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Numerical Integration of 3D Reaction-Diffusion Equations

(Difference methods for parabolic PDEs, boundary value problem)

Reaction-Diffusion Problem:

$$\text{Calcium} \; : \; \frac{\partial [Ca^{2+}]}{\partial t} = D_{Ca} \nabla^2 [Ca^{2+}] + \sum_j R_j + \sum_m a_m \delta(x - x_m) \tag{1}$$

$$\text{Buffer} \; : \; \frac{\partial [B_j]}{\partial t} = D_{B_j} \nabla^2 [B_j] + R_j \tag{2}$$

Reaction term ($Ca + B_j \rightleftharpoons CaB_j$) :

$$R_j = -k_j^+ [B_j][Ca^{2+}] + k_j^- ([B_j]_{total} - [B_j]) \tag{3}$$

- Diffusion/heat equation in one dimension
  - Explicit and implicit difference schemes
  - Stability analysis
  - Non-uniform grid
- Three dimensions: Alternating Direction Implicit (ADI) methods
- Non-homogeneous diffusion equation: dealing with the reaction term

Diffusion/heat equation in one spatial dimension

$$\frac{\partial f}{\partial t} = D\frac{\partial^2 f}{\partial x^2} \tag{4}$$

Discretization of coordinates: $(x,t) \rightarrow (x_j, t_n)$
$x_j = x_0 + j\,\Delta x$; $t_n = t_0 + n\,\Delta t$; $f(x_j, t_n) \equiv f_j^n$

Finite difference approximation for 1st derivative:

$$\frac{f_j^{n+1} - f_j^n}{\Delta t} = \frac{\partial f_j^{n+1/2}}{\partial t} + O(\Delta t^2) = \frac{\partial f_j^n}{\partial t} + O(\Delta t) = \frac{\partial f_j^{n+1}}{\partial t} + O(\Delta t) \tag{5}$$

Finite difference approximation for 2nd derivative:

$$\frac{(f_{j+1}^n - f_j^n)/\Delta x - (f_j^n - f_{j-1}^n)/\Delta x}{\Delta x} = \frac{f_{j-1}^n - 2f_j^n + f_{j+1}^n}{\Delta x^2} = \frac{\partial^2 f_j^n}{\partial x^2} + O(\Delta x^2) \tag{6}$$

1. Euler (explicit) scheme: $f_j^{n+1} - f_j^n = \nu\,(f_{j-1}^n - 2f_j^n + f_{j+1}^n) \equiv \nu\,\delta_x^2 f_j^n$
where $\nu \equiv D\Delta t/\Delta x^2$

- Given f_j^n, values at next time step f_j^{n+1} are computed directly
- Stable for $\nu < 1/2$
- Truncation error: $T = O(\Delta t) + O(\Delta x^2)$

2. Fully implicit scheme: $f_j^{n+1} - f_j^n = \nu\,(f_{j-1}^{n+1} - 2f_j^{n+1} + f_{j+1}^{n+1}) \equiv \nu\,\delta_x^2 f_j^{n+1}$
("backward" Euler method)

- Tridiagonal system of linear equations must be solved at each time step
- Unconditionally stable
- Truncation error: $T = O(\Delta t) + O(\Delta x^2)$

3. Crank-Nicholson (implicit) scheme: $f_j^{n+1} - f_j^n = \nu/2\{\delta_x^2\, f_j^n + \delta_x^2\, f_j^{n+1}\}$

$$\text{symmetric representation:} \quad (1 - \frac{\nu}{2}\,\delta_x^2) f_j^{n+1} = (1 + \frac{\nu}{2}\,\delta_x^2) f_j^n \tag{7}$$

- Truncation error: $T = O(\Delta t^2) + O(\Delta x^2)$
- Unconditionally stable

Solving the fully implicit scheme: tridiagonal system

$$\frac{\partial f}{\partial t} = D\frac{\partial^2 f}{\partial x^2} \quad \Rightarrow \quad f_j^{n+1} - f_j^n = \nu\,(f_{j-1}^{n+1} - 2f_j^{n+1} + f_{j+1}^{n+1}) \tag{8}$$

- **Assume Dirichlet boundary conditions:** $f_0 = f_N = 0$

$$\begin{pmatrix} 1+2\nu & -\nu & 0 & 0 & \cdot & & & \\ -\nu & 1+2\nu & -\nu & 0 & \cdot & & 0 & \\ 0 & -\nu & 1+2\nu & -\nu & \cdot & & & \\ 0 & 0 & -\nu & 1+2\nu & \cdot & & & \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ & & & & \cdot & 1+2\nu & -\nu & 0 \\ & 0 & & & \cdot & -\nu & 1+2\nu & -\nu \\ & & & & \cdot & 0 & -\nu & 1+2\nu \end{pmatrix} \begin{pmatrix} f_0^{n+1} \\ f_1^{n+1} \\ f_3^{n+1} \\ f_4^{n+1} \\ \cdot \\ f_{N-2}^{n+1} \\ f_{N-1}^{n+1} \\ f_N^{n+1} \end{pmatrix} = \begin{pmatrix} f_0^n \\ f_1^n \\ f_3^n \\ f_4^n \\ \cdot \\ f_{N-2}^n \\ f_{N-1}^n \\ f_N^n \end{pmatrix}$$

$$L_j f_{j-1} + C_j f_j + R_j f_{j+1} = H_j \qquad j = 0..N$$

$$L_0 = R_N = 0,\;\; L_j = R_j = -\nu,\;\; C_j = 1 + 2\nu$$

Solve by Gaussian elimination:

1. Forward elimination:
$$R_0 = R_0/C_0\,, \quad H_0 = H_0/C_0 \tag{9}$$
$$C_j = C_j - L_j R_{j-1}, \quad j = 1..N \tag{10}$$
$$H_j = (H_j - L_j H_{j-1})/C_j, \quad j = 1..N \tag{11}$$
$$R_j = R_j/C_j, \quad j = 1..N \tag{12}$$

2. Backward substitution:
$$f_N = H_N \tag{13}$$
$$f_j = H_j - R_j f_{j+1}, \quad j = N-1\ldots 0. \tag{14}$$

- **Operations per time step:** $5N$ **multiply/divide** $+\,3N$ **add/subtract**

Stability Analysis: Fourier Method

- Difference scheme is linear (as well as the PDEs), so the error satisfies the same equation
- Substitute into equations the solution (for the error instability) of the form $f_j^n = \lambda^n \exp(i\, x_j\, k)$ (where $k = \pi m/(N\Delta x)$, $m = 0..N$)
- Method is stable if $\lambda < 1$

1. Forward Euler (explicit scheme): $f_j^{n+1} - f_j^n = \nu_x\,(f_{j-1}^n - 2f_j^n + f_{j+1}^n)$

$$\begin{aligned}
(\lambda^{n+1} - \lambda^n)\exp(i\, x_j\, k) &= \nu_x\, \lambda^n \exp(i\, x_j\, k)\,[\exp(-i\,\Delta x\, k) - 2 + \exp(i\,\Delta x\, k)] \\
\lambda - 1 &= \nu_x\,[\exp(-i\,\Delta x\, k) - 2 + \exp(i\,\Delta x\, k)] \\
\lambda &= 1 - 4\nu_x \sin^2(\Delta x\, k/2) \\
|\lambda| < 1 \;&\rightarrow\; \nu_x < 1/2 \qquad (15)
\end{aligned}$$

2. Backward Euler (implicit scheme): $f_j^{n+1} - f_j^n = \nu_x\,(f_{j-1}^{n+1} - 2f_j^{n+1} + f_{j+1}^{n+1})$

$$\begin{aligned}
(\lambda^{n+1} - \lambda^n)\exp(i\, x_j\, k) &= \nu_x\, \lambda^{n+1} \exp(i\, x_j\, k)\,[\exp(-i\,\Delta x\, k) - 2 + \exp(i\,\Delta x\, k)] \\
\lambda - 1 &= \nu_x\, \lambda\,[\exp(-i\,\Delta x\, k) - 2 + \exp(i\,\Delta x\, k)] \\
\lambda &= \frac{1}{1 + 4\nu_x \sin^2(\Delta x\, k/2)} < 1 \quad \text{(always stable)} \qquad (16)
\end{aligned}$$

Non-Uniform Grid: $x_{i+1} - x_i = \Delta x_i$

Finite difference approximation for the 2nd derivative:

$$\frac{(f^n_{j+1} - f^n_j)/\Delta x_j - (f^n_j - f^n_{j-1})/\Delta x_{j-1}}{(\Delta x_{j-1} + \Delta x_j)/2} = \frac{\partial^2 f^n_j}{\partial x^2} + O(\Delta x^2_{j,j-1}) + O(\Delta x_j - \Delta x_{j-1}) \tag{17}$$

- **To maintain accuracy, set $\Delta x_j = \Delta x_{j-1}(1 \pm \epsilon)$, $\epsilon \ll 1$**

Modified difference scheme:

$$f^{n+1}_j - f^n_j = \nu\,(f^{n+1}_{j-1} - 2f^{n+1}_j + f^{n+1}_{j+1}) \quad \Rightarrow \quad f^{n+1}_j - f^n_j = \nu^-_j f^{n+1}_{j-1} + \nu^0_j f^{n+1}_j + \nu^+_j f^{n+1}_{j+1} \tag{18}$$

where

$$\begin{aligned}
\nu^-_j &= \frac{2D\Delta t}{\Delta x_{j-1}(\Delta x_{j-1} + \Delta x_j)} \\
\nu^0_j &= -\frac{2D\Delta t}{\Delta x_{j-1}\Delta x_j} \\
\nu^+_j &= \frac{2D\Delta t}{\Delta x_j(\Delta x_{j-1} + \Delta x_j)}
\end{aligned}$$

Minimal spacing decreases exponentially with increasing N:

$$\begin{aligned}
\Delta x_j &= (1+\epsilon)\Delta x_{j-1} = (1+\epsilon)^j \Delta x_0 \equiv \gamma^j \Delta x_0 \\
\Delta x_0 &= \frac{\Delta x_N}{\gamma^n}
\end{aligned}$$

$$\text{Flux boundary conditions: } \frac{\partial f_{0,N}}{\partial n} + b f_{0,N} = c \tag{19}$$

Consider field values at (virtual) points outside the boundary:
$f_{-1} = f(x_0 - \Delta x)$, $f_{N+1} = f(x_N + \Delta x)$

$$\begin{aligned} \frac{\partial f_0}{\partial x} &\Rightarrow \frac{f_1 - f_{-1}}{2\Delta x} + O(\Delta x^2) \\ \frac{\partial f_0}{\partial x} + b f_0 = c &\Rightarrow f_1 - f_{-1} + 2\Delta x(b f_0 - c) = 0 \\ f_{-1} &= f_1 + 2\Delta x(b f_0 - c) \end{aligned} \tag{20}$$

Difference equation at point x_0:

$$\begin{aligned} f_0^{n+1} - f_0^n &= \nu\,(f_{-1}^{n+1} - 2f_0^{n+1} + f_1^{n+1}) \\ &= \nu\,(f_1^{n+1} + 2\Delta x(b f_0^{n+1} - c) - 2f_0^{n+1} + f_1^{n+1}) \\ &= 2\nu\,(f_1^{n+1} + (b\Delta x - 1) f_0^{n+1} - c\Delta x) \\ \Rightarrow [2\nu(1 &- b\Delta x) + 1] f_0^{n+1} - 2\nu f_1^{n+1} = f_0^n - 2\nu c \Delta x \end{aligned} \tag{21}$$

Difference equation at point x_N:

$$[2\nu(1 - b\Delta x) + 1] f_N^{n+1} - 2\nu f_{N-1}^{n+1} = f_N^n - 2\nu c \Delta x \tag{22}$$

$$\begin{pmatrix} 1+2\nu(1-b\Delta x) & -2\nu & 0 & \cdot & & & \\ -\nu & 1+2\nu & -\nu & \cdot & & 0 & \\ 0 & -\nu & 1+2\nu & \cdot & & & \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ & & & \cdot & 1+2\nu & -\nu & 0 \\ & 0 & & \cdot & -\nu & 1+2\nu & -\nu \\ & & & \cdot & 0 & -2\nu & 1+2\nu(1-b\Delta x) \end{pmatrix} \begin{pmatrix} f_0^{n+1} \\ f_1^{n+1} \\ f_3^{n+1} \\ \cdot \\ f_{N-2}^{n+1} \\ f_{N-1}^{n+1} \\ f_N^{n+1} \end{pmatrix}$$

$$= \begin{pmatrix} f_0^n - 2\nu c\Delta x \\ f_1^n \\ f_3^n \\ \cdot \\ f_{N-2}^n \\ f_{N-1}^n \\ f_N^n - 2\nu c\Delta x \end{pmatrix}$$

Diffusion/heat equation in three spatial dimensions

$$\frac{\partial f}{\partial t} = D\left[\frac{\partial^2 f}{\partial x^2} + \frac{\partial^2 f}{\partial y^2} + \frac{\partial^2 f}{\partial z^2}\right] \tag{23}$$

1. Euler (explicit) scheme: $f^{n+1} - f^n = \left[\nu_x\,\delta_x^2 + \nu_y\,\delta_y^2 + \nu_z\,\delta_z^2\right] f^n$

where $f^n \equiv f^n_{ijk} \equiv f(x_i, y_j, z_k; t^n)$
$\nu_x \equiv D\Delta t/\Delta x^2$, $\nu_y \equiv D\Delta t/\Delta y^2$, $\nu_z \equiv D\Delta t/\Delta z^2$
$\delta_x^2 f^n \equiv f^n_{i-1jk} - 2f^n_{ijk} + f^n_{i+1jk}$, $\delta_y^2 f^n \equiv f^n_{ij-1k} - 2f^n_{ijk} + f^n_{ij+1k}$
$\delta_z^2 f^n \equiv f^n_{ijk-1} - 2f^n_{ijk} + f^n_{ijk+1}$

- Stability condition: $\nu_x + \nu_y + \nu_z \leq 1/2$

2. Implicit schemes: Alternating Direction Implicit (ADI) Methods

Backward Euler ($f^{n+1} - f^n = \left[\nu_x\,\delta_x^2 + \nu_y\,\delta_y^2 + \nu_z\,\delta_z^2\right] f^{n+1}$) no longer practical: requires solution of a (non-tridiagonal) system of N^3 equations.

Locally One-Dimensional (LOD) method

3D analog of Crank-Nicholson scheme:

$$(1 - \frac{\nu_x}{2}\delta_x^2 - \frac{\nu_y}{2}\delta_y^2 - \frac{\nu_z}{2}\delta_z^2) f^{n+1} = (1 + \frac{\nu_x}{2}\delta_x^2 + \frac{\nu_y}{2}\delta_y^2 + \frac{\nu_z}{2}\delta_z^2) f^n \tag{24}$$

- Factorization (introduces additional terms of order $O(\Delta t^2)$)

$$(1 - \frac{\nu_x}{2}\delta_x^2)(1 - \frac{\nu_y}{2}\delta_y^2)(1 - \frac{\nu_z}{2}\delta_z^2) f^{n+1} = (1 + \frac{\nu_x}{2}\delta_x^2)(1 + \frac{\nu_y}{2}\delta_y^2)(1 + \frac{\nu_z}{2}\delta_z^2) f^n \tag{25}$$

- To solve Eq. (25), break down each iteration into several steps:

$$\begin{aligned}
(1 - \frac{\nu_x}{2}\delta_x^2) f^{n*} &= (1 + \frac{\nu_x}{2}\delta_x^2) f^n \\
(1 - \frac{\nu_y}{2}\delta_y^2) f^{n**} &= (1 + \frac{\nu_y}{2}\delta_y^2) f^{n*} \\
(1 - \frac{\nu_z}{2}\delta_z^2) f^{n+1} &= (1 + \frac{\nu_z}{2}\delta_z^2) f^{n**}
\end{aligned} \tag{26}$$

- Each time step three tridiagonal systems are solved for all points.
- Truncation error: $T = O(\Delta t^2) + O(\Delta x^2) + O(\Delta y^2) + O(\Delta z^2)$
- Always stable

Problem: equations for intermediate values f^{n*}, f^{n**} are not consistent with the full differential equation: additional care required dealing with boundary conditions

Douglas-Gunn ADI Method

Another "deformation" of the Crank-Nicholson method:

$$(1-\frac{A_x}{2})(1-\frac{A_y}{2})(1-\frac{A_z}{2})f^{n+1} = \left[(1+\frac{A_x}{2})(1+\frac{A_y}{2})(1+\frac{A_z}{2}) - \frac{A_x A_y A_z}{4}\right] f^n \quad (27)$$

where $A_x \equiv \nu_x \delta_x^2 = D\frac{\Delta t}{\Delta x^2}\delta_x^2,\ A_y \equiv \nu_y \delta_y^2,\ A_z \equiv \nu_z \delta_z^2$

Multi-step implementation - Douglas-Gunn method

$$(1-\frac{A_x}{2})f^{n*} = (1+\frac{A_x}{2}+A_y+A_z)f^n \quad (28)$$

$$(1-\frac{A_y}{2})f^{n**} = (1+\frac{A_x}{2}+\frac{A_y}{2}+A_z)f^n + \frac{A_x}{2}f^{n*} \quad (29)$$

$$(1-\frac{A_z}{2})f^{n+1} = (1+\frac{A_x}{2}+\frac{A_y}{2}+\frac{A_z}{2})f^n + \frac{A_x}{2}f^{n*} + \frac{A_y}{2}f^{n**} \quad (30)$$

• Each equation is a valid approximation of the full diffusion equation - no modification needed for boundary conditions

Simplify by subtracting Eq.(28) from Eq.(29), and Eq.(29) from Eq.(30):

$$(1-\frac{A_x}{2})f^{n*} = (1+\frac{A_x}{2}+A_y+A_z)f^n \quad (31)$$

$$(1-\frac{A_y}{2})f^{n**} = f^{n*} - \frac{A_y}{2}f^n \quad (32)$$

$$(1-\frac{A_z}{2})f^{n+1} = f^{n**} - \frac{A_z}{2}f^n \quad (33)$$

- **Truncation error:** $T = O(\Delta t^2) + O(\Delta x^2) + O(\Delta y^2) + O(\Delta z^2)$
- **Always stable**

Heterogeneous Diffusion/heat equation in 1D

$$\frac{\partial f}{\partial t} = D\frac{\partial^2 f}{\partial x^2} + H(f,t) \tag{34}$$

Crank-Nicholson scheme:

$$f_j^{n+1} - f_j^n = \nu/2\{\delta_x^2 f_j^n + \delta_x^2 f_j^{n+1}\} + \frac{\Delta t}{2}(H(f^{n+1},t^{n+1}) + H(f^n,t^n)) \tag{35}$$

Symmetric form:

$$(1 - \frac{\nu}{2}\delta_x^2)f_j^{n+1} = (1 + \frac{\nu}{2}\delta_x^2)f_j^n + \frac{\Delta t}{2}(H(f^{n+1},t^{n+1}) + H(f^n,t^n)) \tag{36}$$

• **For non-linear $H(f)$, this scheme can be solved using predictor/corrector or iteration methods, or one has to give up $O(\Delta t^2)$ accuracy:**
$H(f^{n+1}) = H(f^n) + H'(f^n)(f^{n+1} - f^n)/\Delta t + O(\Delta t)$

• **Without loss of accuracy, one can substitute $H^n \equiv H(f^n,t^n) \rightarrow H(f^n,t^{n+1/2})$, $H^{n+1} \equiv H(f^{n+1},t^{n+1}) \rightarrow H(f^{n+1},t^{n+1/2})$. The following is an equivalent scheme:**

$$(1 - \frac{\nu}{2}\delta_x^2)f_j^{n+1} = (1 + \frac{\nu}{2}\delta_x^2)f_j^n + \frac{\Delta t}{2}(H(f^{n+1},t^{n+\frac{1}{2}}) + H(f^n,t^{n+\frac{1}{2}})) \tag{37}$$

Heterogeneous diffusion/heat equation in 3D

$$\frac{\partial f}{\partial t} = D\left[\frac{\partial^2 f}{\partial x^2} + \frac{\partial^2 f}{\partial y^2} + \frac{\partial^2 f}{\partial z^2}\right] + H(f,t) \tag{38}$$

Douglas-Gunn method for heterogeneous equation:

$$(1 - \frac{A_x}{2}) f^{n*} = (1 + \frac{A_x}{2} + A_y + A_z) f^n + \Delta t \,(\, \alpha H(f^n) + \beta H(f^{n*})\,) \tag{39}$$

$$(1 - \frac{A_y}{2}) f^{n**} = (1 + \frac{A_x}{2} + \frac{A_y}{2} + A_z) f^n + \frac{A_x}{2} f^{n*} + \Delta t \,(\, \gamma H(f^n) + \delta H(f^{n**})\,) \tag{40}$$

$$(1 - \frac{A_z}{2}) f^{n+1} = (1 + \frac{A_x}{2} + \frac{A_y}{2} + \frac{A_z}{2}) f^n + \frac{A_x}{2} f^{n*} + \frac{A_y}{2} f^{n**} + \Delta t \,(\, \zeta H(f^n) + \eta H(f^{n+1})\,) \tag{41}$$

where $\alpha + \beta = 1$, $\gamma + \delta = 1$, $\zeta + \eta = 1$.
Choice of coefficients consistent with second order accuracy:
$\alpha = \gamma = 1$, $\beta = \delta = 0$, $\zeta = \eta = 1/2$.

Subtract Eq.(39) from Eq.(40), and Eq.(40) from Eq.(41):

$$(1 - \frac{A_x}{2}) f^{n*} = (1 + \frac{A_x}{2} + A_y + A_z) f^n + \Delta t \, H^n \tag{42}$$

$$(1 - \frac{A_y}{2}) f^{n**} = f^{n*} - \frac{A_y}{2} f^n \tag{43}$$

$$(1 - \frac{A_z}{2}) f^{n+1} = f^{n**} - \frac{A_z}{2} f^n + \frac{\Delta t}{2}(H^{n+1} - H^n) \tag{44}$$

where $H^n \equiv H(f^n, t^n)$, $H^{n+1} \equiv H(f^{n+1}, t^{n+1})$.

Apply operator $(1 - \frac{A_x}{2})(1 - \frac{A_y}{2})$ from the left to recover the difference scheme:

$$(1 - \frac{A_x}{2})(1 - \frac{A_y}{2})(1 - \frac{A_z}{2}) f^{n+1} = \left[(1 + \frac{A_x}{2})(1 + \frac{A_y}{2})(1 + \frac{A_z}{2}) - \frac{A_x A_y A_z}{4}\right] f^n + \frac{\Delta t}{2}(H^n + H^{n+1}) - \frac{\Delta t}{2}(A_x + A_y - \frac{A_x A_y}{2})(H^{n+1} - H^n) \tag{45}$$

- **Without loss of accuracy, one can substitute** $H^n \equiv H(f^n, t^n) \to H(f^n, t^{n+1/2})$**,** $H^{n+1} \equiv H(f^{n+1}, t^{n+1}) \to H(f^{n+1}, t^{n+1/2})$**.**

Reaction-diffusion with one buffer (Hines method)

$$\text{Calcium} \;:\; \frac{\partial[Ca]}{\partial t} = D_{Ca}\nabla^2[Ca] + R + \sum_m a_k\delta(x - x_m) \qquad (46)$$

$$\text{Buffer} \;:\; \frac{\partial[B]}{\partial t} = D_B\nabla^2[B] + R \qquad (47)$$

$$\text{Reaction term} \;:\; R = -k^+[B][Ca] + k^-([B]_{total} - [B]) \qquad (48)$$

- Difference scheme for source term: $H_{source}(x_i, y_j, z_k) = \sum c_m \delta^i_{i_m}\delta^j_{j_m}\delta^k_{k_m}$

$$\text{Heterogeneity for [Ca]:} \qquad H_{Ca}([Ca], t) = H_{source} + R([Ca], [B])$$

$$\text{Heterogeneity for [B]:} \qquad H_B([B], t) = R([Ca], [B]) \qquad (49)$$

- **Problem:** to solve for $[Ca]^{n+1}$, knowledge of $[B]^{n+1}$ is required; to solve for $[B]^{n+1}$, knowledge of $[Ca]^{n+1}$ is required.

- **Solution:** compute $[Ca]$ and $[B]$ on time grids staggered by $\Delta t/2$

$$\begin{aligned}
(1 - \frac{A_x}{2})[Ca]^{n*} &= (1 + \frac{A_x}{2} + A_y + A_z)[Ca]^n + \Delta t\, H_{Ca}([Ca]^n, [B]^{n+\frac{1}{2}})\\
(1 - \frac{A_y}{2})[Ca]^{n**} &= [Ca]^{n*} - \frac{A_y}{2}[Ca]^n\\
(1 - \frac{A_z}{2})[Ca]^{n+1} &= [Ca]^{n**} - \frac{A_z}{2}[Ca]^n + \frac{\Delta t}{2}(H_{Ca}([Ca]^{n+1}, [B]^{n+\frac{1}{2}}) - H_{Ca}([Ca]^n, [B]^{n+\frac{1}{2}}))
\end{aligned}$$

$$\begin{aligned}
(1 - \frac{A_x}{2})[B]^{n-\frac{1}{2}*} &= (1 + \frac{A_x}{2} + A_y + A_z)[B]^{n-\frac{1}{2}} + \Delta t\, H_B([B]^{n-\frac{1}{2}}, [Ca]^n)\\
(1 - \frac{A_y}{2})[B]^{n-\frac{1}{2}**} &= [B]^{n-\frac{1}{2}*} - \frac{A_y}{2}[B]^{n-\frac{1}{2}}\\
(1 - \frac{A_z}{2})[B]^{n+\frac{1}{2}} &= [B]^{n-\frac{1}{2}**} - \frac{A_z}{2}[B]^{n-\frac{1}{2}} + \frac{\Delta t}{2}(H_B([B]^{n+\frac{1}{2}}, [Ca]^n) - H_B([B]^{n-\frac{1}{2}}, [Ca]^n))
\end{aligned}$$

Fully implicit difference scheme in 3D with heterogeneity

Fully implicit ADI method (Douglas-Rachford):

$$\begin{aligned}(1-A_x)f^{n*} &= (1+A_y+A_z)f^n + H^n\Delta t \quad (50)\\ (1-A_y)f^{n**} &= (1+A_z)f^n + A_x f^{n*} + H^n\Delta t \quad (51)\\ (1-A_z)f^{n+1} &= f^n + A_x f^{n*} + A_y f^{n**} + H^{n+1}\Delta t \quad (52)\end{aligned}$$

- **Each equation is a valid approximation of the full diffusion equation - no modification needed for boundary conditions**

Agrees with the following "deformation" of the fully implicit difference scheme:

$$\begin{aligned}(1-A_x)(1-A_y)(1-A_z)f^{n+1} &= (1+A_xA_y+A_yA_z+A_xA_z-A_xA_yA_z)f^n\\ &+ H^{n+1}\Delta t + A_xA_y(H^{n+1}-H^n)\Delta t \quad (53)\end{aligned}$$

where $A_x \equiv \nu_x\delta_x^2 = D\frac{\Delta t}{\Delta x^2}\delta_x^2,\ A_y \equiv \nu_y\delta_y^2,\ A_z \equiv \nu_z\delta_z^2$

Simplify by subtracting Eq.(50) from Eq.(51), and Eq.(51) from Eq.(52):

$$\begin{aligned}(1-A_x)f^{n*} &= (1+A_y+A_z)f^n + H^n\Delta t \quad (54)\\ (1-A_y)f^{n**} &= -A_y f^n + f^{n*} \quad (55)\\ (1-A_z)f^{n+1} &= -A_z f^n + f^{n**} + (H^{n+1}-H^n)\Delta t \quad (56)\end{aligned}$$

- **Truncation error:** $T = O(\Delta t) + O(\Delta x^2) + O(\Delta y^2) + O(\Delta z^2)$
- **Always stable**

Heterogeneous diffusion/heat equation in 2D

$$\frac{\partial f}{\partial t} = D\left[\frac{\partial^2 f}{\partial x^2} + \frac{\partial^2 f}{\partial y^2}\right] + H(f,t) \tag{57}$$

1. Douglas-Gunn/Crank-Nicholson method:

$$(1 - \frac{A_x}{2})f^{n*} = (1 + \frac{A_y}{2})f^n + \frac{\Delta t}{2}H(f^n, t^n) \tag{58}$$

$$(1 - \frac{A_y}{2})f^{n+1} = (1 + \frac{A_x}{2})f^{n*} + \frac{\Delta t}{2}H(f^{n+1}, t^{n+1}) \tag{59}$$

Corresponding difference scheme:

$$\begin{aligned}(1 - \frac{A_x}{2})(1 - \frac{A_y}{2})f^{n+1} &= (1 + \frac{A_x}{2})(1 + \frac{A_y}{2})f^n + \\ &\frac{\Delta t}{2}(H^n + H^{n+1}) + \frac{\Delta t}{4}A_x(H^n - H^{n+1})\end{aligned} \tag{60}$$

where $A_x \equiv \nu_x \delta_x^2 = D\frac{\Delta t}{\Delta x^2}\delta_x^2,\ A_y \equiv \nu_y \delta_y^2$

2. Fully implicit method:

$$(1 - A_x)f^{n*} = (1 + A_y)f^n + \Delta t\, H(f^n, t^n) \tag{61}$$

$$(1 - A_y)f^{n+1} = f^n + A_x f^{n*} + \Delta t\, H(f^{n+1}, t^{n+1}) \tag{62}$$

Corresponding "deformation" of the fully implicit difference scheme:

$$(1 - A_x)(1 - A_y)f^{n+1} = (1 + A_x A_y)f^n + H^{n+1}\Delta t + A_x(H^n - H^{n+1})\Delta t \tag{63}$$