Multiscale modeling of diffusion processes in dendrites and dendritic spines

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Outline

- Motivation
- Theory
- Details of the coupling
- Verification
- Application
- Results
- Concluding remarks

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Physical models on different length scales

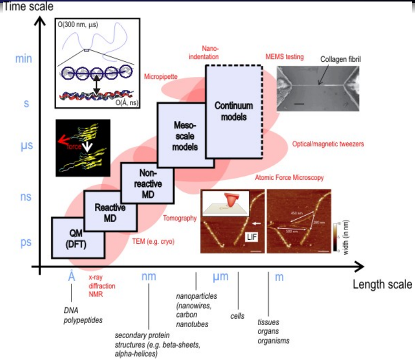

Figure: Illustration of physical models on different length scales, from Markus J. Buehler, MIT

Physical models on different length scales

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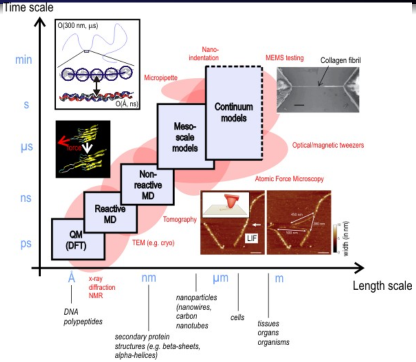

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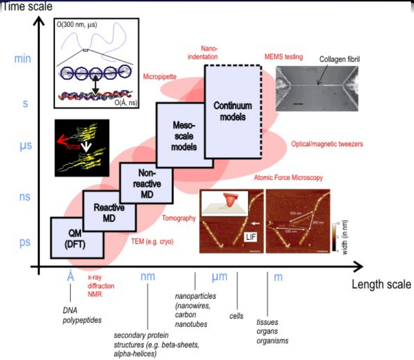

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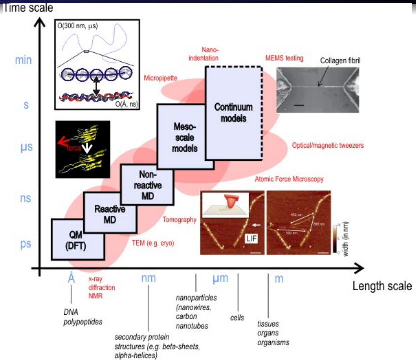
- Problems might arise between these length scales



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Physical models on different length scales

Existing meso scale models

Some meso scale models exist already, but mostly these are aimed at specific problems and/or closed source.

- Dissipative Particle Dynamics
- Dendritc solidification modeling by
- Hybrid fluid flow models by

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- Test and verify implementation thoroughly.
- Apply developed software to physical problem in order to verify functionality.

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Figures/randomwalk-eps-conve

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Figures/randomwalk-eps-conve

Finite difference methods

- For partial differential equations

Figures/FDM_stencils-

Finite difference methods
- For partial differential equations

- Approximate derivatives by finite differences using the definition of the derivative and omitting the limit:

$$\frac{du}{dt} = \lim_{\Delta t \to 0} \frac{u(t) - u(t+\Delta t)}{\Delta t}$$
$$\approx \frac{u(t) - u(t+\Delta t)}{\Delta t}$$

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- Repeat for all derivatives in the PDE.
- Solve equation on discrete mesh points.

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Finite difference methods

Finite difference methods

- The two discretizations used are summarized in the theta-rule description

$$\frac{u^{k+1} - u^k}{\Delta t} = \theta D \frac{\partial^2 u^{k+1}}{\partial x^2} + (1 - \theta) D \frac{\partial^2 u^k}{\partial x^2}. \qquad (1)$$

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- In order to accommodate a larger time step, the Backward Euler discretization ($\theta = 1$) must be implemented:

$$u_i^{k+1} = \frac{D\Delta t}{\Delta x^2}\left((u_{i+1}^{k+1} - u_i^{k+1}) - (u_i^{k+1} - u_{i-1}^{k+1})\right) + u_i^k.$$

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- By insertion the BE scheme results in a tridiagonal linear system in 1D.

Tridiagonal linear systems

Tridiagonal linear systems are efficiently solved by a specialized Gaussian elimination algorithm.

```
g[0] = up[0]/b[0];
H[0] = c[0]/b[0];
for(int i=1; i<n; i++){
    //forward substitution
    H[i]  = -c[i]/(b[i] + a[i]*H[i-1]);
    g[i] = (up[i] - a[i]*g[i-1])/(b[i] + a[i]*H[i
        -1]);
}
u[n-1] = g[n-1];
for(int i=(n-2);i>=0;i--){
    //Backward substitution
    u[i] = g[i] - H[i]*u[i+1];
}
```

Code 1 : The tridiag algoritm

Finite difference methods

Backward Euler in 2D

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Finite difference methods

Backward Euler in 2D

- In 2D the solution to the discrete diffusion equation is a matrix.
- Rewriting the matrix as a vector results in a banded linear system:

$$\left(\begin{array}{ccc|ccc|ccc}
\gamma & -2\beta & 0 & -2\alpha & 0 & 0 & 0 & 0 & 0 \\
-\beta & \gamma & -\beta & 0 & -2\alpha & 0 & 0 & 0 & 0 \\
0 & -2\beta & \gamma & 0 & 0 & -2\alpha & 0 & 0 & 0 \\
\hline
-\alpha & 0 & 0 & \gamma & -2\beta & 0 & -\alpha & 0 & 0 \\
0 & -\alpha & 0 & -\beta & \gamma & -\beta & 0 & -\alpha & 0 \\
0 & 0 & -\alpha & 0 & -2\beta & \gamma & 0 & 0 & -\alpha \\
\hline
0 & 0 & 0 & -2\alpha & 0 & 0 & \gamma & -2\beta & 0 \\
0 & 0 & 0 & 0 & -2\alpha & 0 & -\beta & \gamma & -\beta \\
0 & 0 & 0 & 0 & 0 & -2\alpha & 0 & -2\beta & \gamma
\end{array}\right)\mathbf{u} = \mathbf{u}_p$$

Tridiagonal linear systems

Block tridiagonal solver

The tridiag algorithm can be rewritten to solve block tridiagonal systems by replacing divisions with matrix inverses:

$$
\begin{aligned}
H_0 &= -B_0^{-1} C_0 \\
\mathbf{g}_0 &= B_0^{-1} \mathbf{u}_{p0} \\
H_i &= -\left(B_i + A_i H_{i-1}\right)^{-1} C_i \\
\mathbf{g}_i &= \left(B_i + A_i H_{i-1}\right)^{-1} \left(\mathbf{u}_{pi} - A_i \mathbf{g}_{i-1}\right)
\end{aligned}
$$

$$
\begin{aligned}
\mathbf{u}_{n-1} &= \mathbf{g}_{n-1} \\
\mathbf{u}_i &= \mathbf{g}_i + H_i \mathbf{u}_{i+1}
\end{aligned}
$$

Tridiagonal linear systems

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- The Block tridiagonal solver requires inversion of $2n$ matrices, but only once.
- In total $\mathcal{O}(n^{2d-1})$ operations are required for a general system, one order less than e.g. LU decomposition.
- Memory impact can also be reduced to $8 \cdot n^{2d-1}$ bytes, as opposed to $8 \cdot n^{2d}$ bytes.

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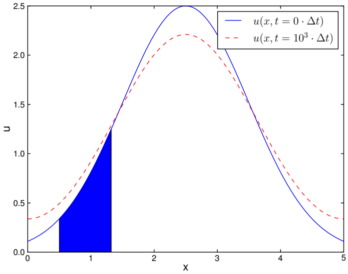
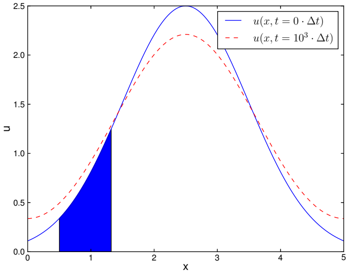
- $\mathbf{u}_p$ is then used as input to calculate the next time step.

Conversion between length scales



Conversion between length scales

- A single, real integer converts the concentration in one mesh point to a number of random walkers.



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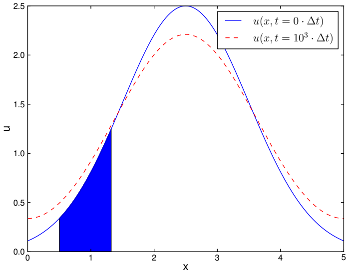
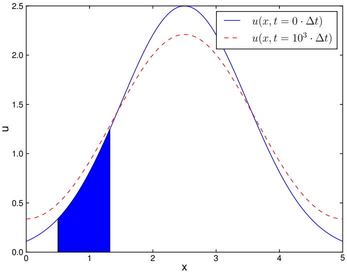


Conversion between length scales

- A single, real integer converts the concentration in one mesh point to a number of random walkers.
- $$C_{ij} = Hc \cdot u_{ij}$$
- The conversion must be done at each time step because the concentration over an area of the mesh might change.



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- Rewriting this results in the desired restriction which is placed on the step length:

$$l = \sqrt{2dD\frac{\Delta t}{\tau}}$$

Boundary conditions on the random walk

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- Requires some work on the PDE boundary conditions etc.

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- From the residuals, we know how the error should behave.
- For a given exact solution, u_e, the error is defined by:

$$\varepsilon(t^k) = ||u(t^k) - u_e(t^k)||_2$$

$$\approx \sqrt{\Delta x \Delta y \sum_{i=0}^{k} \sum_{i=0}^{k} (u(t^k, x_i, y_j) - u_e(t^k, x_i, y_j))^2}.$$

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- Many useful variations of this method.
- Tests are done using

$$u(x,y,t) = e^{-\pi^2 t}\cos(\pi x)\cos(\pi y) + 1,$$

which fulfills boundary conditions and has $s(x,t) = 0$.

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- Often difficult tests.

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- Forward Euler solution (1D):

$$u^{k+1} = \sum_{i=0}^{k} \binom{k}{i} (D\Delta t)^i \frac{2^i}{\Delta x^{2i}} (\cos(\pi \Delta x) - 1)^i \cos(\pi x).$$

- Backward Euler solution:

$$\vec{u}^k = \left(\mathbf{M}^{-1}\right)^k \vec{u}^0.$$

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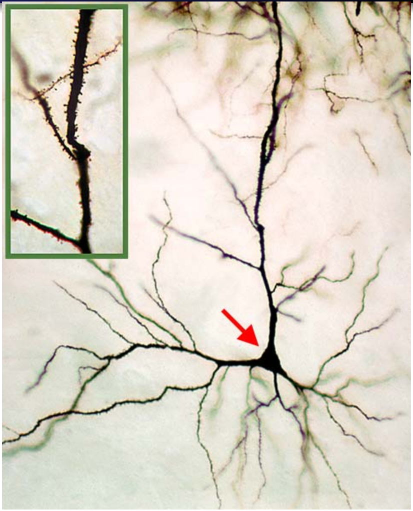
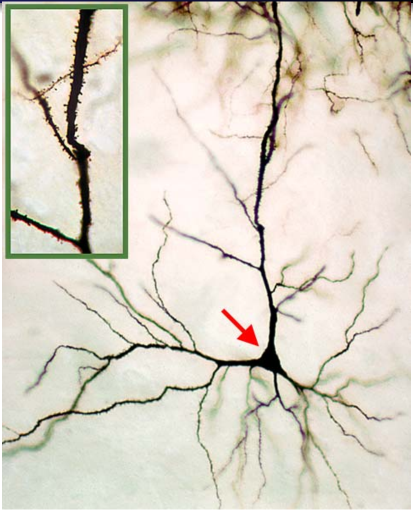
The problem



The problem

- Pyramidal neuron



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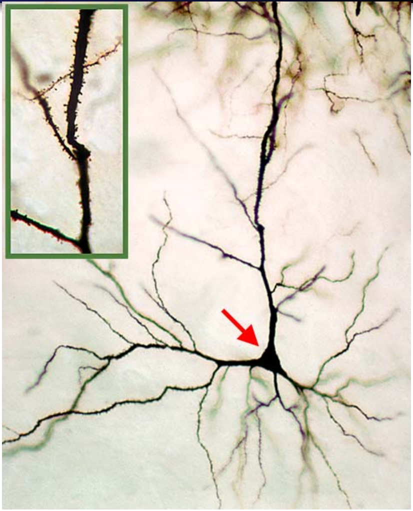
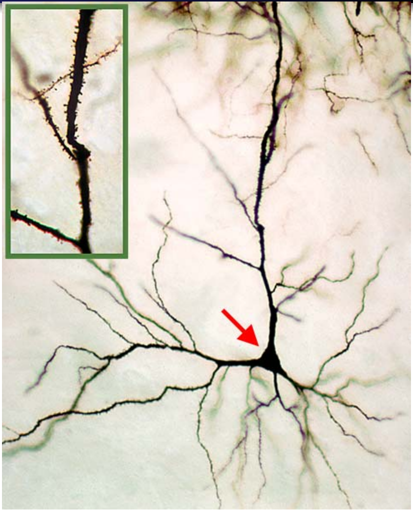


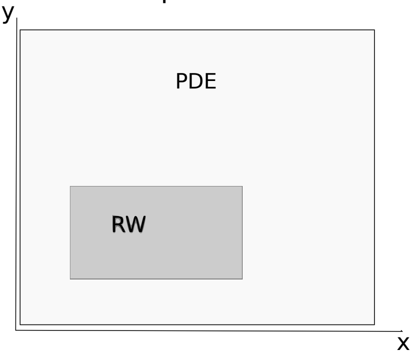
The problem

- Pyramidal neuron
- Protein Kinase Cγ
- Dendritic spines

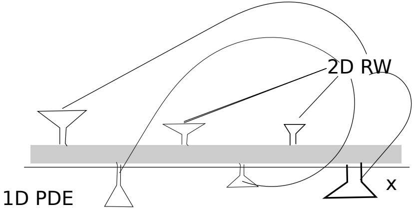


Computational model

Default setup



Modified setup



Parameters and other details

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- Spine geometries chosen at random to correspond with Arellano et.al.
- Initial condition is modified to accommodate absorption effects (`http://jcb.rupress.org/content/170/7/1147/suppl/DC1`).

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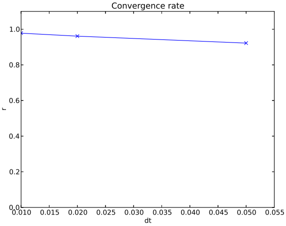
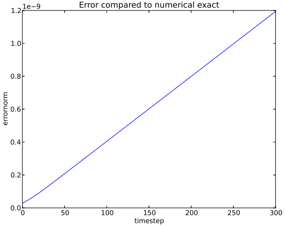
What we are looking for

- Successful tests of PDE solvers.
- Successful tests of RW solver.
- Successful test of hybrid solver given sufficient number of walkers.

PDE solvers

BE





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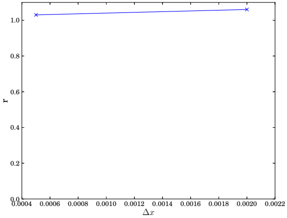
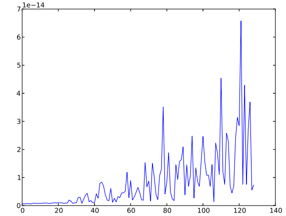
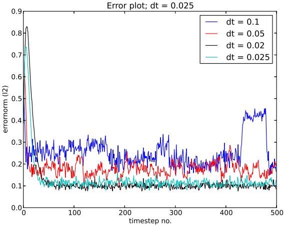
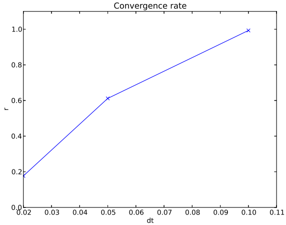




RW solver


Error plot; dt = 0.025
dt = 0.1
dt = 0.05
dt = 0.02
dt = 0.025
errornorm (l2)
timestep no.
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
0
100
200
300
400
500


Convergence rate
r
dt
0.0
0.2
0.4
0.6
0.8
1.0
0.02
0.03
0.04
0.05
0.06
0.07
0.08
0.09
0.10
0.11

RW solver

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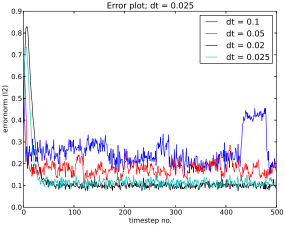

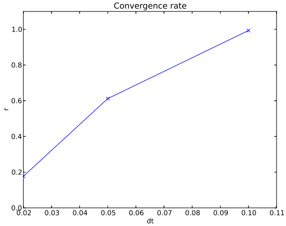

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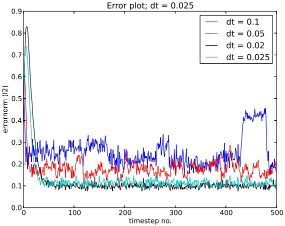
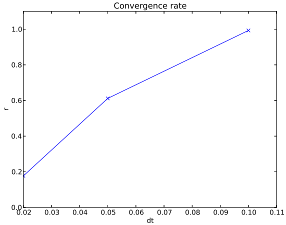
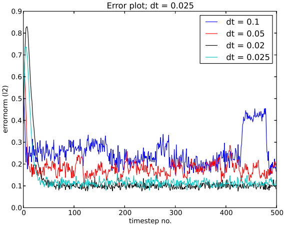
- No numerical exact solution.

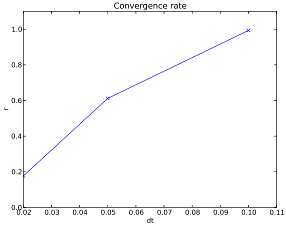




RW solver

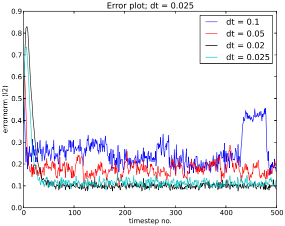
- Needs a new initial condition, otherwise similar.
- No numerical exact solution.
- Expected convergence rate of 0.5.

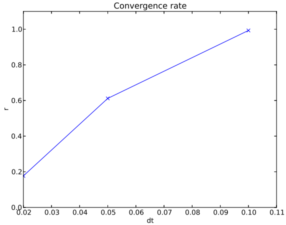




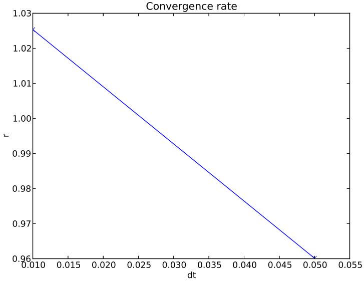
RW solver

- Needs a new initial condition, otherwise similar.
- No numerical exact solution.
- Expected convergence rate of 0.5.
- Verifies that the coupling works.





Hybrid solver



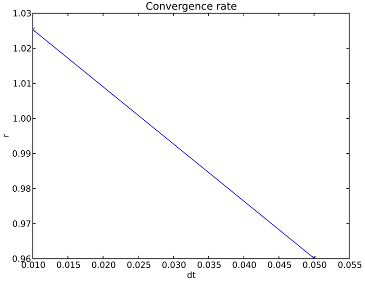
Hybrid solver

- New error term:

$$\varepsilon(t) = C_t \Delta t + C_x \Delta x^2 + \frac{C_{RW}}{\sqrt{Hc}}$$

- A lot of walkers are required:

$$Hc \geq \frac{1}{\Delta t^2}$$



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- New error term:

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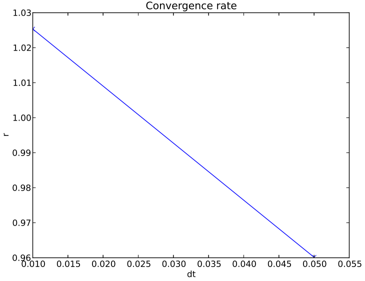


Hybrid solver

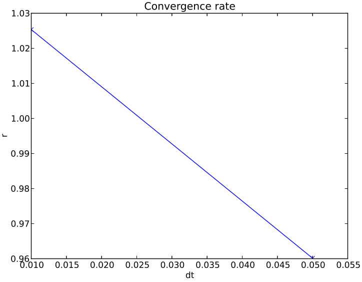
- New error term:

$$\varepsilon(t) = C_t \Delta t + C_x \Delta x^2 + \frac{C_{RW}}{\sqrt{Hc}}$$

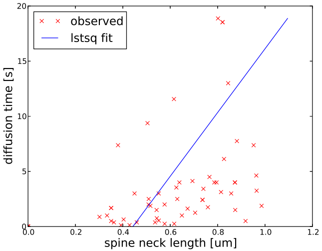
- A lot of walkers are required:

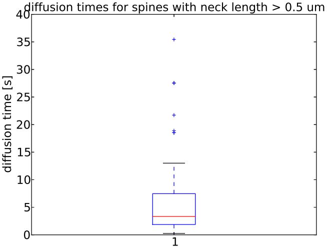
$$Hc \geq \frac{1}{\Delta t^2}$$

- Expect first order convergence.
- The extra error can be controlled (at a large cost).



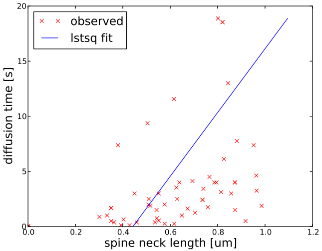
Results from application

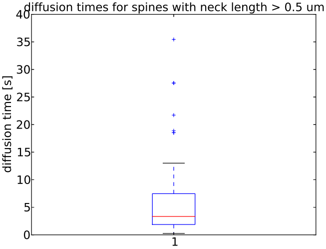




Results from application

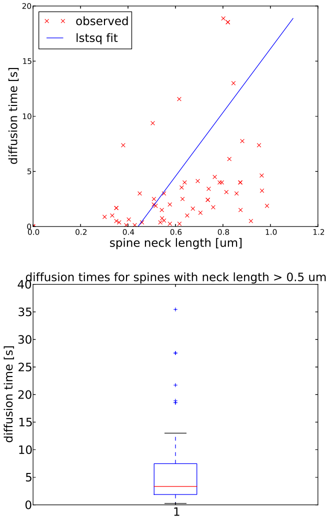
- Consistently towards lower range of results by Craske et.al.





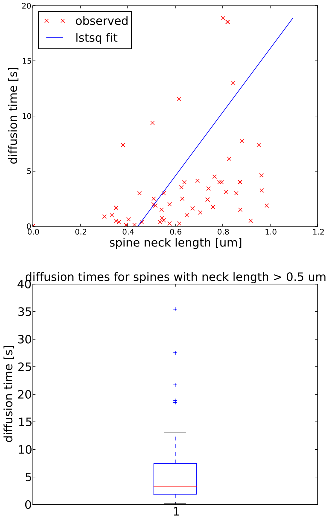
Results from application

- Consistently towards lower range of results by Craske et.al.
- Otherwise relatively good.



Results from application

- Consistently towards lower range of results by Craske et.al.
- Otherwise relatively good.
- $\sim$ 2-3 seconds can be added.



Outline

- Motivation
- Theory
- Details of the coupling
- Verification
- Application
- Results
- Concluding remarks

Conclusions

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- Both PDE, RW and hybrid solvers are implemented correctly.
- Software can be modified to model real applications.
- Proof of concept.

Further work

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- Implement flux exchange boundary conditions

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- Find other physical applications - anisotropy.

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- Implement flux exchange boundary conditions
- Find other physical applications - anisotropy.
- Implement Finite element PDE solver.

Thank you for your attention!

References I

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