James B. Rawlings

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University of Wisconsin–Madison

September 6, 2007
Outline

1. Research group overview

2. Research project opportunities
   - Modeling and control of multi-component, dispersed-phase systems
   - Stochastic methods in chemical reaction engineering
   - New and continuing research projects

3. Closing
The best, quick overview of our research activities is provided by the website: http://jbrwww.che.wisc.edu

The best way to get a feel for what we do is to talk to the graduate students. They are very friendly!
<table>
<thead>
<tr>
<th>PROJECT</th>
<th>RESEARCHER</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. On-line image processing for particle size and shape distribution</td>
<td>P. Larsen Ph.D.</td>
</tr>
<tr>
<td>2. Multi-scale modeling of solid-phase formation and growth</td>
<td>E. Mastny Ph.D.</td>
</tr>
<tr>
<td>(joint with Prof. dePablo)</td>
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<tr>
<td>3. Performance monitoring for nonlinear model predictive control</td>
<td>M. Rajamani Ph.D.</td>
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<td>4. Virus modeling</td>
<td>S. Hensel M.S.</td>
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<tr>
<td>(joint with Prof. Yin)</td>
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<td>5. Octave: computational modeling</td>
<td>J. Eaton Postdoc</td>
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<td>6. Implementing distributed large-scale model predictive control</td>
<td>B. Stewart Ph.D.</td>
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<tr>
<td>7. Optimizing economic performance with model predictive control</td>
<td>R. Amrit Ph.D.</td>
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<td>8. Data based disturbance modeling</td>
<td>F. Lima Postdoc</td>
</tr>
<tr>
<td>9. Modeling and control of multi-component, dispersed-phase systems</td>
<td>new</td>
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<tr>
<td>10. Stochastic methods in chemical reaction engineering</td>
<td>new</td>
</tr>
</tbody>
</table>
Challenges for dispersed-phase systems

- **Objectives:** Control size distribution, shape, internal structure, purity.
- **Challenges:** Measurement limitations, Lack of manipulated variables.

Needles, glycine, \(\alpha\) polymorph, glycine, \(\gamma\) polymorph
Population balances and stochastic simulation

**Stochastic Solution**
Average of 100 Simulations

**Deterministic Solution**
Via Orthogonal Collocation

Discrete particle sizes
Integer-valued particle accounting

Continuous particle sizes
Real-valued particle accounting
Multi-phase CFD

http://www.uni-magdeburg.de/isut/LSS/Forschung/TOP4/2phaseCFD.gif
Advanced image analysis for needles$^1,^2$

Original image

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$^1$Larsen, Rawlings, and Ferrier, ChE Sci, 2006
$^2$Patent filed by WARF, P05340US
Advanced image analysis for needles\textsuperscript{1,2}

Original image

Linear feature detection

\textsuperscript{1}Larsen, Rawlings, and Ferrier, ChE Sci, 2006
\textsuperscript{2}Patent filed by WARF, P05340US
Advanced image analysis for needles$^1,2$

Original image  | Linear feature detection  | Collinearity identification

$^1$Larsen, Rawlings, and Ferrier, ChE Sci, 2006

$^2$Patent filed by WARF, P05340US
Advanced image analysis for needles\textsuperscript{1,2}

- Original image
- Linear feature detection
- Collinearity identification
- Parallelism identification

\textsuperscript{1}Larsen, Rawlings, and Ferrier, ChE Sci, 2006
\textsuperscript{2}Patent filed by WARF, P05340US
Advanced image analysis for needles\textsuperscript{1,2}

Original image \hspace{2cm} Linear feature detection \hspace{2cm} Collinearity identification

Parallelism identification \hspace{2cm} Cluster properties

\textsuperscript{1}Larsen, Rawlings, and Ferrier, ChE Sci, 2006
\textsuperscript{2}Patent filed by WARF, P05340US
Computer vision for faceted particles\textsuperscript{3,4}

(a) Original image

\textsuperscript{3}Larsen, Rawlings, and Ferrier, ChE Sci, 2007
\textsuperscript{4}Patent filed by WARF, P06449US
Computer vision for faceted particles $^3,^4$

(a) Original image  (b) Linear features

$^3$Larsen, Rawlings, and Ferrier, ChE Sci, 2007
$^4$Patent filed by WARF, P06449US
Computer vision for faceted particles $^{3,4}$

(a) Original image  
(b) Linear features  
(c) Salient line group

$^{3}$Larsen, Rawlings, and Ferrier, ChE Sci, 2007  
$^{4}$Patent filed by WARF, P06449US
Computer vision for faceted particles \(^3,^4\)

(a) Original image  
(b) Linear features  
(c) Salient line group  

(d) Model initialization

\(^3\)Larsen, Rawlings, and Ferrier, ChE Sci, 2007  
\(^4\)Patent filed by WARF, P06449US
Computer vision for faceted particles \(^3,^4\)

(a) Original image  
(b) Linear features  
(c) Salient line group

(d) Model initialization  
(e) Further matches

\(^3\)Larsen, Rawlings, and Ferrier, ChE Sci, 2007  
\(^4\)Patent filed by WARF, P06449US
Computer vision for faceted particles \(^3,^4\)

(a) Original image  
(b) Linear features  
(c) Salient line group

(d) Model initialization  
(e) Further matches  
(f) Optimized Fit

\(^3\)Larsen, Rawlings, and Ferrier, ChE Sci, 2007  
\(^4\)Patent filed by WARF, P06449US
Size and shape control with video feedback
On-line process optimization and state estimation

Size distribution measurement uncertainty for 100 images

probability

size class

PSD
Fully-equipped laboratory

High-speed, in situ video imaging (provided by GlaxoSmithKline).

Brand new, $100k, in situ IR spectroscopic probe for multicomponent reaction monitoring (Mettler-Toledo ReactIR iC10)
Stochastic Kinetics

- Small species populations
- Species numbers are integers, reactions cause integer jumps
- Large fluctuations in species numbers and reaction rates
- Biological networks and catalyst particles
Stochastic Kinetics

- Small species populations
- Species numbers are integers, reactions cause integer jumps
- Large fluctuations in species numbers and reaction rates
- Biological networks and catalyst particles

Research objective

Develop reduced models from stochastic chemical reactions. These models must meet the following requirements:

- Simpler than the full model (fewer reactions, fewer parameters, or faster simulation times)
- Converges to the full model as a specified parameter goes to zero
Reactions on small length scales

When reactions depend on features at small length scales:
- random fluctuations may significantly change the production rates.
- mean field closures may not apply.

Catalytic converter

Pt on Al$_2$O$_3$.
2nm particle $\approx$ 7 units cells (40 reaction sites).
Fluctuations due to small particle numbers may
- cause jumps from high to low coverage
- lead to different production rates from different particle sizes
Reactions on small length scales: Virus infection

Simple Viral Infection Model

Virus

Cell

cccDNA

Viral Proteins

Degraded

rcDNA

New Virus

k_1

k_2

k_3

k_4

k_5

Deterministic Average Stoch

Average concentrations of small systems are not necessarily the same as the deterministic evolution.
Reactions on small length scales: Virus infection

Average concentrations of small systems are not necessarily the same as the deterministic evolution.
Stochastic simulation method - Kinetic Monte Carlo

\[ A \xrightleftharpoons[k_2]{k_1} B \]

\[ k_1 = 2 \quad k_2 = 1 \]

\[ n_{A0} = 6 \quad n_{B0} = 3 \]
Stochastic simulation method - Kinetic Monte Carlo

$A \xrightleftharpoons[k_2]{k_1} B$

$k_1 = 2 \quad k_2 = 1$

$n_{A0} = 6 \quad n_{B0} = 3$

KMC Algorithm

1. Choose which reaction

Which reaction:

\[ \frac{r_1}{r_1 + r_2} = \frac{12}{12 + 3} \quad \frac{r_2}{r_1 + r_2} = \frac{3}{3 + 12} \]
Stochastic simulation method - Kinetic Monte Carlo

\[ A \xrightleftharpoons[k_2]{k_1} B \]

\[ k_1 = 2 \quad k_2 = 1 \]

\[ n_{A0} = 6 \quad n_{B0} = 3 \]

KMC Algorithm

1. Choose which reaction
2. Choose time step

- Which reaction:
  \[ \frac{r_1}{r_1 + r_2} = \frac{12}{12 + 3} \]
  \[ \frac{r_2}{r_1 + r_2} = \frac{3}{3 + 12} \]

- Time step: Sample from an exponential distribution where the distribution mean is the sum of reaction rates.
Stochastic simulation method - Kinetic Monte Carlo

\[ A \xrightarrow{k_1} B \]
\[ k_1 = 2 \quad k_2 = 1 \]
\[ n_{A0} = 6 \quad n_{B0} = 3 \]

**KMC Algorithm**

1. Choose which reaction
2. Choose time step
3. Repeat

\[ \text{Which reaction: } \begin{cases} 
0 & \text{Random number} \\
1 & \frac{r_1}{r_1+r_2} = \frac{12}{12+3} \\
1 & \frac{r_2}{r_1+r_2} = \frac{3}{3+12}
\end{cases} \]

- Time step: Sample from an exponential distribution where the distribution mean is the sum of reaction rates.
KMC simulations and probability

Multiple KMC simulations, $A \xrightarrow{k_1} \xleftarrow{k_2} B$

$\begin{align*}
\text{time (sec)} & \quad 0 & 0.5 & 1 & 1.5 & 2 & 2.5 & 3 \\
n_A & \quad 100 & 80 & 60 & 40 & 20 & 0 \\
n_B & \quad 0 & 20 & 40 & 60 & 80 & 100
\end{align*}$

KMC simulations are samples of a probability distribution that evolves in time. We can write the evolution equation for the probability density (master equation).
KMC simulations and probability

- KMC simulations are samples of a probability distribution that evolves in time.
- We can write the evolution equation for the probability density (master equation).
Chemical master equation

\[
\frac{dP(x)}{dt} = \sum_{j=1}^{N_{rxn}} r_j(x - \nu_j)P(x - \nu_j) - r_j(x)P(x)
\]

rate into state \( x \)

rate out of state \( x \)

\[
\frac{dP}{dt} = AP
\]
Chemical master equation

\[
\frac{dP(x)}{dt} = \sum_{j=1}^{N_{rxn}} r_j(x - \nu_j)P(x - \nu_j) - r_j(x)P(x)
\]

rate into state \(x\)
rate out of state \(x\)

\[
\frac{dP}{dt} = AP
\]

Master equation example

- A \(\xrightarrow{k_1} B\) \(\xleftarrow{k_2}\)
- \(n_{A0} = 100, n_{B0} = 0\)
- \(k_1 = 2, k_2 = 1\)
- 101 possible states
- 101 Coupled ODEs
Kinetics of multiple time scales

\[
A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B \xrightarrow{k_2} C
\]

**Deterministic - One Time Scale**

\[
k_1 = 2 \quad k_{-1} = 0.5 \quad k_2 = 0.5
\]

**KMC - One Time Scale**

\[
k_1 = 2 \quad k_{-1} = 0.5 \quad k_2 = 0.5
\]

**One time scale**
Kinetics of multiple time scales

\[ A \xrightleftharpoons[k_1\backslash k_{-1}]{} B \xrightarrow{k_2} C \]

**Deterministic - One Time Scale**

\[ k_1 = 2, \quad k_{-1} = 0.5, \quad k_2 = 0.5 \]

**KMC - One Time Scale**

\[ k_1 = 2, \quad k_{-1} = 0.5, \quad k_2 = 0.5 \]

**Deterministic - Two Time Scales**

\[ k_1 = 10, \quad k_{-1} = 10, \quad k_2 = 0.5 \]

**KMC - Two Time Scales**

\[ k_1 = 10, \quad k_{-1} = 10, \quad k_2 = 0.5 \]

One time scale

Reaction equilibrium
Kinetics of multiple time scales

\[ A \xrightarrow{k_1} B \xrightarrow{k_2} C \]

Deterministic - One Time Scale

\[ k_1 = 2 \quad k_{-1} = 0.5 \quad k_2 = 0.5 \]

KMC - One Time Scale

\[ k_1 = 2 \quad k_{-1} = 0.5 \quad k_2 = 0.5 \]

Deterministic - Two Time Scales

\[ k_1 = 10 \quad k_{-1} = 10 \quad k_2 = 0.5 \]

KMC - Two Time Scales

\[ k_1 = 10 \quad k_{-1} = 10 \quad k_2 = 0.5 \]

Deterministic - Two Time Scales

\[ k_1 = 2 \quad k_{-1} = 20 \quad k_2 = 20 \]

KMC - Two Time Scales

\[ k_1 = 2 \quad k_{-1} = 20 \quad k_2 = 20 \]

One time scale

Reaction equilibrium

Reactive intermediate
Comparison of mechanisms

\[
\begin{align*}
A & \iff 2B \\
B & \rightarrow C
\end{align*}
\]

\[

t_1 = k_1 a, \quad r_{-1} = k_{-1}/2b(b - 1) \\
\quad r_2 = k_2 b
\]
Comparison of mechanisms

\[ A \rightleftharpoons 2B \]
\[ B \rightarrow C \]
\[ r_1 = k_1 a, \quad r_{-1} = k_{-1}/2b(b - 1) \]
\[ r_2 = k_2 b \]

Stoch SPA

\[ A \rightarrow 2C \]
\[ r = \left( \frac{k_1 k_2}{k_{-1}/2 + k_2} \right) a \]
Comparison of mechanisms

\[ A \rightleftharpoons 2B \]
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\[ r_1 = k_1 a, \quad r_{-1} = k_{-1}/2b(b - 1) \]
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**Stoch SPA**

\[ A \rightarrow 2C \]
\[ r = \left( \frac{k_1 k_2}{k_{-1}/2 + k_2} \right) a \]

**Det SPA**

\[ A \rightarrow 2C \]
\[ r = k_1 a \]
Comparison of mechanisms

\[ A \leftrightarrow 2B \]
\[ B \rightarrow C \]
\[ r_1 = k_1 a, \quad r_{-1} = k_{-1}/2b(b - 1) \]
\[ r_2 = k_2 b \]

**Stoch SPA**

\[ A \rightarrow 2C \]
\[ r = \left( \frac{k_1 k_2}{k_{-1}/2 + k_2} \right) a \]

**Det SPA**

\[ A \rightarrow 2C \]
\[ r = k_1 a \]

**Det QSSA**

\[ A \rightarrow 2C \]
\[ r = k_2 \left[ -k_2 + \sqrt{k_2^2 + 8k_1 k_{-1}a} \right] \]
\[ 4k_{-1} \]
Comparison of mechanisms

\[ A \iff 2B \]

\[ B \rightarrow C \]

\[ r_1 = k_1 a, \quad r_{-1} = k_{-1}/2b(b - 1) \]

\[ r_2 = k_2 b \]

**Stoch SPA**

\[ A \rightarrow 2C \]

\[ r = \left( \frac{k_1 k_2}{k_{-1}/2 + k_2} \right) a \]

**Det SPA**

\[ A \rightarrow 2C \]

\[ r = k_1 a \]

**Det QSSA**

\[ A \rightarrow 2C \]

\[ r = k_2 \left[ -k_2 + \sqrt{k_2^2 + 8k_1 k_{-1} a} \right] \quad \frac{4k_{-1}}{} \]

\[ n_{A0} = 25, \quad n_{B0} = 0, \quad n_{C0} = 0 \]

\[ k_1 = 1 \]

\[ k_{-1} = 1000 \]

\[ k_2 = 1000 \]
New and continuing research projects

Opportunities for new MS/PhD students in the following areas

1. Stochastic methods in chemical reaction engineering
   - Systems engineering of stochastic reaction models
   - Model reduction
   - Application to biological systems (joint with Prof. Yin)

2. Modeling and control of multi-component, dispersed-phase systems
   - Modeling particle populations, both stochastic and deterministic methods
   - Modeling particle interaction with fluid flow (joint with Prof. Graham)
   - State estimation and feedback control based on real-time video imaging
   - New measurement: multicomponent reaction monitoring (Mettler-Toledo ReactIR iC10)
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   - state estimation and feedback control based on realtime video imaging
   - new measurement: multicomponent reaction monitoring (Mettler-Toledo ReactIR iC10)
<table>
<thead>
<tr>
<th>Student</th>
<th>Organization</th>
<th>Sector</th>
</tr>
</thead>
<tbody>
<tr>
<td>John Eaton</td>
<td>Research Fellow – UW</td>
<td><a href="http://www.octave.org">www.octave.org</a></td>
</tr>
<tr>
<td>Rolf Findeisen</td>
<td>U. Magdeburg</td>
<td>Academic</td>
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<tr>
<td>Eric Haseltine</td>
<td>Postdoc, Systems Biology</td>
<td>Academic</td>
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<tr>
<td>Scott Meadows</td>
<td>U. Alberta</td>
<td>Academic</td>
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<tr>
<td>Ken Muske</td>
<td>Villanova U.</td>
<td>Academic</td>
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<tr>
<td>Chris Rao</td>
<td>U. Illinois</td>
<td>Academic</td>
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<tr>
<td>Walt Witkowski</td>
<td>Sandia</td>
<td>Academic</td>
</tr>
<tr>
<td>Peter Findeisen</td>
<td>Daimler</td>
<td>Automotive</td>
</tr>
<tr>
<td>Andy Fordyce</td>
<td>Novo Nordisk</td>
<td>Biochemical</td>
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<tr>
<td>Rahul Bindlish</td>
<td>Dow</td>
<td>Chemicals</td>
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<tr>
<td>Paul Larsen</td>
<td>Dow</td>
<td>Chemicals</td>
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<tr>
<td>Rock Matthews</td>
<td>Corning</td>
<td>Chemicals, fibers</td>
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<tr>
<td>Steve Miller</td>
<td>Eastman Chemical</td>
<td>Chemicals</td>
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<tr>
<td>John Campbell</td>
<td>Aspentech</td>
<td>Control vendor</td>
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<tr>
<td>Sankash Venkatesh</td>
<td>ZS Associates</td>
<td>Operations Research</td>
</tr>
<tr>
<td>Scott Middlebrooks</td>
<td>ASML</td>
<td>Microelectronics</td>
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<tr>
<td>Jenny Wang</td>
<td>IBM</td>
<td>Microelectronics</td>
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<tr>
<td>Wai Man Chan</td>
<td>Shell (Brazil)</td>
<td>Petrochemicals</td>
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<tr>
<td>Ethan Mastny</td>
<td>BP Alaska</td>
<td>Petrochemicals</td>
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<tr>
<td>Brian Odelson</td>
<td>BP</td>
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<tr>
<td>Murali Rajamani</td>
<td>BP</td>
<td>Petrochemicals</td>
</tr>
<tr>
<td>Matt Tenny</td>
<td>ExxonMobil</td>
<td>Petrochemicals</td>
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<tr>
<td>Aswin Venkat</td>
<td>Shell</td>
<td>Petrochemicals</td>
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<tr>
<td>Dan Patience</td>
<td>GlaxoSmithKline</td>
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</tbody>
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Questions?