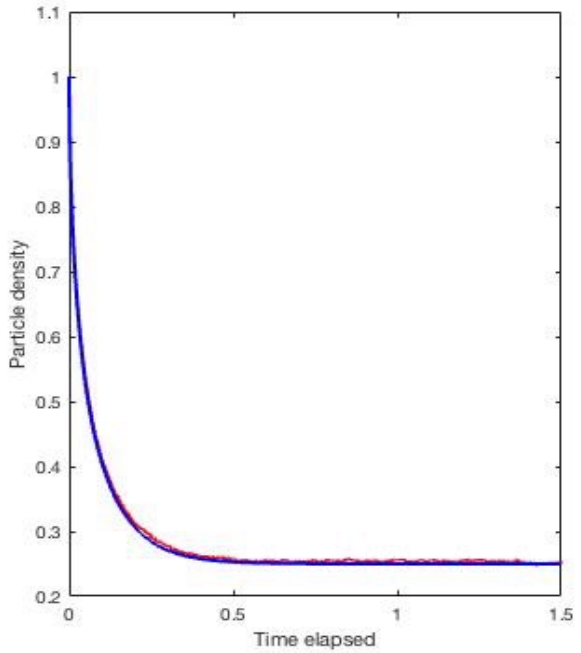
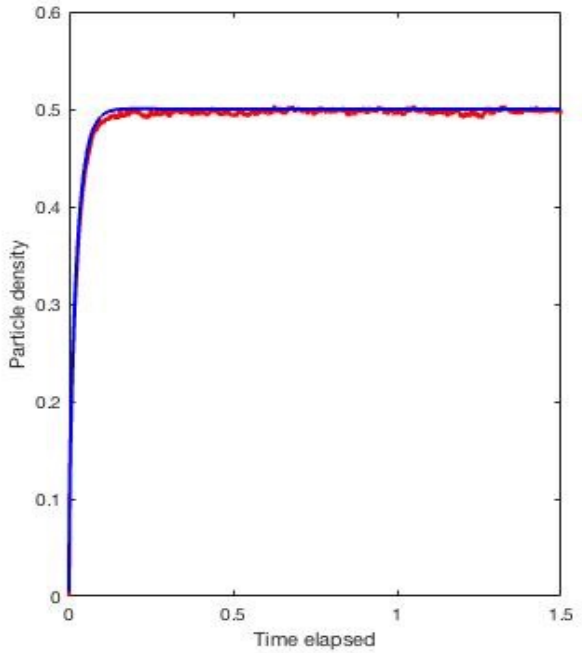


Fig 1: The system displayed at progressive times with particle concentrations shown in the pure-compartment (blue), blending (green) and Brownian (yellow) regions respectively. The deterministic PDE is shown in red.

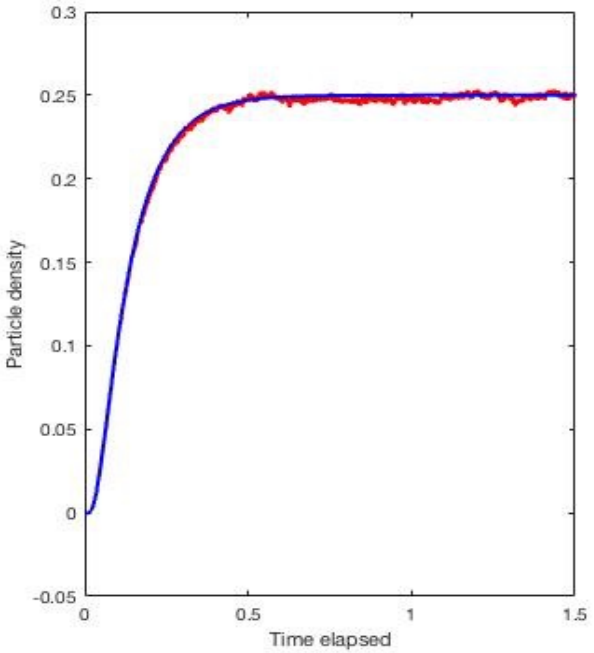
EXAMPLE CONT.



(a)
Pure-compartment region



(b)
Blending region



(c)
Pure-Brownian region

Fig 2: Plots of the analytical probability of finding a particle in the each region (blue) against the simulated probability (red).

MORPHOGEN EXAMPLE

Working over $\Omega = [-1,1]$ with interfaces located at $I_1 = -0.5$, $I_1 = 0.5$. $D = 1/40$, $\lambda = 1000$ and $\mu = 0.1$ the following deterministic equation governs the system:

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2} - \mu u$$

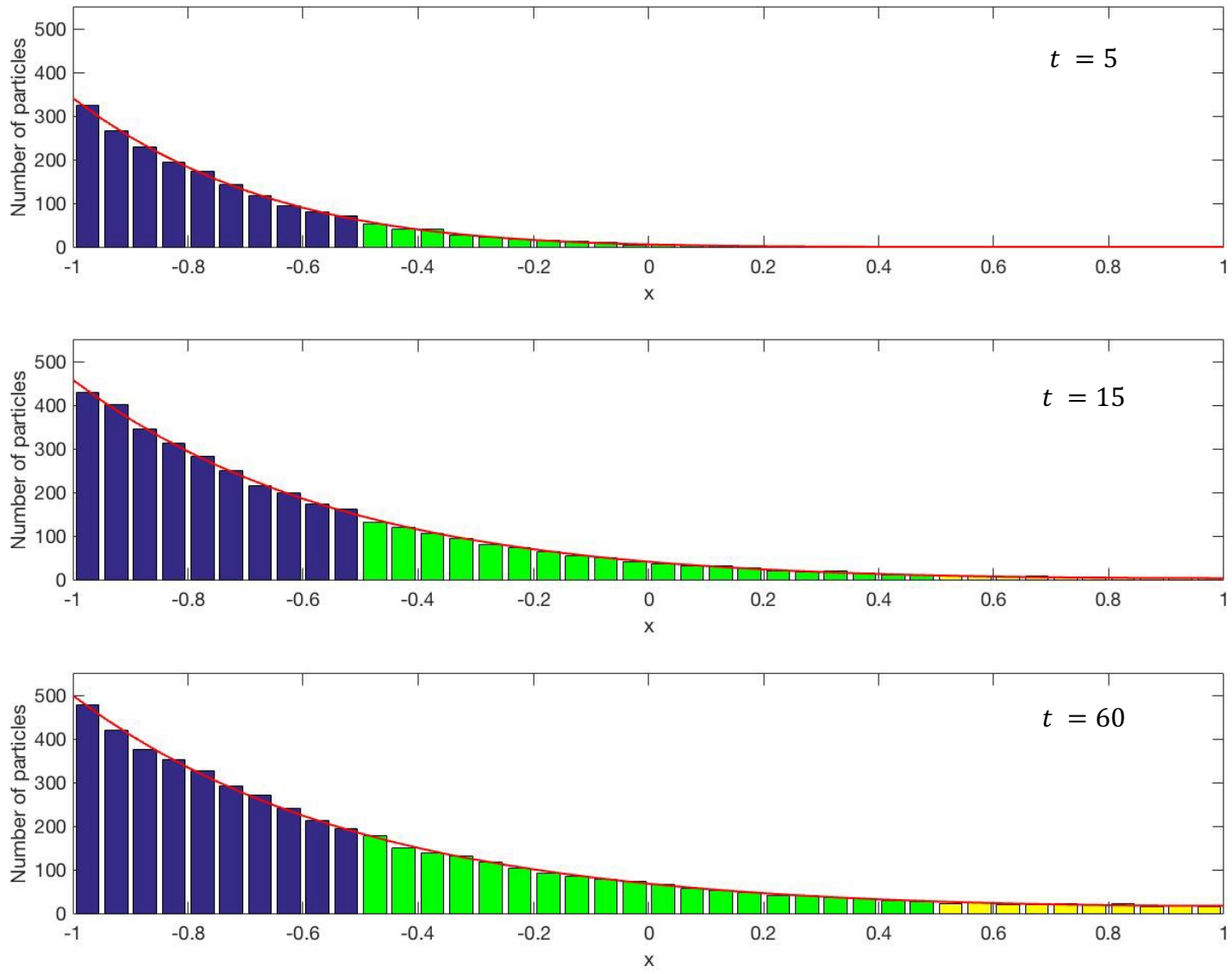
where $u(x,0) = 0, u_x(-1,t) = -\lambda$ and $u_x(1,t) = 0$.

Plotting the deterministic solution below against simulations gives a very good fit again:

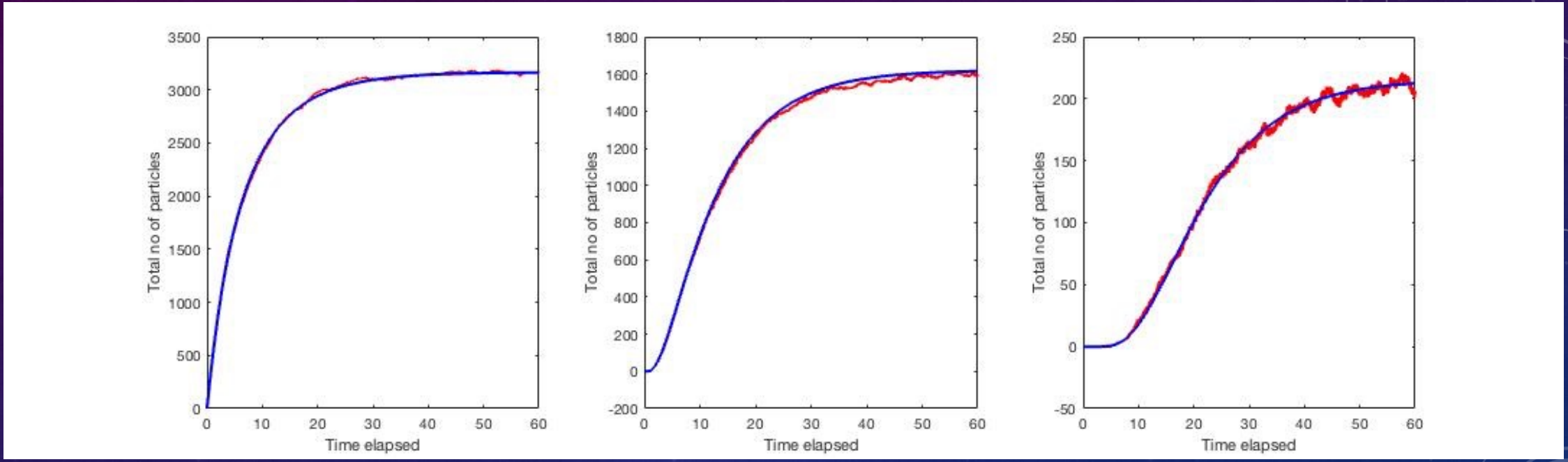
$$u(x,t) = \lambda\sqrt{\frac{D}{\mu}}\frac{\cosh(\sqrt{\frac{\mu}{D}}(x-1))}{\sinh(2\sqrt{\frac{\mu}{D}})} - \frac{\lambda D}{2\mu}e^{-\mu t} - 4\lambda D\sum_{i=1}^{\infty}\frac{\cos(n\pi(x+1)/2)}{D(n\pi)^2+4\mu}e^{-(\frac{D(n\pi)^2}{4}+\mu)t}$$

EXAMPLE CONT.

Fig 3: The system displayed at progressive times with particle concentrations shown in the pure-compartment (blue), blending (green) and Brownian (yellow) regions respectively. The deterministic PDE is shown in red.



EXAMPLE CONT.



(a)
Pure-compartment region

(b)
Blending region

(c)
Pure-Brownian region

Fig 4: Plots of the total analytical particle numbers in each region (blue) against the total simulated particle numbers (red).

CONCLUSIONS

- Verified that particles may can migrate between each region easily and that the interchange between the Gillespie algorithm and the Brownian SDE work well in the blending region.

- Ability to interchange modelling approach allows greater detail in Brownian regimes and less in compartment, saving computational resources.

- We focus on a specific diffusion function for these example however any combination can be used as long as $D_c(x) + D_p(x) = D \; \forall x \in \Omega$.

- PDE to compartment-based blending also seems to work, however I am still working on this as it's a little more complicated!