



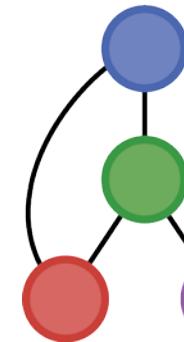
# Robust Simulation of Transient PDE Models under Uncertainty

Chenyu Wang, Matthew D. Stuber

2019 AIChE Annual Meeting  
Orlando, FL, November 14th

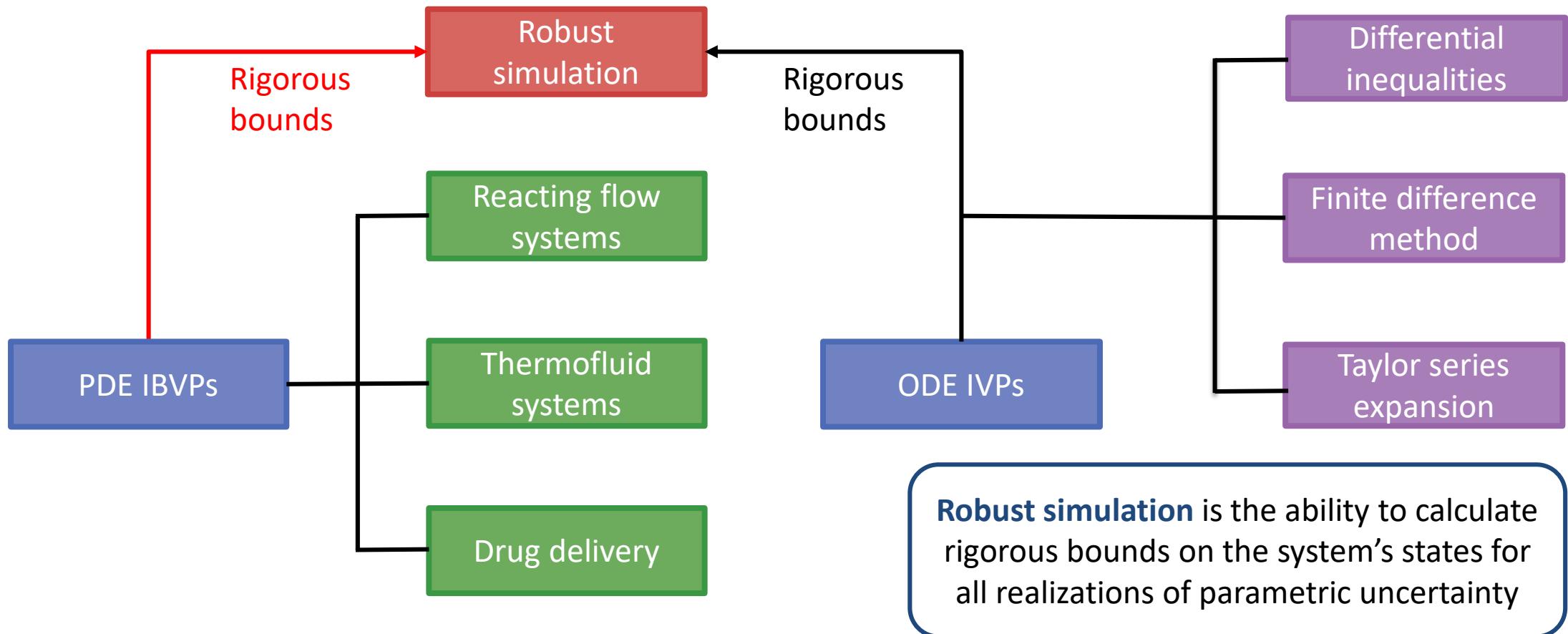


19 AIChE  
Annual Meeting, Orlando, FL



Process Systems and  
Operations Research  
Laboratory

# Robust Simulation



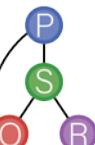
- [1] M. D. Stuber and P. I. Barton, "Robust simulation and design using semi-infinite programs with implicit functions," *International Journal of Reliability and Safety*, vol. 5, no. 3-4, pp. 378-397, 2011.
- [2] J. K. Scott and P. I. Barton, "Bounds on the reachable sets of nonlinear control systems," *Automatica*, vol. 49, no. 1, pp. 93-100, 2013.
- [3] G. F. Corliss, "Survey of interval algorithms for ordinary differential equations," *Applied Mathematics and Computation*, vol. 31, pp. 112-120, 1989.

# Parametric Partial Differential Equations

- Provide valid and efficient bounds for parametric PDE system (IBVP)

$$\begin{aligned}\partial_t \mathbf{x}(y, \mathbf{p}, t) &= \mathbf{f}(y, \mathbf{x}(y, \mathbf{p}, t), \partial_y \mathbf{x}(y, \mathbf{p}, t), \partial_{yy} \mathbf{x}(y, \mathbf{p}, t), \mathbf{p}, t) \\ \mathbf{x}(y(\mathbf{p}, t_0), t_0) &= \mathbf{x}_0(\mathbf{p}), \quad \mathbf{p} \in P \\ \mathbf{x}(y^L(\mathbf{p}, t), t) &= \mathbf{x}^L(\mathbf{p}), \quad \mathbf{p} \in P \\ \mathbf{x}(y^U(\mathbf{p}, t), t) &= \mathbf{x}^U(\mathbf{p}), \quad \mathbf{p} \in P\end{aligned}$$

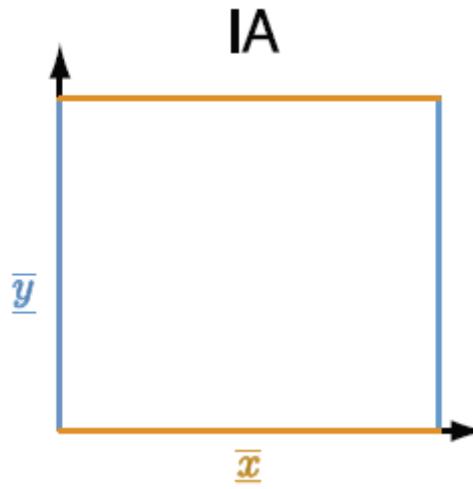
- Assumptions:
  - $\mathbf{f} : C \times D \times \mathbb{R}^{n_x} \times \mathbb{R}^{n_x} \times P \times I \rightarrow \mathbb{R}^{n_x}$  is locally Lipschitz continuous;
  - For every  $\mathbf{p} \in P$ , there exists a unique solution over the time domain  $I$ .
- Reachable set:  $Re(y, t) \equiv \{\mathbf{x}(y, \mathbf{p}, t) : \mathbf{p} \in P\}$ .
- Objective: efficiently compute bounds on the reachable set with less conservatism.



# Interval Arithmetic and Affine Arithmetic

## Interval Arithmetic (IA)

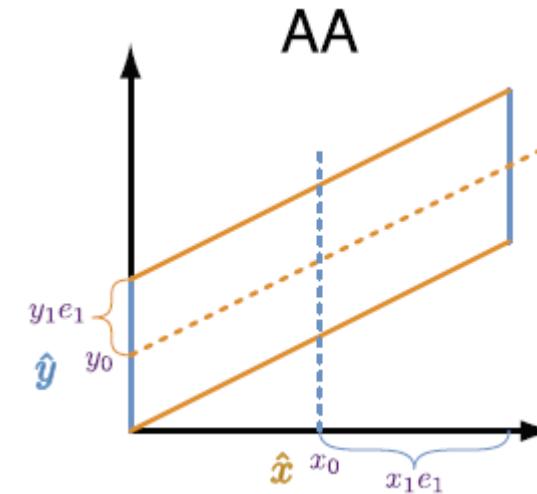
$$x \in [x^L, x^U] = X$$



## Affine Arithmetic (AA)

$$\hat{X} = x_0 + \sum_{i=1}^n x_i \varepsilon_i,$$

$$\begin{aligned} x_0 &= (x^L + x^U)/2, \\ x_1 &= (x^U - x^L)/2, \\ x_i &= 0, \forall i > 1. \end{aligned}$$



- $F(X) \supseteq \mathbf{f}(X) = \{\mathbf{f}(\mathbf{x}) | \mathbf{x} \in X\}$
- Dependency problems: overestimation

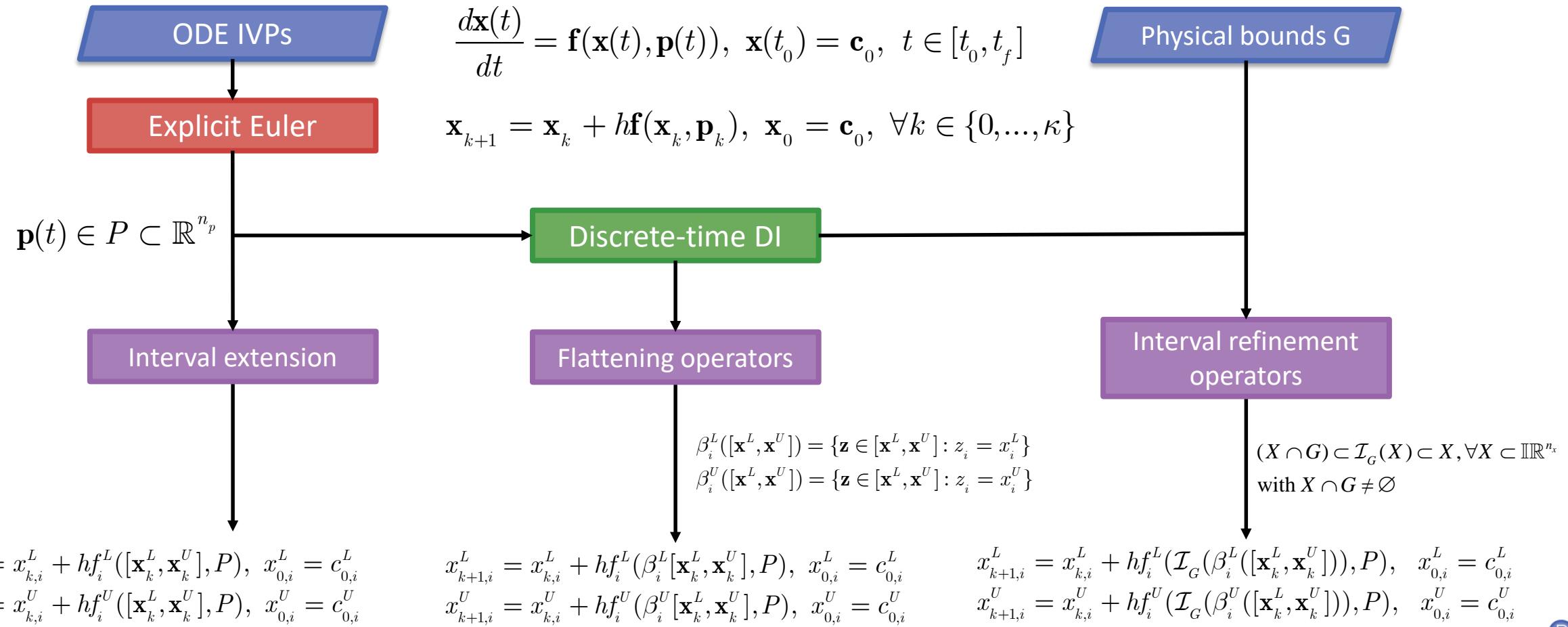
- Keep track of the dependency;
- Enhance the efficacy of interval operations

[4] J. Comba, J. Stolfi, "Affine arithmetic and its applications to computer graphics," *anais do vii sibgrapi*, 9-18 (1993).

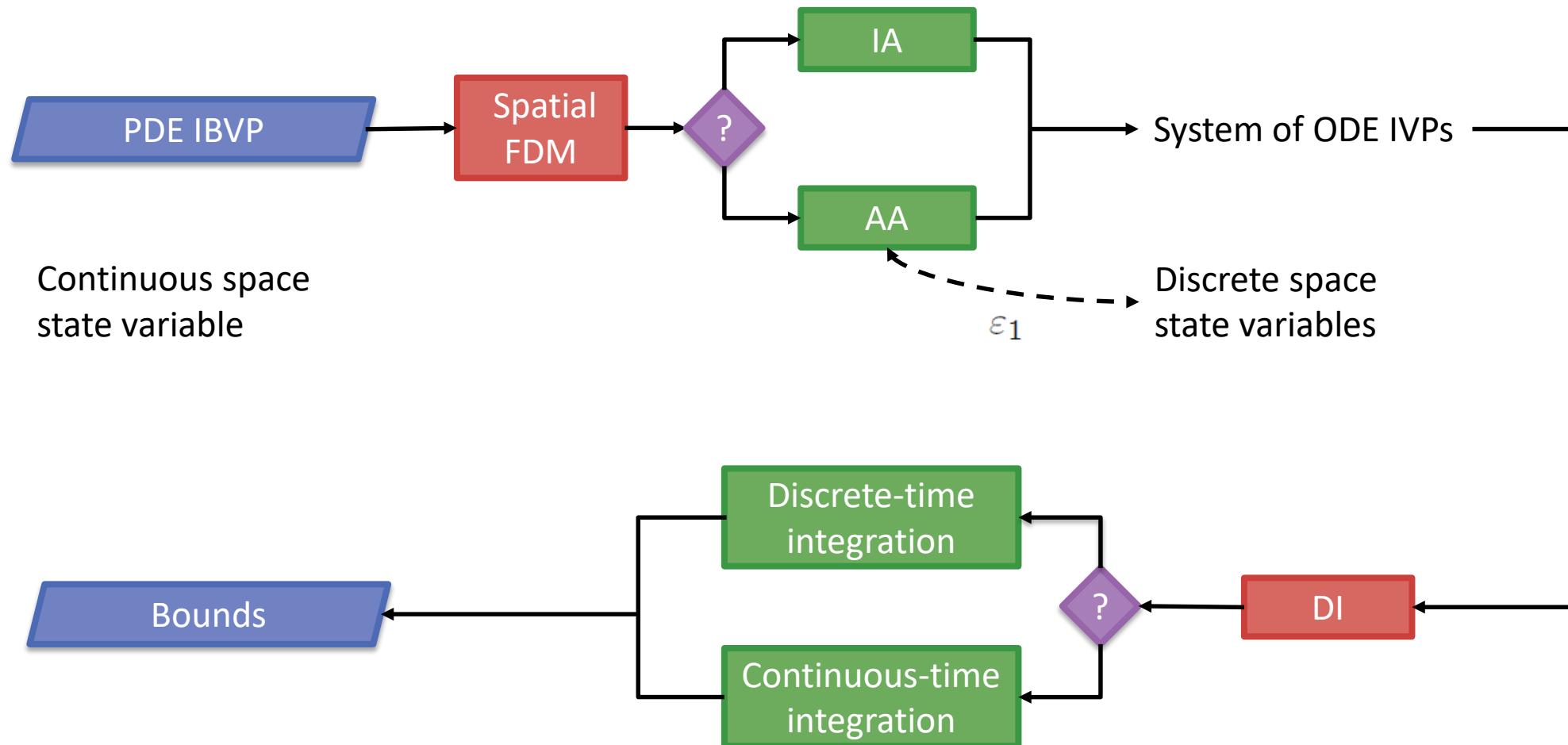
[5] J. Stolfi, L. H. de Figueiredo, "An introduction to affine arithmetic," *Trends in Applied and Computational Mathematics*, 4 (3) (2003) 297–312.

[6] L. H. De Figueiredo, J. Stolfi, "Affine arithmetic: concepts and applications," *Numerical Algorithms*, 37 (1-4) (2004) 147–158.

# Differential Inequalities



# Bounding PDE

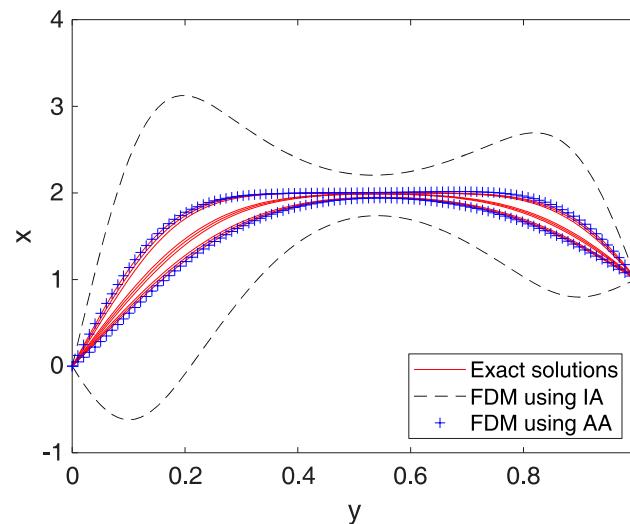


# Convection-Diffusion System

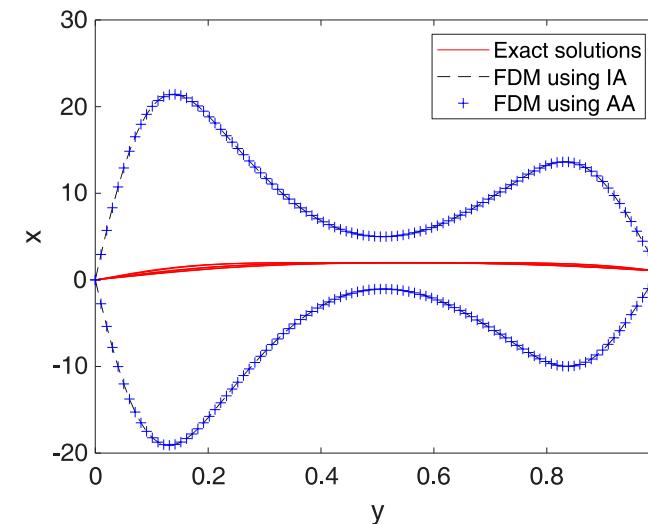
$$\frac{\partial x}{\partial t} = p_1 \frac{\partial^2 x}{\partial y^2} - p_2 \frac{\partial x}{\partial y}, \quad t \in [0, 1], \quad y \in [0, 1]$$

$$p_1 \in [0.1, 0.3] \quad p_2 \in [0.2, 0.6]$$

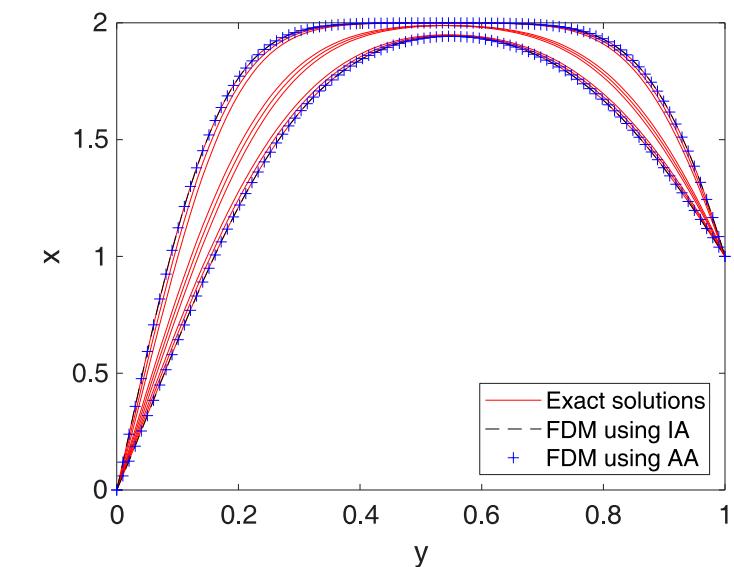
$t = 0.5$



Centered finite difference



Forward finite difference



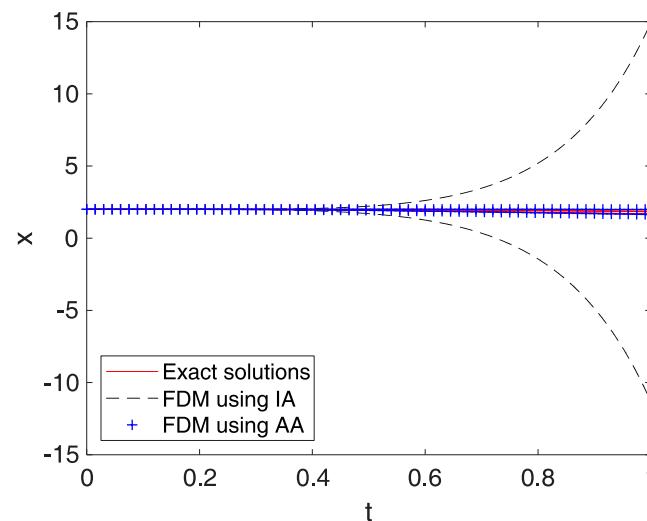
Backward finite difference

# Convection-Diffusion System

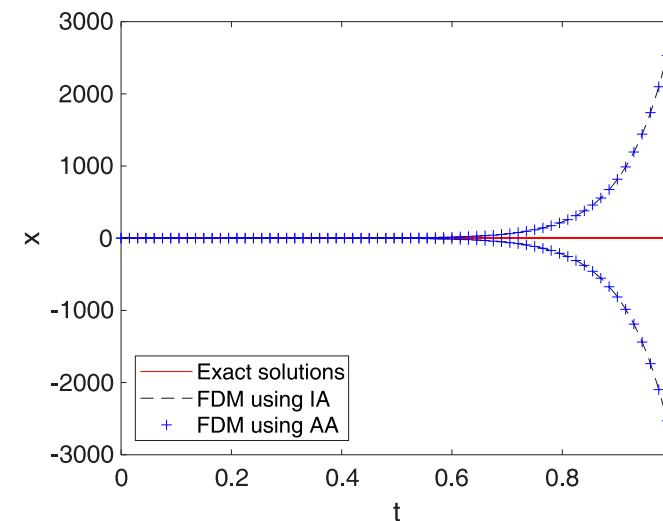
$$\frac{\partial x}{\partial t} = p_1 \frac{\partial^2 x}{\partial y^2} - p_2 \frac{\partial x}{\partial y}, \quad t \in [0, 1], \quad y \in [0, 1]$$

$$p_1 \in [0.1, 0.3] \quad p_2 \in [0.2, 0.6]$$

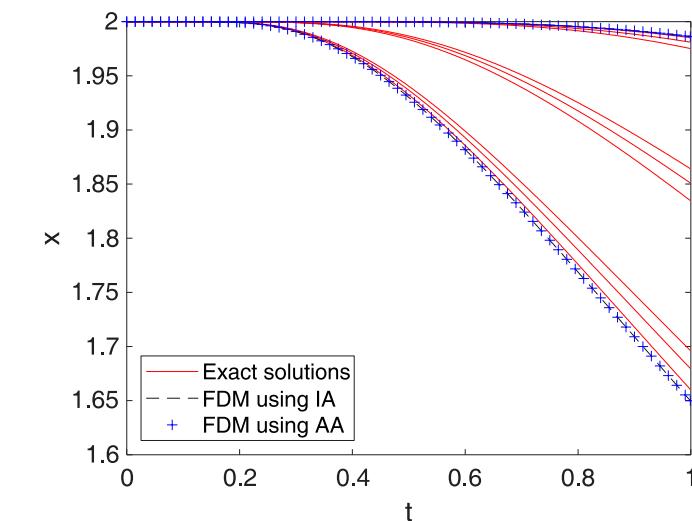
$y = 0.5$



Centered finite difference



Forward finite difference

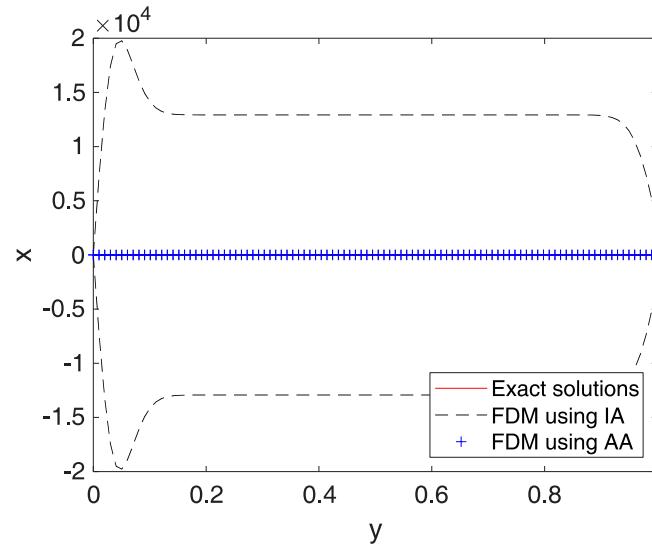


Backward finite difference

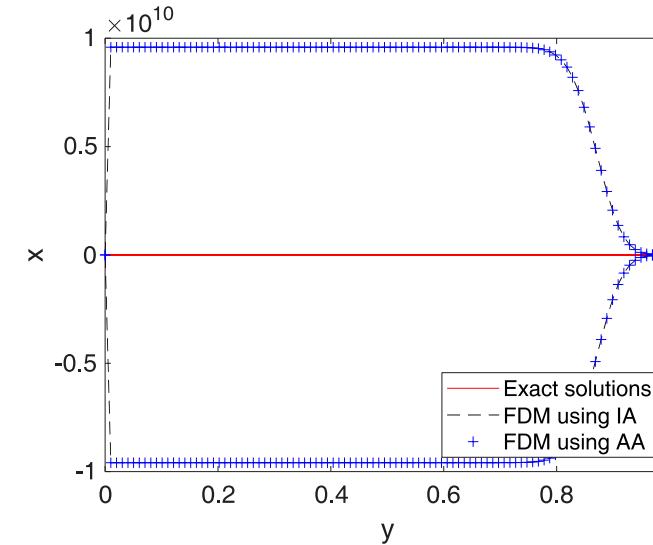
# Convection-Reaction System

$$\frac{\partial x}{\partial t} = -p_1 \frac{\partial x}{\partial y} - p_2 x, \quad t \in [0, 1], \quad y \in [0, 1]. \quad p_1 \in [0.1, 0.3] \quad p_2 \in [0.2, 0.6]$$

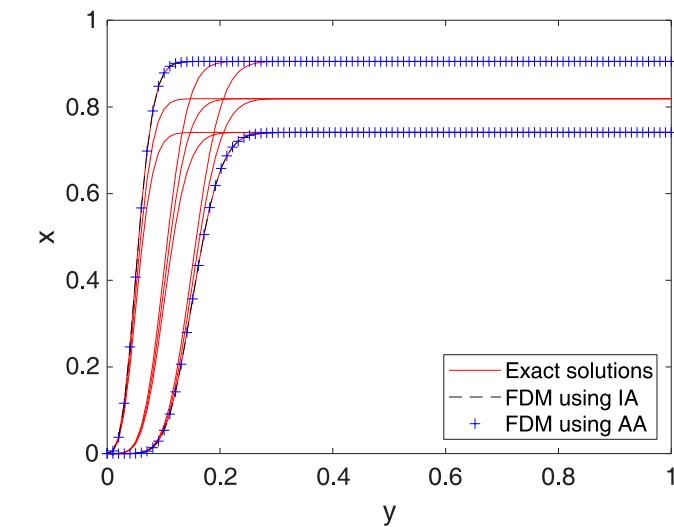
$t = 0.5$



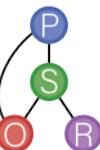
Centered finite difference



Forward finite difference



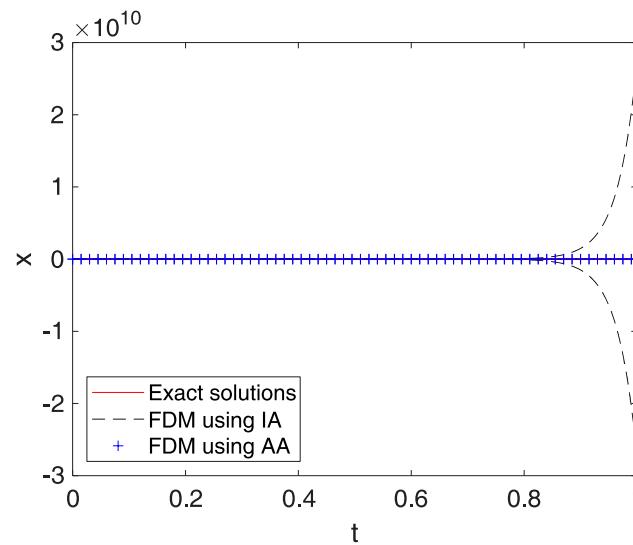
Backward finite difference



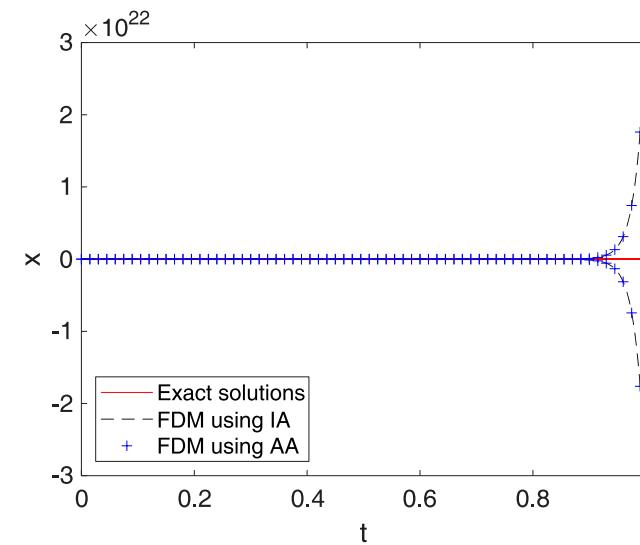
# Convection-Reaction System

$$\frac{\partial x}{\partial t} = -p_1 \frac{\partial x}{\partial y} - p_2 x, \quad t \in [0, 1], \quad y \in [0, 1]. \quad p_1 \in [0.1, 0.3] \quad p_2 \in [0.2, 0.6]$$

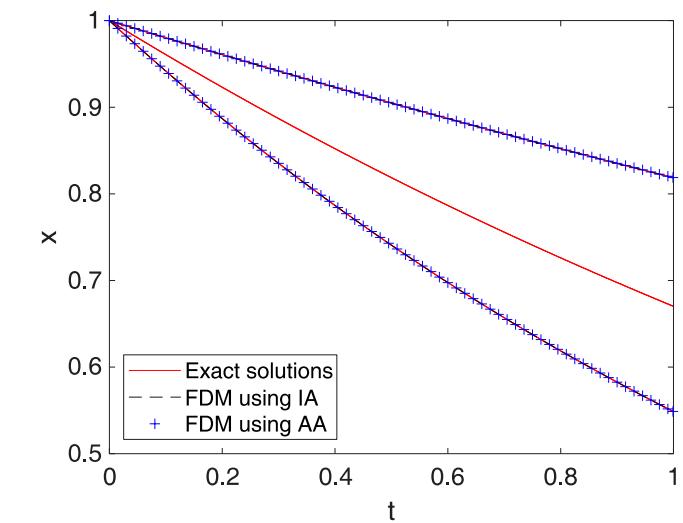
$y = 0.5$



Centered finite difference



Forward finite difference

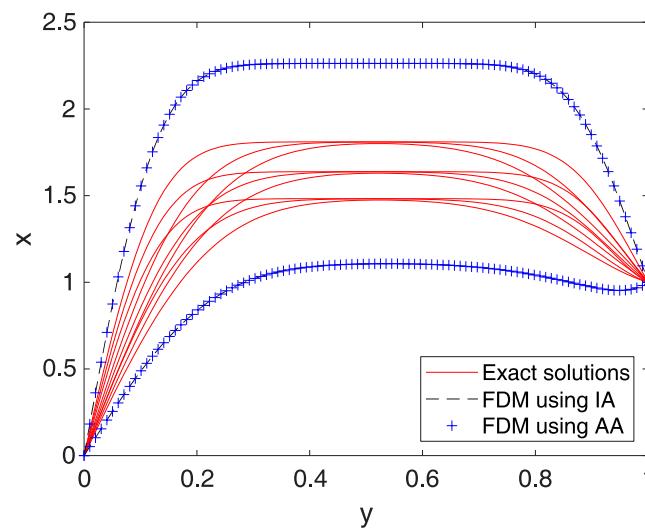


Backward finite difference

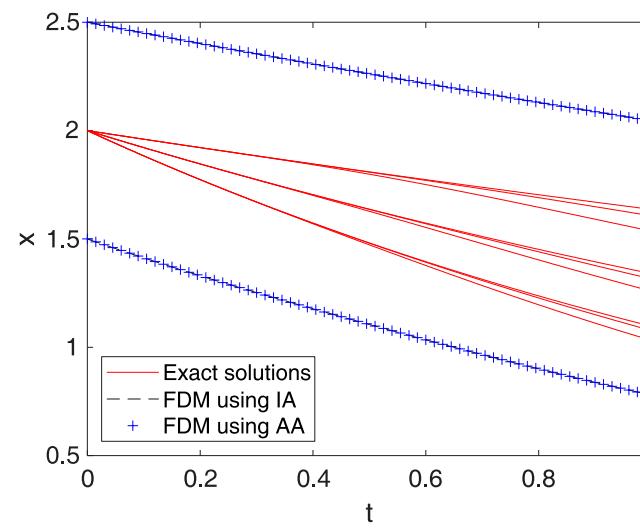
# Diffusion-Reaction System

$$\frac{\partial x}{\partial t} = p_1 \frac{\partial^2 x}{\partial y^2} - p_2 x, \quad t \in [0, 1], \quad y \in [0, 1] \quad p_1 \in [0.01, 0.03] \quad p_2 \in [0.2, 0.6]$$

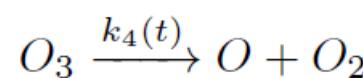
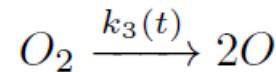
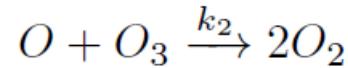
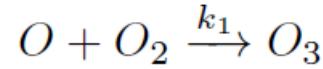
$t = 0.5$



$y = 0.5$



# Coupled IBVPs



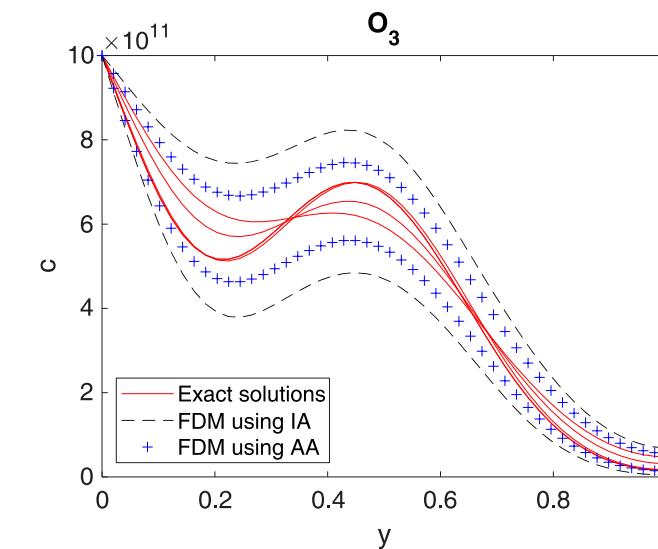
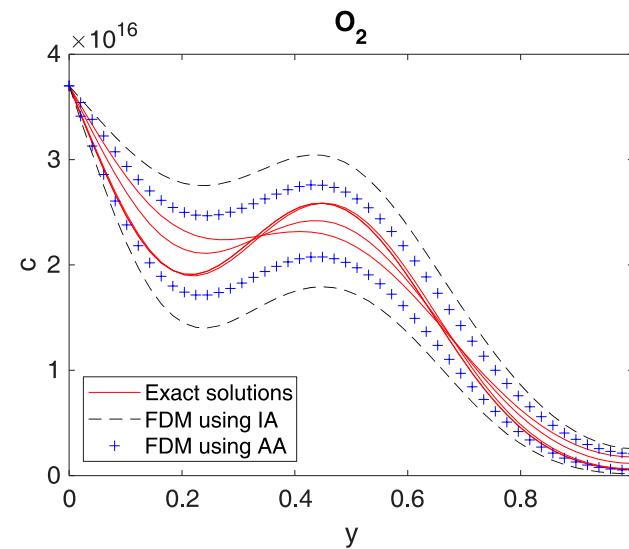
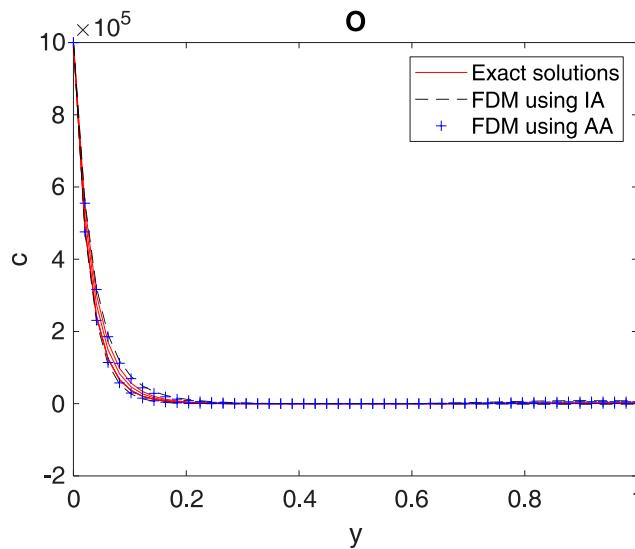
$$\frac{\partial c_O}{\partial t} + u_1 \frac{\partial c_O}{\partial y} = D_1 \frac{\partial^2 c_O}{\partial y^2} + r_{c_O},$$

$$\frac{\partial c_{O_2}}{\partial t} + u_2 \frac{\partial c_{O_2}}{\partial y} = D_2 \frac{\partial^2 c_{O_2}}{\partial y^2} + r_{c_{O_2}},$$

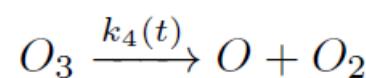
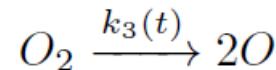
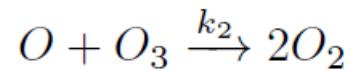
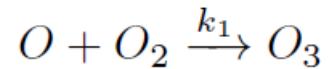
$$\frac{\partial c_{O_3}}{\partial t} + u_3 \frac{\partial c_{O_3}}{\partial y} = D_3 \frac{\partial^2 c_{O_3}}{\partial y^2} + r_{c_{O_3}},$$

$$u \in [4e-3, 6e-3]$$

$$D \in [4e-3, 6e-3]$$



# Coupled IBVPs



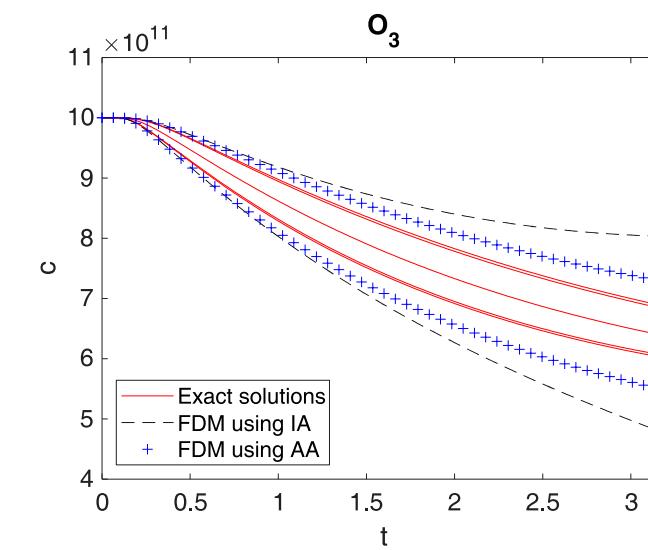
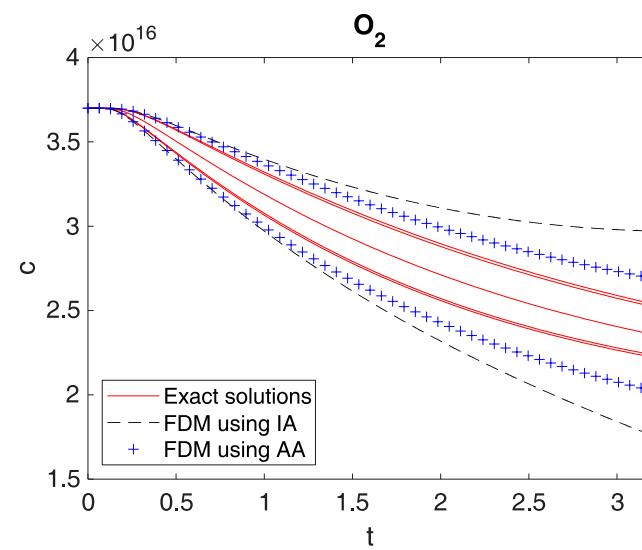
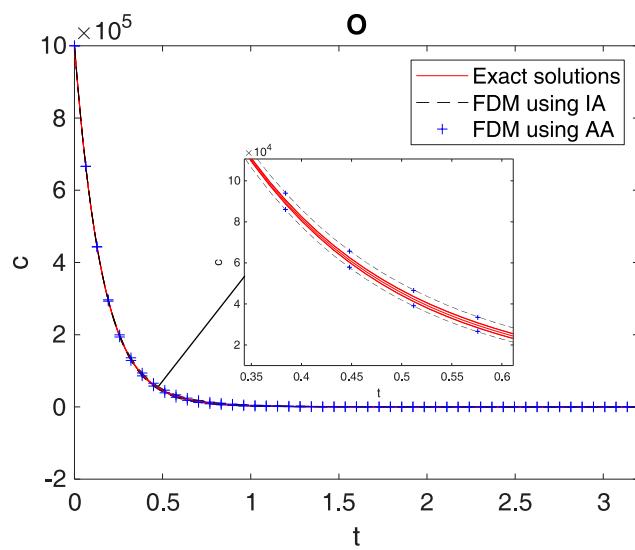
$$\frac{\partial c_O}{\partial t} + u_1 \frac{\partial c_O}{\partial y} = D_1 \frac{\partial^2 c_O}{\partial y^2} + r_{c_O},$$

$$\frac{\partial c_{O_2}}{\partial t} + u_2 \frac{\partial c_{O_2}}{\partial y} = D_2 \frac{\partial^2 c_{O_2}}{\partial y^2} + r_{c_{O_2}},$$

$$\frac{\partial c_{O_3}}{\partial t} + u_3 \frac{\partial c_{O_3}}{\partial y} = D_3 \frac{\partial^2 c_{O_3}}{\partial y^2} + r_{c_{O_3}},$$

$$u \in [4e-3, 6e-3]$$

$$D \in [4e-3, 6e-3]$$



# Transport Model in Tumor

- Fluid Transport Model

- Darcy's law  $u = -K \frac{dp}{dr}$
- Continuity equation  $\nabla \cdot \mathbf{u} = \phi_v(r)$

$$\left. \begin{aligned} \phi_v(r) &= L_p \frac{S}{V} (p_v - p) \\ \end{aligned} \right\} \nabla^2 p = \frac{\alpha^2}{R^2} (p - p_{ss})$$

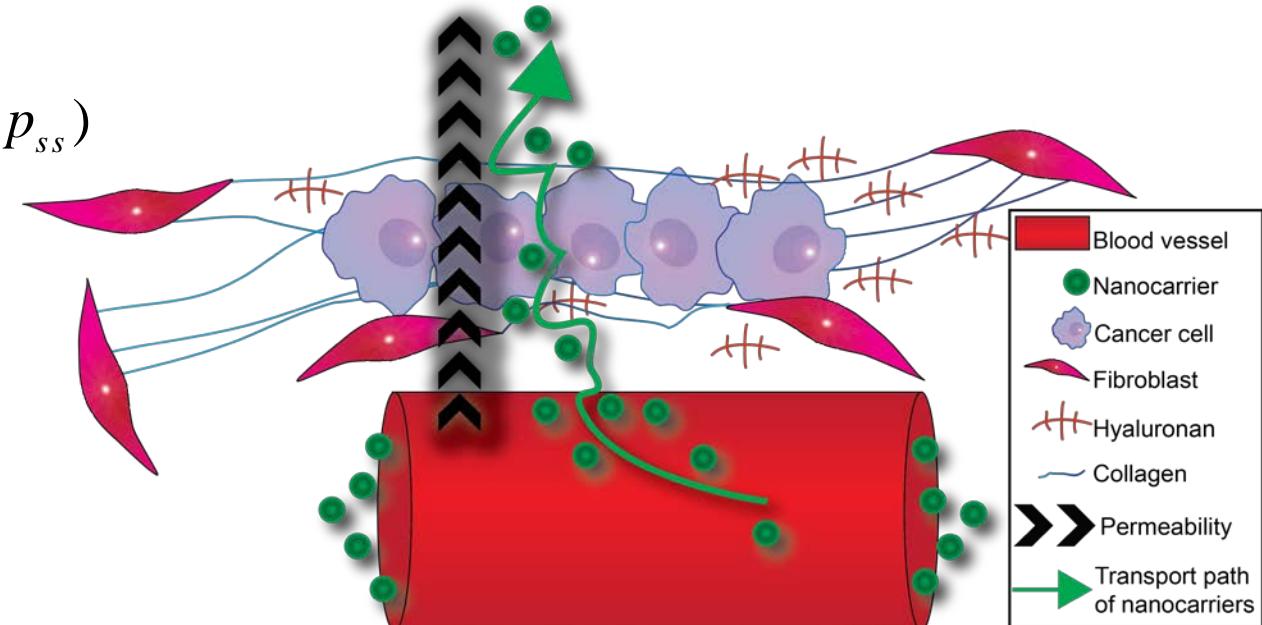
- Solute Transport Model

$$\frac{\partial C}{\partial t} + \frac{1}{r^2} \frac{\partial (r^2 u C)}{\partial r} = D \frac{1}{r^2} \frac{\partial}{\partial r} (r^2 \frac{\partial C}{\partial r}) + \phi_s$$

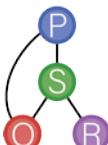
Convection      Diffusion

- Pore Theory

$$L_p = \frac{\gamma r_o^2}{8\mu L} \quad P = \frac{\gamma H D_o}{L} \quad \sigma = 1 - W$$

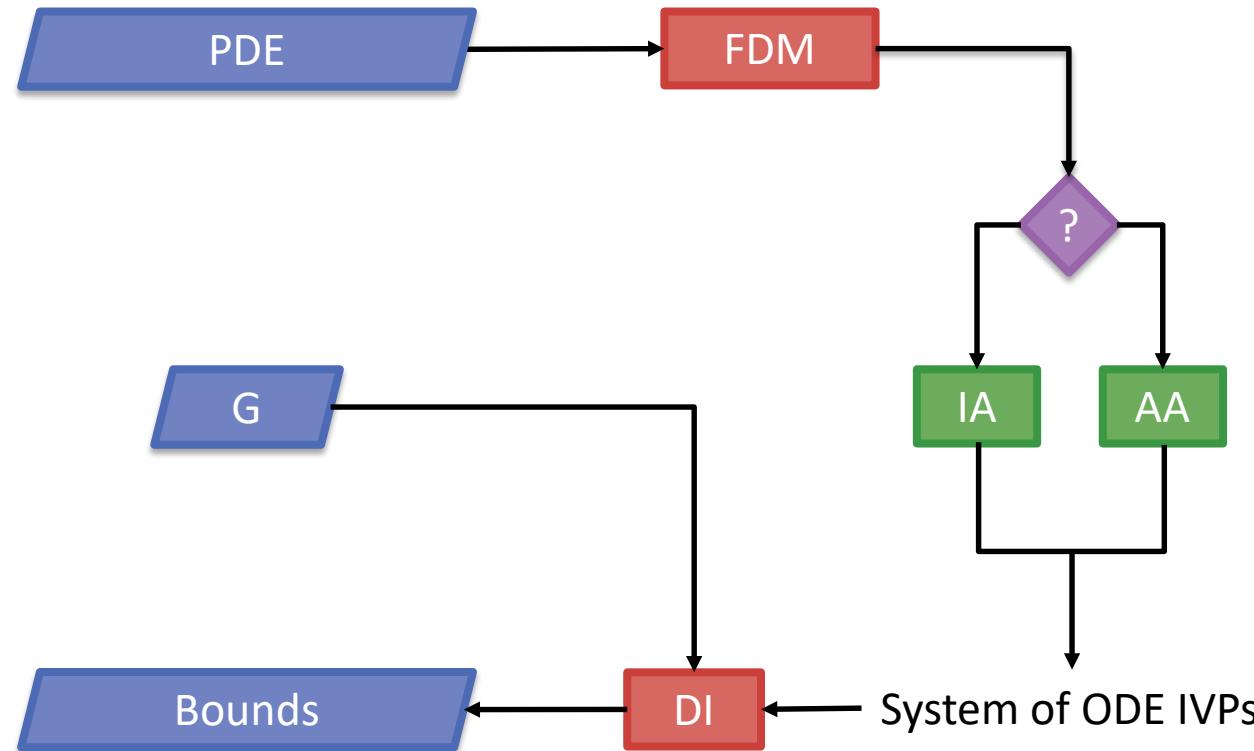


[9] J. D. Martin, M. Panagi, C. Wang, T. T. Khan, M. R. Martin, C. Voutouri, K. Toh, P. Papageorgis, F. Mpekris, C. Polydorou, et al., "Dexamethasone increases cisplatin-loaded nanocarrier delivery and efficacy in metastatic breast cancer by normalizing the tumor microenvironment," *ACS nano*.

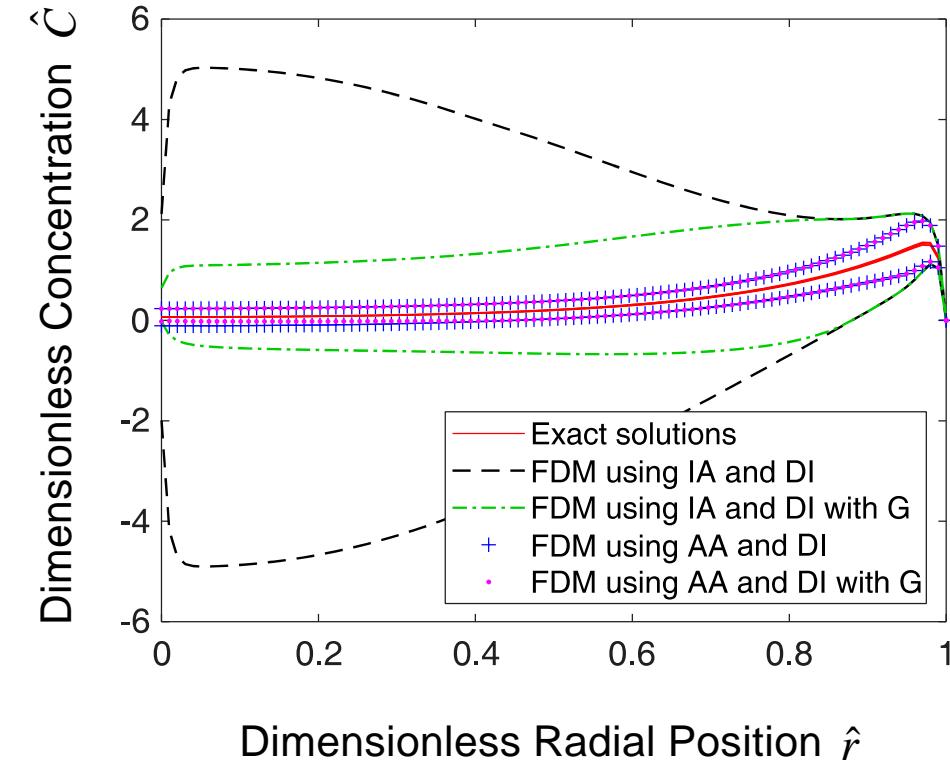


# Transport Model in Tumor

$$K \in [2.75\text{E-}7, 2.85\text{E-}7] \quad L_p \in [1.65\text{E-}6, 1.75\text{E-}6]$$

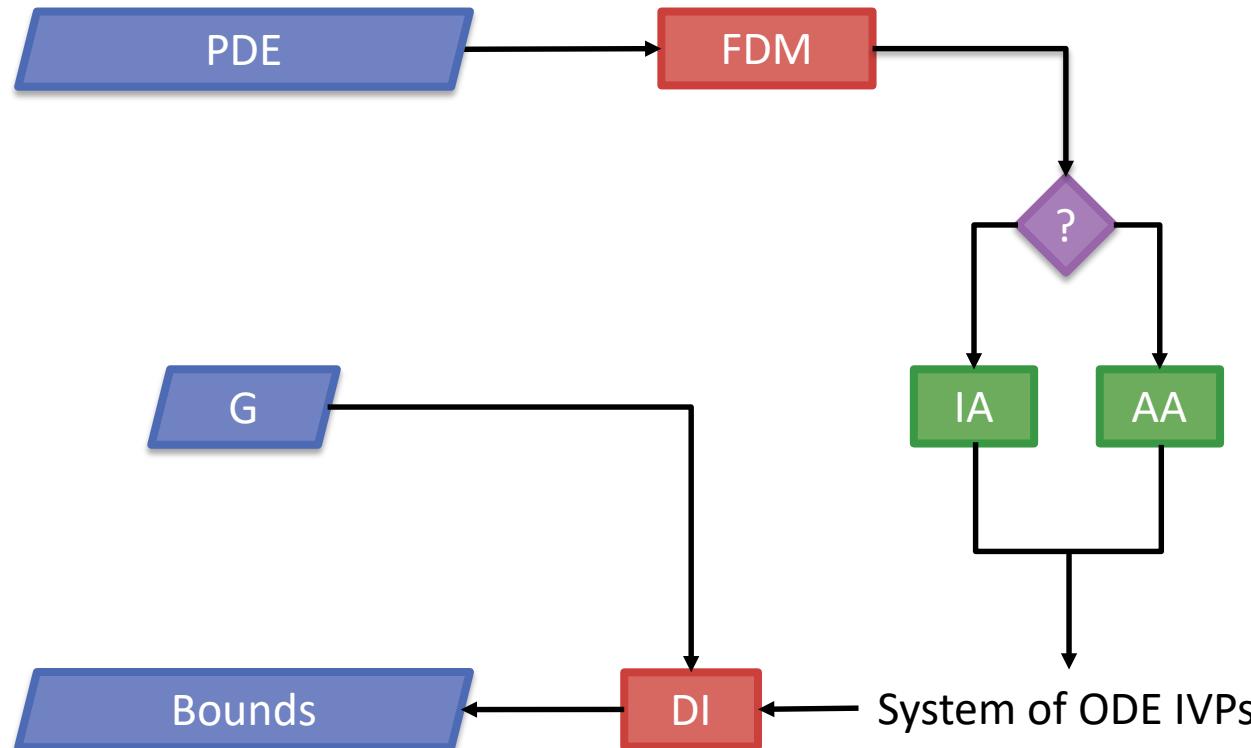


Concentration at 30 min post injection

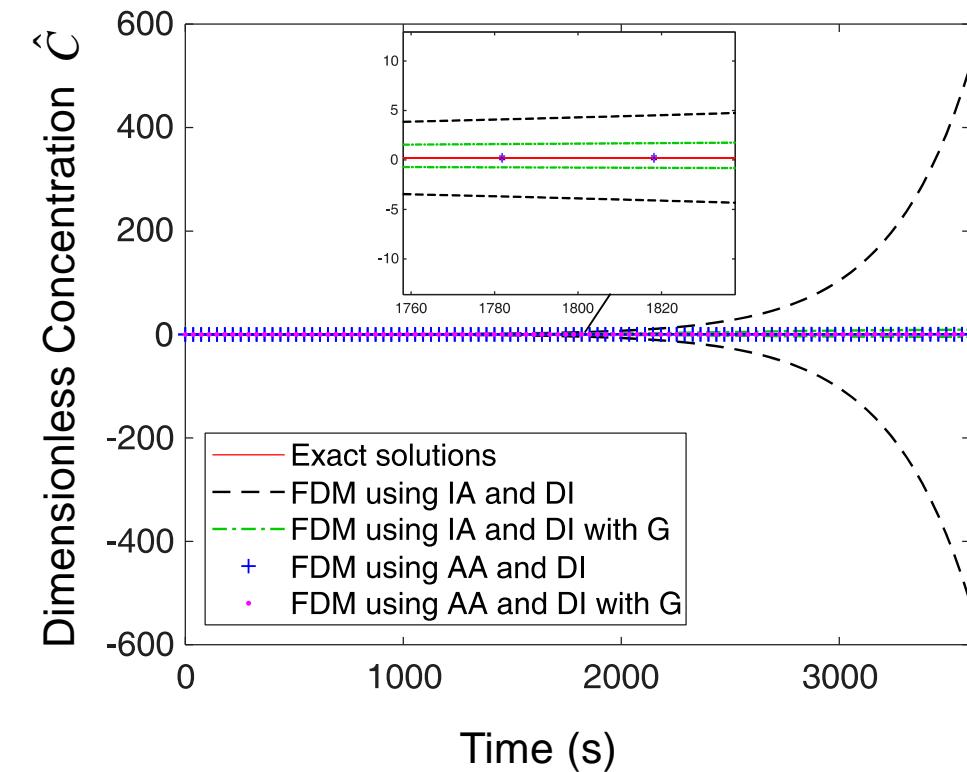


# Transport Model in Tumor

$$K \in [2.75\text{E-}7, 2.85\text{E-}7] \quad L_p \in [1.65\text{E-}6, 1.75\text{E-}6]$$

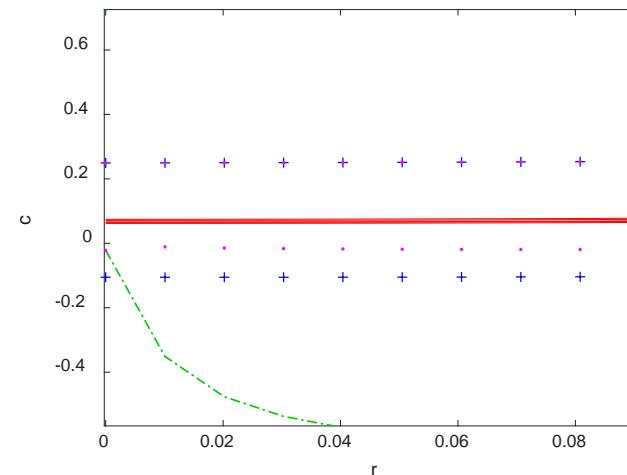


Concentration at medium radius

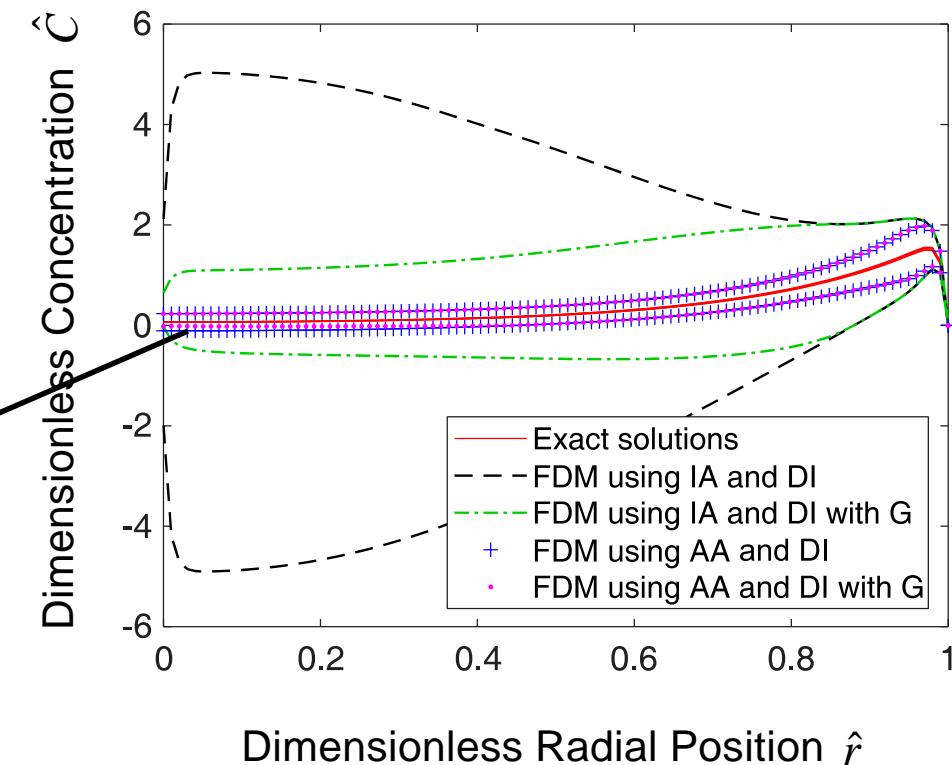


# Transport Model in Tumor

Method	Time (s)
Exact solutions	0.156898524
FDM using IA and DI	4.366923814
FDM using IA and DI with G	212.759461536
FDM using AA and DI	4.033772619
FDM using AA and DI with G	201.610427039



Concentration at 30 min post injection



# Summary

	Conv-Diff	Conv-Rxn	Diff-Rxn	Tumor Model
FD	$V_{IA}=V_{AA}$	$V_{IA}=V_{AA}$	X	Unstable
BD	$V_{IA}=V_{AA}$	$V_{IA}=V_{AA}$	X	$V_{IA}>V_{AA}$
CD	$V_{IA}>V_{AA}$	$V_{IA}>V_{AA}$	$V_{IA}>V_{AA}$	Unstable

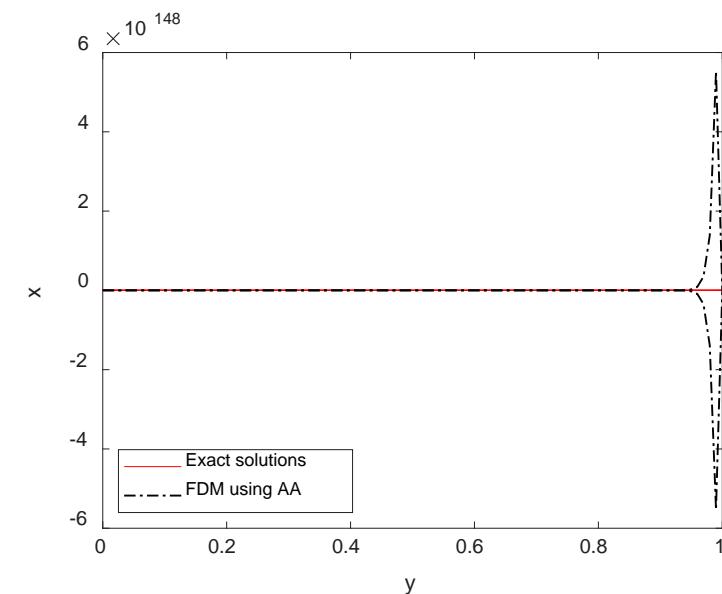
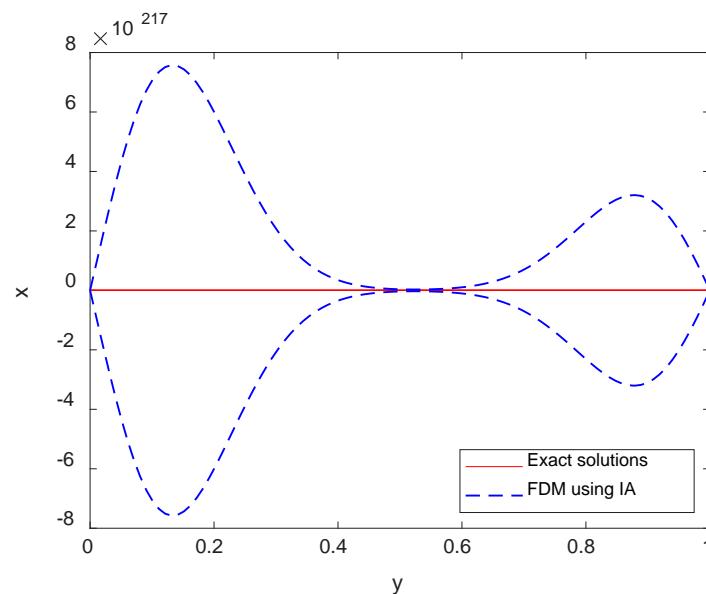
$$\frac{\partial x}{\partial t} = p_1 \frac{\partial^2 x}{\partial y^2} - p_2 \frac{\partial x}{\partial y}, \quad t \in [0, 1], \quad y \in [0, 1]$$

$$p_1 \in [0.1, 0.3] \quad p_2 \in [0.2, 0.6]$$

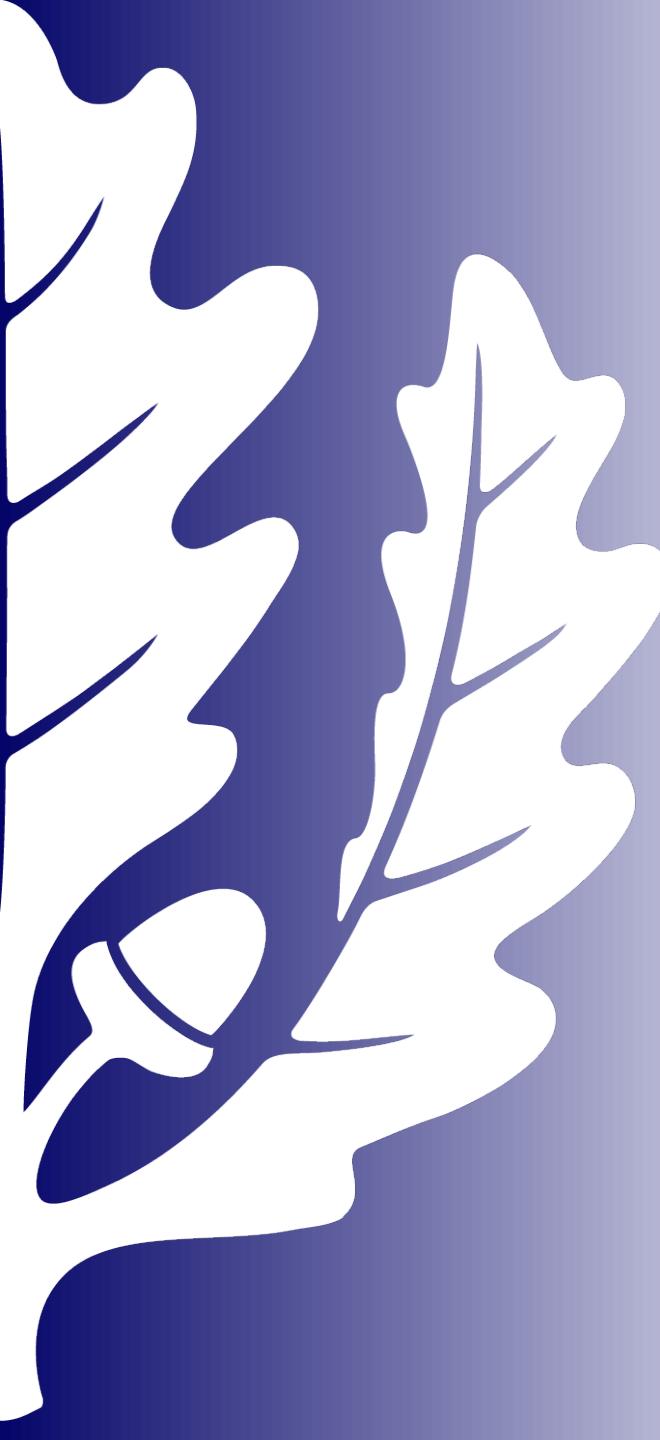
Backward finite difference



Interval Extension



# Acknowledgements



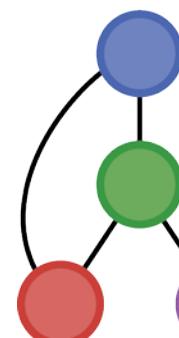
## Group members

- Prof. Matthew D. Stuber,
- Matthew Wilhelm,
- William Hale
- Other group members

## Funding

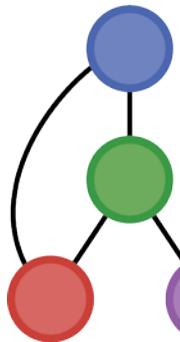
- University of Connecticut
- National Science Foundation, Award No.: 1560072, 1706343, 1932723

Any opinions, findings and conclusions or recommendations expressed in this material are those of the authors and do not necessarily reflect the views of the National Science Foundation



Process Systems and  
Operations Research  
Laboratory

Any questions?

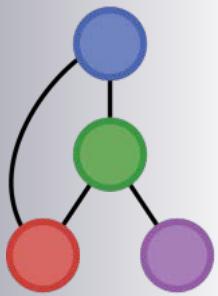


Process Systems and  
Operations Research  
Laboratory



# Backup Slides

# Discrete-time Differential Inequalities



$$\frac{dx(t)}{dt} = f(x(t), \pi(t)), \quad x(t_0) = c_0, \quad t \in [t_0, t_f]$$

Explicit Euler

$$x_{k+1} = x_k + hf(x_k, \pi_k), \quad x_0 = c_0, \quad \forall k \in \{0, \dots, \kappa\}$$

Interval extension

$$\begin{aligned} x_{k+1,i}^L &= x_{k,i}^L + hf_i^L([x_k^L, x_k^U], \Pi), \quad x_{0,i}^L = c_{0,i}^L \\ x_{k+1,i}^U &= x_{k,i}^U + hf_i^U([x_k^L, x_k^U], \Pi), \quad x_{0,i}^U = c_{0,i}^U \end{aligned}$$

Flattening operators

$$\beta_i^L([x^L, x^U]) = \{z \in [x^L, x^U] : z_i = x_i^L\}$$

$$\beta_i^U([x^L, x^U]) = \{z \in [x^L, x^U] : z_i = x_i^U\}$$

$$\begin{aligned} x_{k+1,i}^L &= x_{k,i}^L + hf_i^L(\beta_i^L[x_k^L, x_k^U], \Pi), \quad x_{0,i}^L = c_{0,i}^L \\ x_{k+1,i}^U &= x_{k,i}^U + hf_i^U(\beta_i^U[x_k^L, x_k^U], \Pi), \quad x_{0,i}^U = c_{0,i}^U \end{aligned}$$

Prior enclosure G

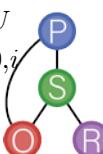
$$\begin{aligned} x_{k+1,i}^L &= x_{k,i}^L + hf_i^L(\mathcal{I}_G(\beta_i^L([x_k^L, x_k^U])), \Pi), \quad x_{0,i}^L = c_{0,i}^L \\ x_{k+1,i}^U &= x_{k,i}^U + hf_i^U(\mathcal{I}_G(\beta_i^U([x_k^L, x_k^U])), \Pi), \quad x_{0,i}^U = c_{0,i}^U \end{aligned}$$

- For continuous-time system, a trajectory  $x(t; c_0, \pi)$  cannot leave the enclosure  $[x^L(t), x^U(t)]$  without crossing its boundary
- Thus, at any  $t \in [t_0, t_f]$ , it is only necessary for  $x_i^L(t)$  to decrease faster than all trajectories  $x_i(t; c_0, \pi)$  that are already incident on the  $i^{\text{th}}$  lower face of  $[x^L(t), x^U(t)]$ .

Example:  $[x^L, x^U] = \{[1, 5], [2, 4], [1, 7]\}$

$$\beta_2^L([x^L, x^U]) = \{[1, 5], [2, 2], [1, 7]\}$$

$$\beta_2^U([x^L, x^U]) = \{[1, 5], [4, 4], [1, 7]\}$$



# I.C. and B.C.

$$\frac{\partial x}{\partial t} = p_1 \frac{\partial^2 x}{\partial y^2} - p_2 \frac{\partial x}{\partial y}, \quad t \in [0, 1], \quad y \in [0, 1]$$

$$x(y, 0) = 2$$

$$x(0, t) = 0, \quad x(1, t) = 1$$

$$\frac{\partial x}{\partial t} = -p_1 \frac{\partial x}{\partial y} - p_2 x, \quad t \in [0, 1], \quad y \in [0, 1]$$

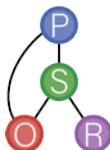
$$x(y, 0) = 1$$

$$x(0, t) = 0, \quad \frac{dx}{dy}|_{y=1} = 0$$

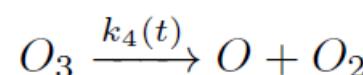
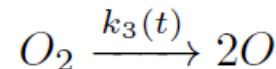
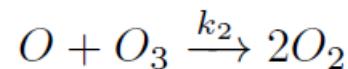
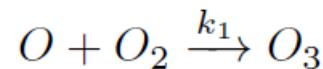
$$\frac{\partial x}{\partial t} = p_1 \frac{\partial^2 x}{\partial y^2} - p_2 x, \quad t \in [0, 1], \quad y \in [0, 1]$$

$$x(y, 0) = 2$$

$$x(0, t) = 0, \quad x(1, t) = 1$$



# Coupled IBVPs



$$\frac{\partial c_O}{\partial t} + u_1 \frac{\partial c_O}{\partial y} = D_1 \frac{\partial^2 c_O}{\partial y^2} + r_{c_O}, \quad u \in [4e-3, 6e-3]$$

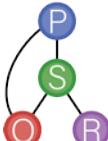
$$\frac{\partial c_{O_2}}{\partial t} + u_2 \frac{\partial c_{O_2}}{\partial y} = D_2 \frac{\partial^2 c_{O_2}}{\partial y^2} + r_{c_{O_2}}, \quad D \in [4e-3, 6e-3]$$

$$\frac{\partial c_{O_3}}{\partial t} + u_3 \frac{\partial c_{O_3}}{\partial y} = D_3 \frac{\partial^2 c_{O_3}}{\partial y^2} + r_{c_{O_3}},$$

$$r_{c_O} = \frac{dc_O}{dt} = -k_1 c_O c_{O_2} - k_2 c_O c_{O_3} + 2k_3(t) c_{O_2} + k_4(t) c_{O_3},$$

$$r_{c_{O_2}} = \frac{dc_{O_2}}{dt} = -k_1 c_O c_{O_2} + k_2 c_O c_{O_3} - k_3(t) c_{O_2} + k_4(t) c_{O_3},$$

$$r_{c_{O_3}} = \frac{dc_{O_3}}{dt} = k_1 c_O c_{O_2} - k_2 c_O c_{O_3} - k_4(t) c_{O_3}.$$



# Coupled IBVPs

Here, the rate constants  $k_1$  and  $k_2$  are constants:  $k_1 = 1.63 \times 10^{-16}$ ,  $k_2 = 4.66 \times 10^{-16}$ . The other two rate constants  $k_3(t)$  and  $k_4(t)$  follow a two-day periodical cycle as:

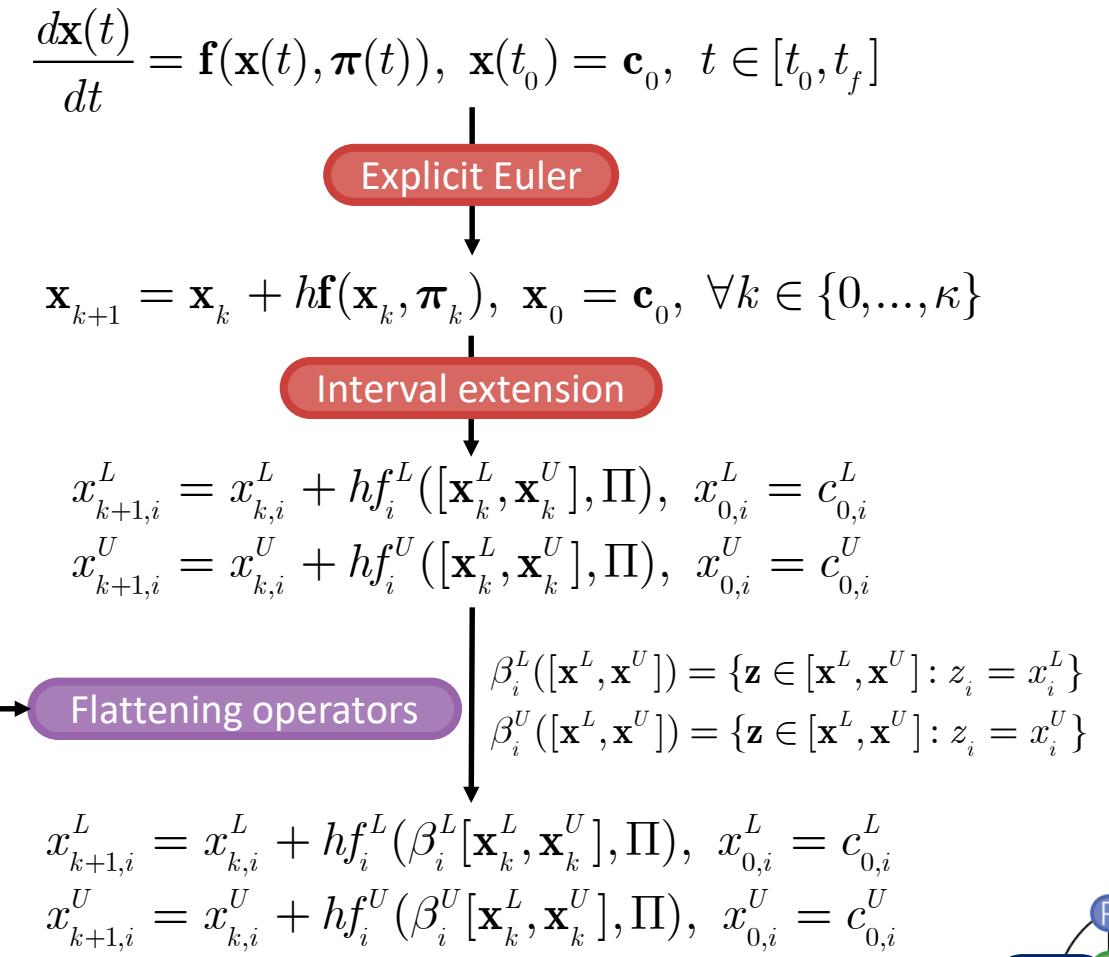
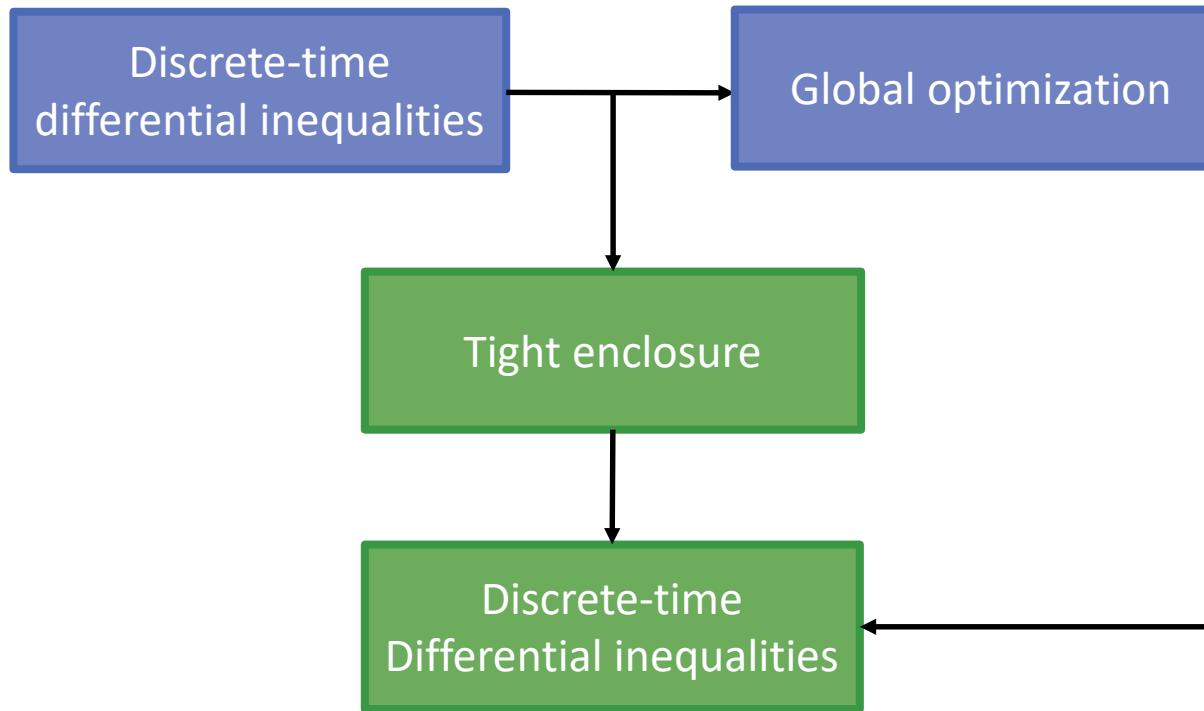
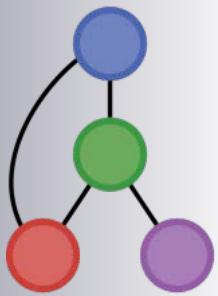
$$k_i(t) = \begin{cases} \exp(-c_i / \sin(\omega t)) & \text{if } \sin(\omega t) \geq 0 \\ 0 & \text{if } \sin(\omega t) > 0, \quad i = 3, 4, \end{cases}$$

where  $c_3 = 22.62$ ,  $c_4 = 7.601$ , and  $\omega = \pi/43200 \text{ s}^{-1}$ . The rate constants  $k_3$  and  $k_4$  will increase quickly at the beginning ( $t = 0$ ), rise to a peak at noon ( $t = 6 \times 3600 \text{ s}$ ), then drop to zero at sunset ( $t = 12 \times 3600 \text{ s}$ ). The initial conditions of this ozone model is given by

$$\begin{aligned} c_O(x, 0) &= \begin{cases} 10^6 & \text{if } 0.3 \leq x \leq 0.6 \\ 0 & \text{otherwise,} \end{cases} \\ c_{O_2}(x, 0) &= \begin{cases} 3.7 \times 10^{16} & \text{if } 0.3 \leq x \leq 0.6 \\ 0 & \text{otherwise,} \end{cases} \\ c_{O_3}(x, 0) &= \begin{cases} 10^{12} & \text{if } 0.3 \leq x \leq 0.6 \\ 0 & \text{otherwise.} \end{cases} \end{aligned}$$

At the bottom of the atmosphere layer, the boundary conditions are given by  $c_O(0, t) = 10^6$ ,  $c_{O_2}(0, t) = 3.7 \times 10^{16}$ ,  $c_{O_3}(0, t) = 10^6$ , while at the top of the atmosphere, we assume the no-flux boundary conditions given by  $\frac{dc_O}{dy}\Big|_{y=1} = \frac{dc_{O_2}}{dy}\Big|_{y=1} = \frac{dc_{O_3}}{dy}\Big|_{y=1} = 0$ .

# Discrete-time Differential Inequalities



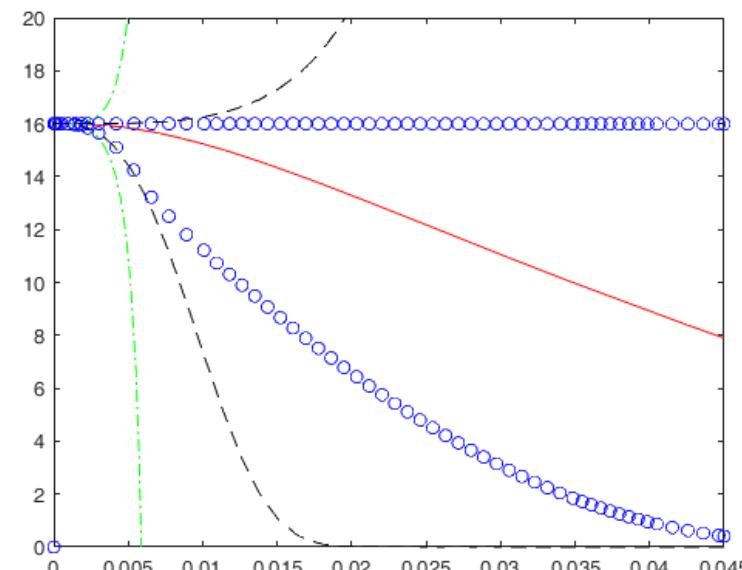
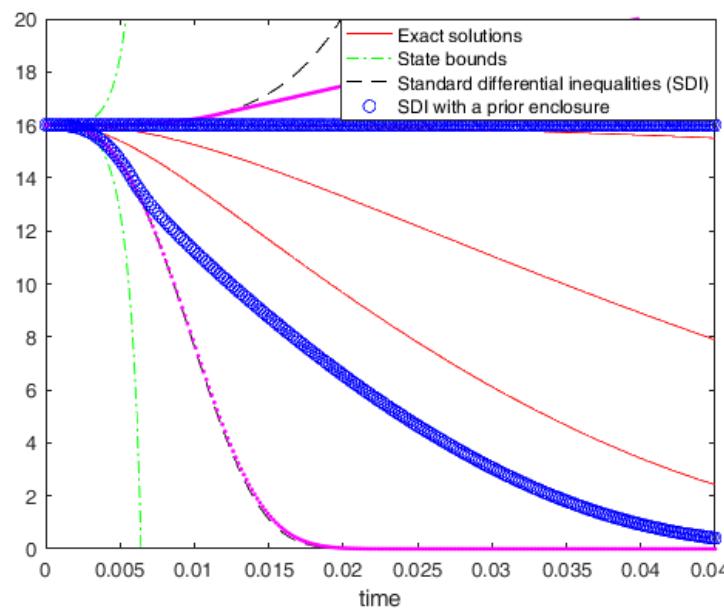
[9] X. Yang and J. K. Scott, "Efficient reachability bounds for discrete-time nonlinear systems by extending the continuous-time theory of differential inequalities," in 2018 Annual American Control Conference (ACC), pp. 6242-6247, IEEE, 2018.

# Discrete-time DI vs Continuous-time DI

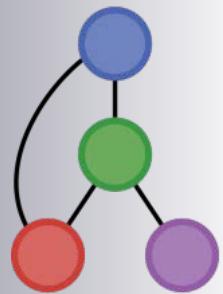


Discrete-time methods	Time per step	Time
exact	0.0001506623	0.035599025
Interval	<b>0.001027332844</b>	<b>0.241191195</b>
SDI	0.000212136452	0.048447647
IGB	0.0005043008	0.122923914
BIG	0.000196413496	0.052653721
MG	0.000389502404	0.096926013

Continuous-time methods	Time	Steps	Time per step	Literature
exact	0.167765429	44	0.0038128507	0.004
Interval	0.28842996	63	0.0045782533	
SDI	0.374489244	1160	0.0003228356	0.014
MG	0.097186758	64	0.0015185431	0.055



# Hukuhara = Affine



$$X = [x^L, x^U], Y = [y^L, y^U]$$

$$m_x = \frac{x^L + x^U}{2}, r_x = \frac{x^U - x^L}{2}, m_y = \frac{y^L + y^U}{2}, r_y = \frac{y^U - y^L}{2}$$

$$\bar{X} = m_x + r_x \epsilon$$

$$\bar{Y} = m_y + r_y \epsilon$$

when  $r_x \geq r_y$

$$\begin{aligned} \bar{X} - \bar{Y} &= (m_x + r_x \epsilon) - (m_y + r_y \epsilon) \\ &= (m_x - m_y) + (r_x - r_y) \epsilon \\ &= \left( \frac{x^L + x^U}{2} - \frac{y^L + y^U}{2} \right) + \left( \frac{x^U - x^L}{2} - \frac{y^U - y^L}{2} \right) \epsilon \\ &= \frac{1}{2}(x^L - y^L + x^U - y^U) + \frac{1}{2}(x^U - y^U - x^L + y^L)[-1,1] \\ &= \frac{1}{2}(x^L - y^L + x^U - y^U) + \frac{1}{2}[-x^U + y^U + x^L - y^L, x^U - y^U - x^L + y^L] \\ &= [x^L - y^L, x^U - y^U] \end{aligned}$$

when  $r_x < r_y$

$$\begin{aligned} \bar{X} - \bar{Y} &= (m_x + r_x \epsilon) - (m_y + r_y \epsilon) \\ &= (m_x - m_y) + (r_x - r_y) \epsilon \\ &= \left( \frac{x^L + x^U}{2} - \frac{y^L + y^U}{2} \right) + \left( \frac{x^U - x^L}{2} - \frac{y^U - y^L}{2} \right) \epsilon \\ &= \frac{1}{2}(x^L - y^L + x^U - y^U) + \frac{1}{2}(x^U - y^U - x^L + y^L)[-1,1] \\ &= \frac{1}{2}(x^L - y^L + x^U - y^U) + \frac{1}{2}[x^U - y^U - x^L + y^L, -x^U + y^U + x^L - y^L] \\ &= [x^U - y^U, x^L - y^L] \end{aligned}$$

