



MAX PLANCK INSTITUTE  
FOR DYNAMICS OF COMPLEX  
TECHNICAL SYSTEMS  
MAGDEBURG



PROCESS SYSTEMS  
ENGINEERING



# Systematic Methods for Reaction Solvent Design

Teng Zhou

8th June, 2017

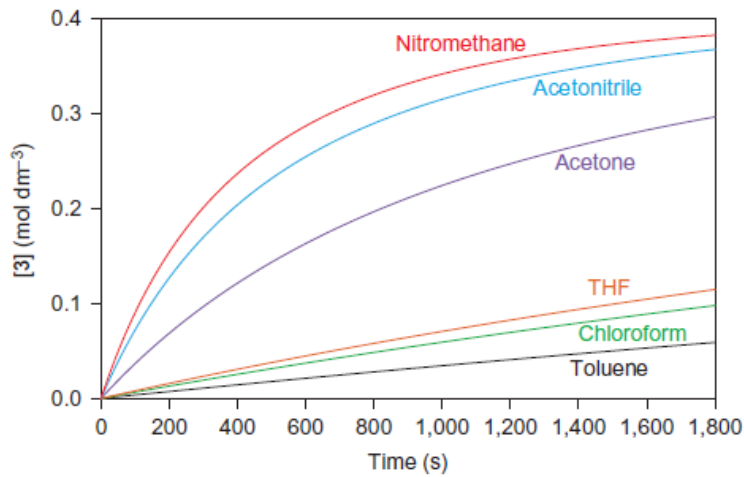
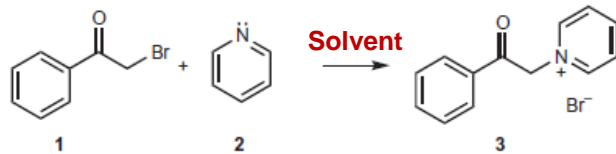
Max Planck Institute for Dynamics of Complex Technical Systems, Magdeburg, Germany  
Technical University of Denmark, Lyngby, Denmark

KT Consortium Annual Meeting, 2017

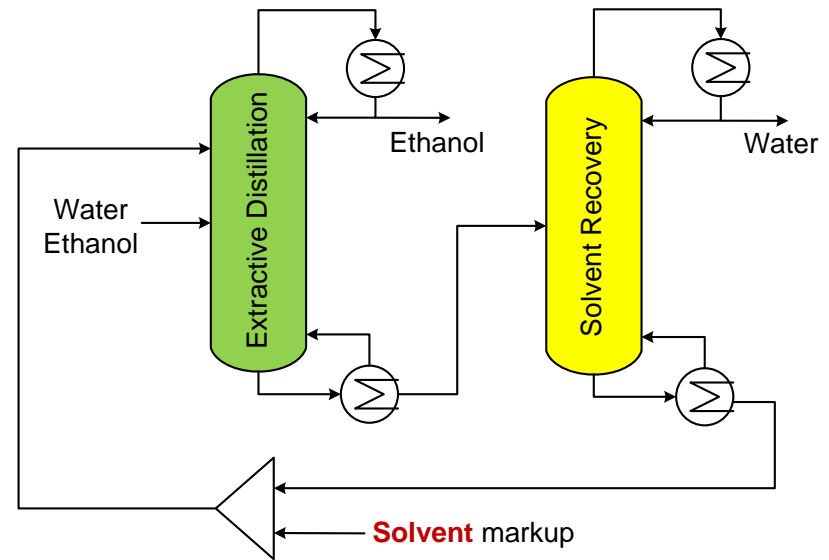


# Role of Solvents in the Process Industry

## Solvent for Reaction



## Solvent for Separation



- ❑ Solvents are widely used as reaction media and separation agents.
- ❑ Can we find the best solvent that gives the highest reaction or separation performances?
  - We need **systematic methods for solvent design** !



# Computer-Aided Molecular Design (CAMD)

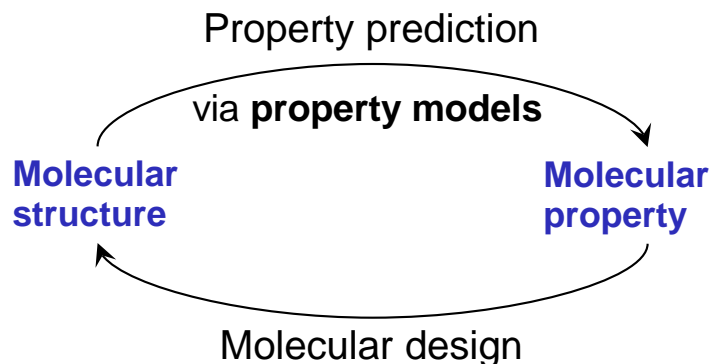
Typical CAMD problems:

Find the best **reaction medium** for a chemical reaction

**working fluid** for a organic rankine cycle (ORC) process

**refrigerant** for a refrigeration process

**solvent** for an extraction process



**Target property:**

Reaction rate

Thermal efficiency

Refrigeration performance

Extraction selectivity

Huge number of molecules → difficult to enumerate and test all

**CAMD via mathematical optimization** is able to identify promising molecules without testing all possible candidates.



# A Typical CAMD Program

Given a set of molecular building groups, find the compound with a minimal viscosity.

Group $j$	Group classes	Valence $v_j$
CH <sub>3</sub>	G <sub>M</sub>	1
CH <sub>2</sub>	G <sub>M</sub>	2
CH	G <sub>M</sub>	3
C	G <sub>M</sub>	4
OH	G <sub>F</sub>	1
CH <sub>3</sub> CO	G <sub>F</sub>	1
CH <sub>2</sub> CO	G <sub>F</sub>	2
CHO	G <sub>F</sub>	1
CH <sub>3</sub> COO	G <sub>F</sub>	1
CH <sub>2</sub> COO	G <sub>F</sub>	2
HCOO	G <sub>F</sub>	1
OCH <sub>3</sub>	G <sub>F</sub>	1
OCH <sub>2</sub>	G <sub>F</sub>	2
OCH	G <sub>F</sub>	3
COOH	G <sub>F</sub>	1

$$\min_{n_j (j \in G)} \eta$$

Subject to:

(1) Structure-property relationship model:

$$\eta = \eta_0 + \sum_{j=1}^N n_j \eta_j$$

(2) Structural feasibility constraints:

$$\sum_{j=1}^N (2 - v_j) n_j - 2m = 0$$

$$n_j (v_j - 1) + 2m - \sum_{k=1}^N n_k \leq 0 \quad (j = 1 \dots N)$$

(3) Structural complexity constraints:

$$n_{low} \leq \sum_{j=1}^N n_j \leq n_{upp}$$

$$0 \leq n_j \leq n_{max}(j)$$

“Mixed-Integer Linear Program (MILP)”

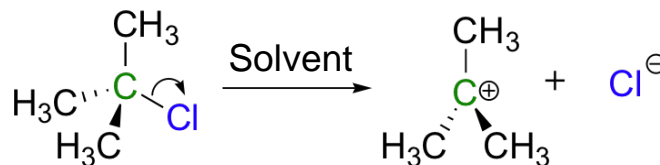
$$n_{j\_opt} = [1 \ 3 \ 0 \ 0 \ 1 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0] \longrightarrow \text{CH}_3(\text{CH}_2)_3\text{OH (Butanol)}$$



# Solvent Design via CAMD

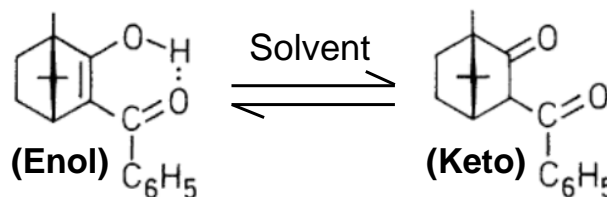
- ✓ CAMD of separation solvents has been widely studied
- ✓ We mainly focus on reaction solvent design

## Solvent effects on reaction rate



Solvent	C <sub>2</sub> H <sub>5</sub> OH	CH <sub>3</sub> OH	HCONH <sub>2</sub>	HCOOH	H <sub>2</sub> O
Relative rate const.	1	9	430	12200	335000

## Solvent effects on chemical equilibrium



Solvent	Diethyl ether	Ethyl acetate	Ethanol	Methanol	Acetone
Enol/Keto	6.81	1.98	1.67	0.87	0.85

**Our Task:** to use CAMD **a)** to design solvents to **increase reaction rates**; and **b)** to design solvents to **improve reaction equilibrium conversions**.



# Methods to quantify/predict solvent effects on reaction rates

- ❑ Experimental measurements
  - + accurate
  - expensive and time-consuming
  - not predictive
  
- ❑ Computational chemistry methods
  - + classical theory based
  - inaccurate on absolute reaction rate values
  - computationally expensive
  
- ❑ QSPR methods  $k = k_0 + aA + bB + \dots$  ( $A, B$ : solvent parameters or descriptors)
  - + fast and predictive
  - + accurate based on a limited set of reliable experimental data
  - 1) Conventional QSPR methods use empirical solvent parameters (e.g. Folić et al., 2007)
  - 2) We use theoretical-descriptor-based QSPR methods
    - + molecular structure or charge related
    - + easy to generate, do not require any experiment

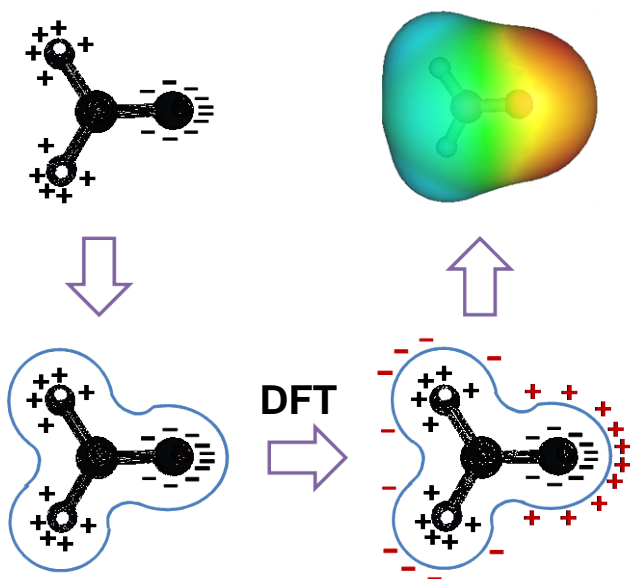
---

QSPR: Quantitative Structure–Property Relationship

Folić M, Adjiman CS, Pistikopoulos EN. AIChE Journal 2007, 53, 1240-1256.



# Conductor-like Screening Model (COSMO)



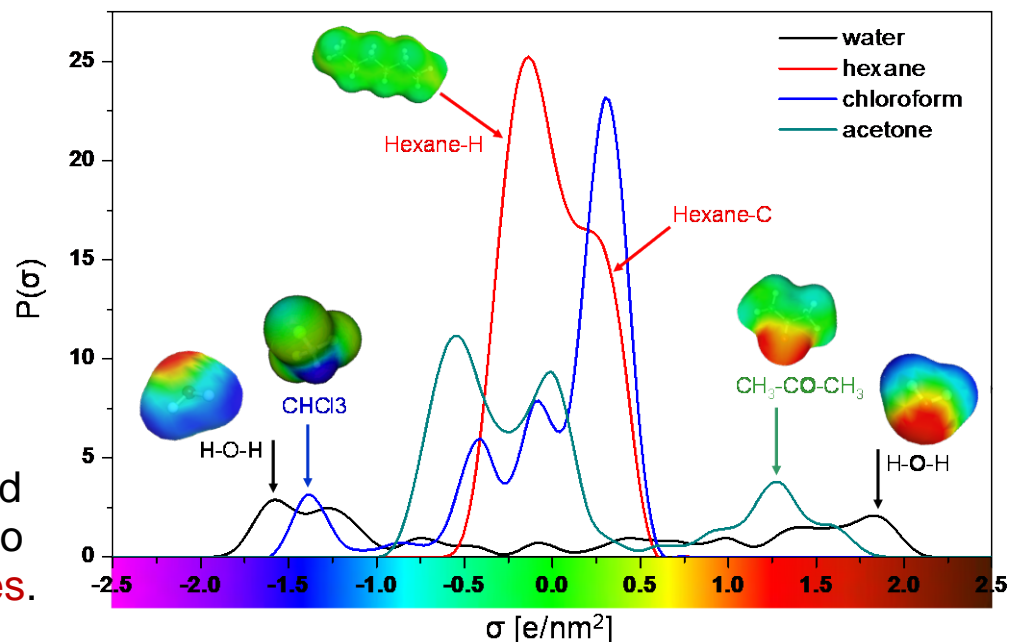
Surface Screening Charge Density

$$\sigma_i = q_i / a_i$$

**$\sigma$ -profile is molecule-specific.**

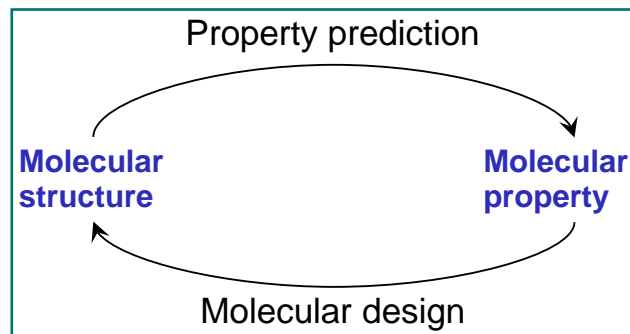
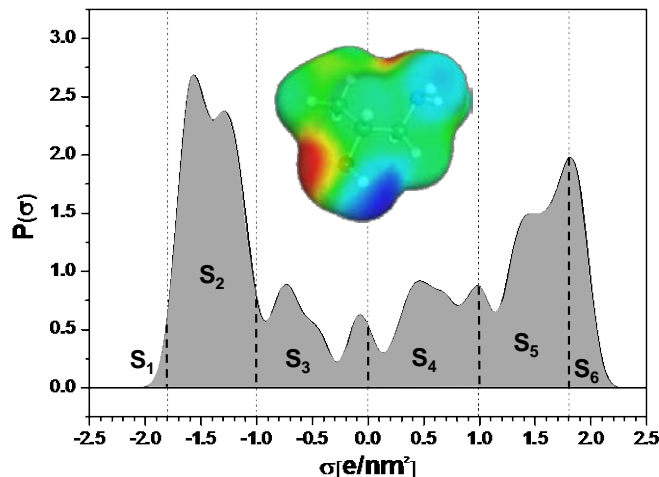
It is a good “molecular fingerprint”, based on which we derive solvent descriptors to correlate solvent effects on reaction rates.

The 3D distribution of Screening Charge Density is converted into a 2D composition function, so called “ $\sigma$ -profile”,  $P(\sigma)$



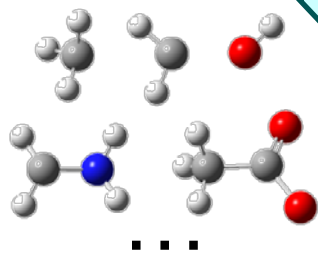


# Solvent Structure – Reaction Rate Relationship



Group contribution model

$$S_i = s_{i0} + \sum_{j=1}^N n_j s_{ij}$$



Solvent descriptors  $S_1 \sim S_6$

Property prediction

QSPR correlation with exp. rate constants in a few solvents

$$\log k_{cal} = \log k_0 + \sum_{i=1}^6 h_i S_i$$

Solvent-sensitive rate constant

Structure

Property





# Computer-Aided Solvent Design

Group j	Group ID, Classes
CH <sub>3</sub>	G1, G <sub>M</sub>
CH <sub>2</sub>	G2, G <sub>M</sub>
CH	G3, G <sub>M</sub>
C	G4, G <sub>M</sub>
OH	G5, G <sub>F</sub>
CH <sub>3</sub> CO	G6, G <sub>F</sub>
...	...
...	...
OCH	G14, G <sub>F</sub>
COOH	G15, G <sub>F</sub>

$$\max_{n_j (j \in G)} \log k$$

$$S_i = s_{i0} + \sum_{j=1}^N n_j s_{ij} \quad (\text{solvent structure} - \text{solvent descriptor relation})$$

$$\log k = \log k_0 + \sum_{i=1}^6 h_i S_i \quad (\text{solvent descriptor} - \text{rate constant relation})$$

Structural feasibility rules:

$$\sum_{j=1}^N (2 - v_j) n_j - 2m = 0$$

$$n_j (v_j - 1) + 2m - \sum_{k=1}^N n_k \leq 0 \quad (j = 1 \dots N)$$

Structural complexity constraints:

$$0 \leq n_j \leq n_{\max}(j)$$

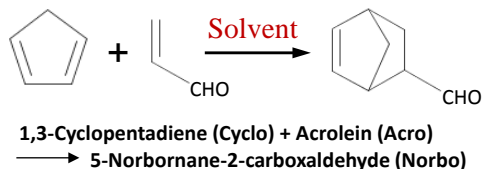
$$n_{\text{low}} \leq \sum_{j=1}^N n_j \leq n_{\text{upp}}$$

## Results: Top 5 solvents designed

Group combinations	Solvent structures	Log $k_{\text{pred}}$
2 CH <sub>3</sub> , 1 C, 1 OH, 1 COOH	(CH <sub>3</sub> ) <sub>2</sub> C(OH)COOH	<b>-1.875</b>
3 CH <sub>2</sub> , 1 OH, 1 COOH	OHCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> COOH	-1.934
1 CH <sub>3</sub> , 1 CH <sub>2</sub> , 1 CH, 1 OH, 1 COOH	CH <sub>3</sub> CH(OH)CH <sub>2</sub> COOH	-1.942
2 CH <sub>2</sub> , 1 OH, 1 COOH	OHCH <sub>2</sub> CH <sub>2</sub> COOH	-1.962
1 CH <sub>3</sub> , 1 CH, 1 OH, 1 COOH	CH <sub>3</sub> CH(OH)COOH	-1.971

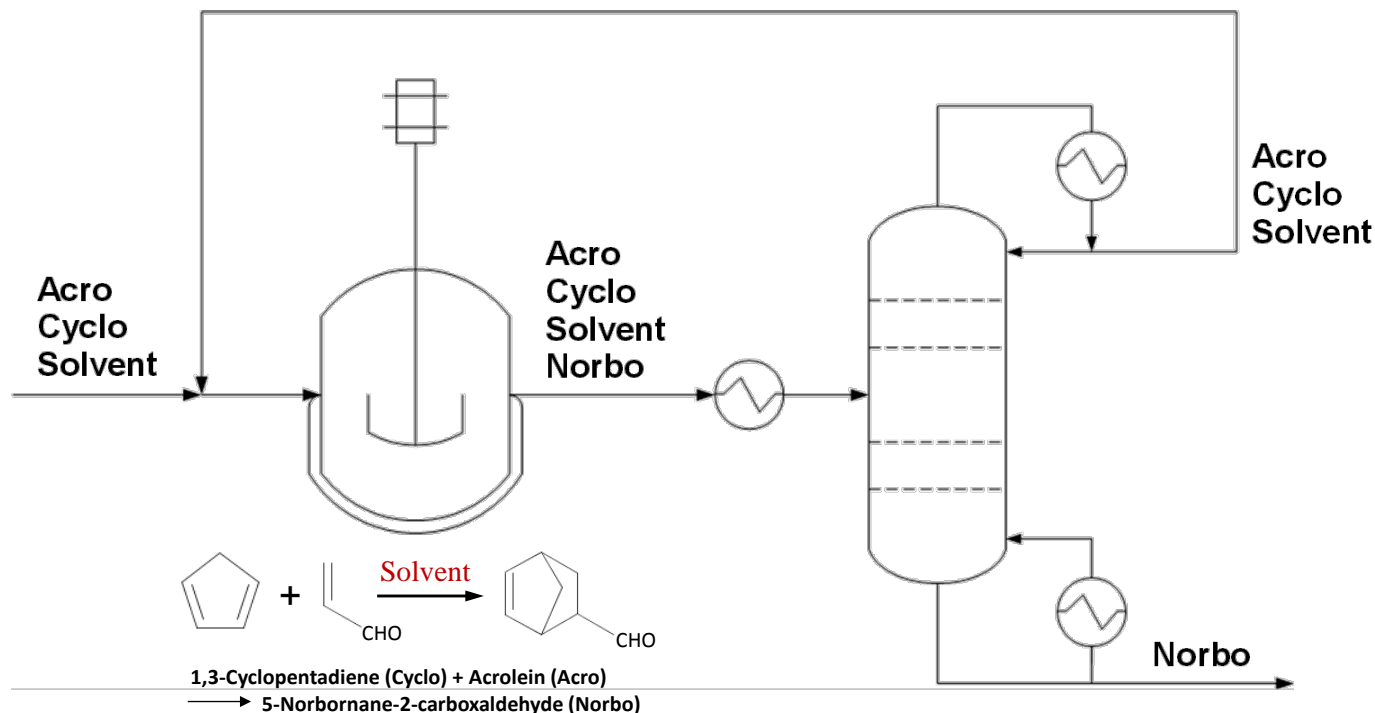
Best solvent found experimentally: acetic acid (Log  $k = -2.491$ )

Example: Diels-Alder reaction





# The best reaction solvent also best for the whole process ?



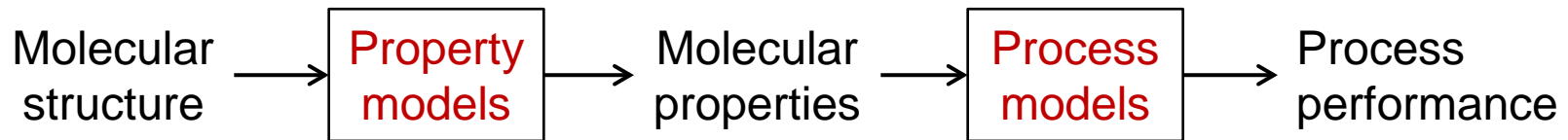
- ✓ Solvents **affect not only** reactions, **but also** other process properties, such as heat utilities, solvent-product separations.
- ✓ In order to find the best solvent for the whole process, it is necessary to perform "**integrated solvent and process design**" where solvent molecular structure and process operating conditions are **simultaneously** optimized.
- ✓ **Process performance instead of reaction performance** should be maximized.



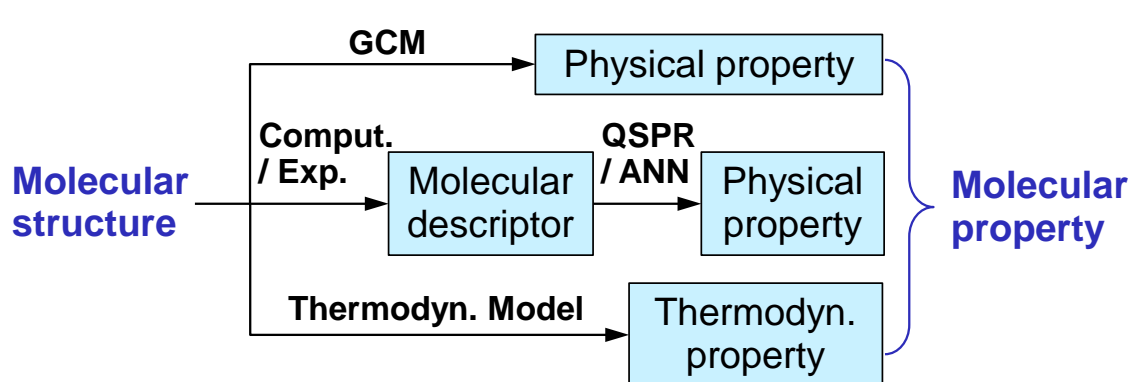
# Integrated Molecular and Process Design

Computer Aided Molecular Design:  
molecular structure – property relation

Integrated Molecular and Process Design:  
molecular structure – process performance relation



- Property models: group contribution (GC) models, QSPR models, UNIFAC



$$T_b = 222.543 \ln \left( \sum_{j=1}^N n_j t_{b,j} \right)$$

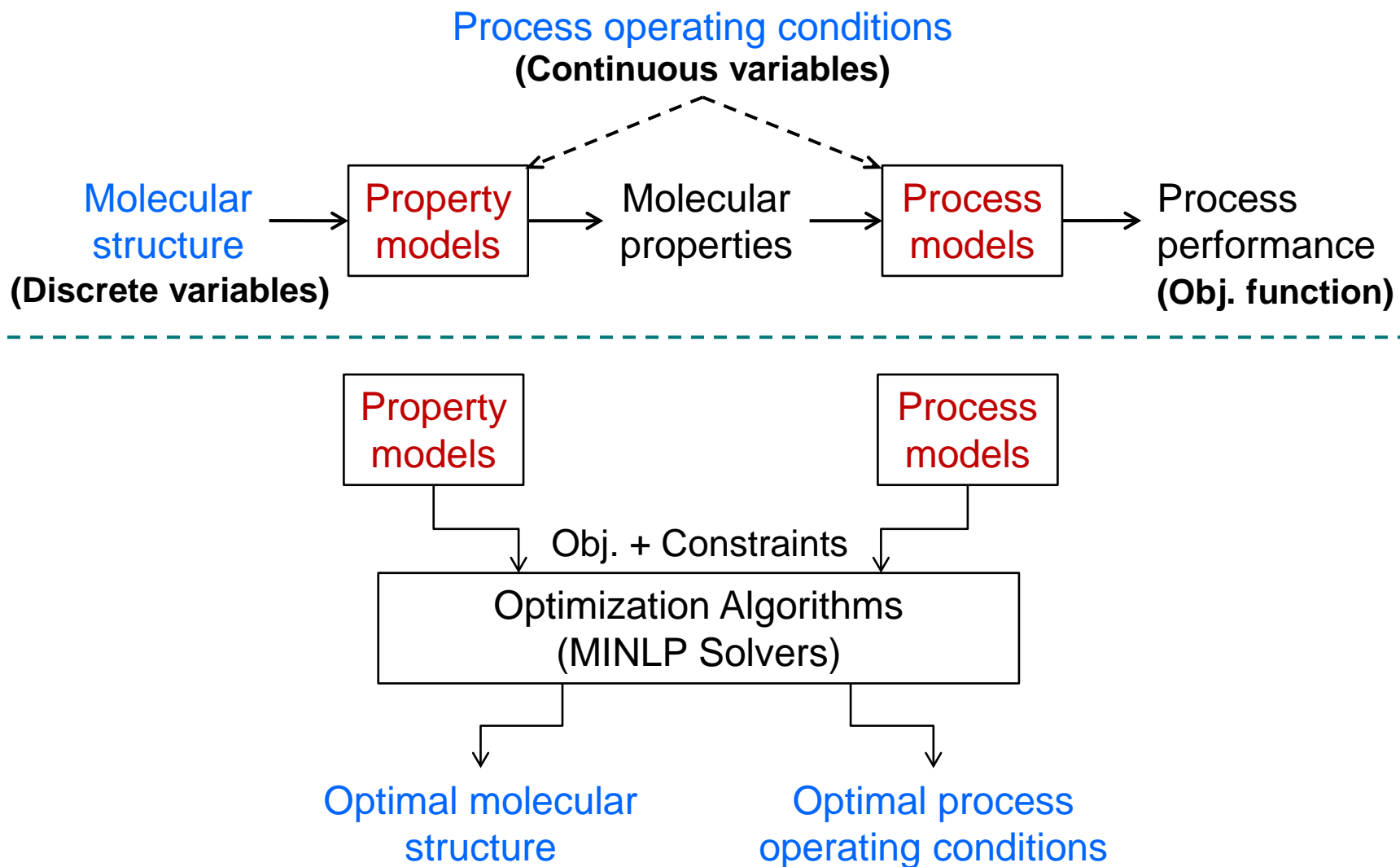
$$\log k = \log k_0 + \sum_{i=1}^6 h_i S_i$$

$$\ln(\gamma_i) = \ln(\gamma_i^C) + \ln(\gamma_i^R)$$

- Process models: mass balance, energy balance, etc.



# Integrated Molecular and Process Design



MINLP: Mixed-Integer Nonlinear Programming



# MINLP Formulation

**Maximize:** Process economic profit  $F$

**Variables:** Integer  $n_j$  (group  $j = 1, 2, \dots, N$ )  
Reaction conversion  $X$  and product recovery  $\xi_{\text{nor}}$

**Subject to:** **Variable boundaries:**

$$\left. \begin{array}{l} 0.50 \leq X \leq 0.99 \\ 0 \leq \xi_{\text{nor}} \leq 0.2 \end{array} \right\} \text{(continuous process variables)}$$

$$0 \leq n_j \leq n_j^{\text{upp}} \text{ (discrete molecular variables)}$$

**Solvent structure constraints:**

Structural feasibility

Structural complexity

**Solvent property models:**

Reaction rate constant (previously mentioned method)

Physical property (existing GC models)

**Process and cost models:**

Reactor; Heat exchanger; Distillation column

Capital investment; Utility cost



# Integrated solvent and process design results

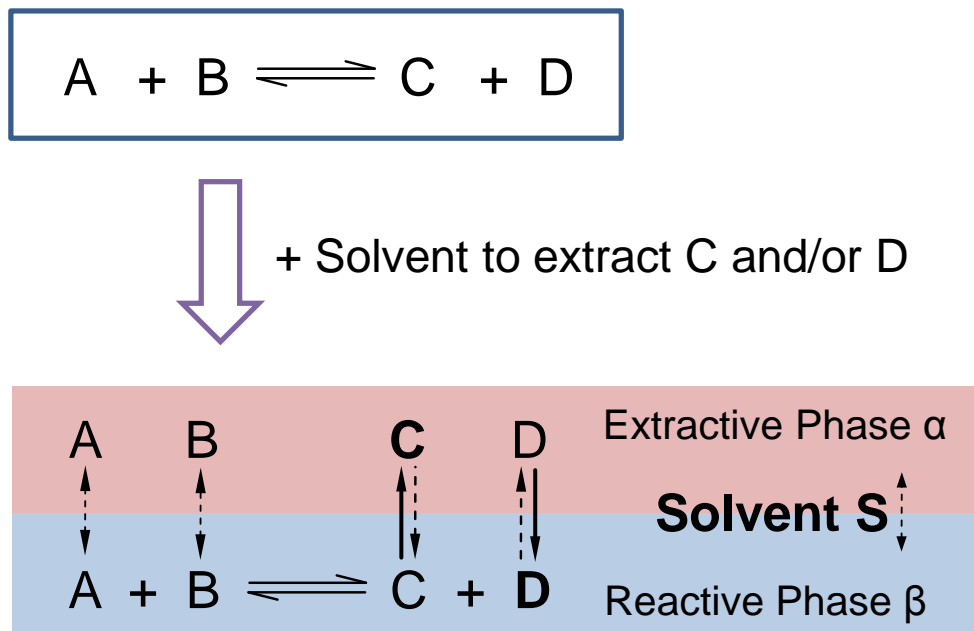
	Integrated Design (MINLP)	Reference Case (NLP)
<b>Optimal solvent</b>	<b>Isopropanol</b>	<b>Acetic acid (Fixed)</b>
Opt. react. conversion	0.755	0.872
Opt. product recovery	99.45%	97.77%
<b>Total profit (\$/year)</b>	<b>27918.1</b>	<b>22776.4</b>
<i>EP</i> (\$/year)	65319.7	74118.8
<i>CI<sub>R</sub></i> (\$/year)	10145.0	5750.3
<i>CI<sub>column</sub></i> (\$/year)	7662.7	17133.2
<i>UC<sub>reb</sub></i> (\$/year)	13399.3	20816.1
log <i>k</i>	-3.294	-2.551

**Tradeoffs** between different solvent properties **are fully captured** via integrated solvent and process design

Zhou T, McBride K, Zhang X, Qi Z, Sundmacher K. (2015). *AIChE J.* 61, 147-158.



## 2<sup>nd</sup> Task: CAMD of solvents to improve reaction conversion via the “extractive reaction” strategy



Solvents = Reaction media + Separation agents

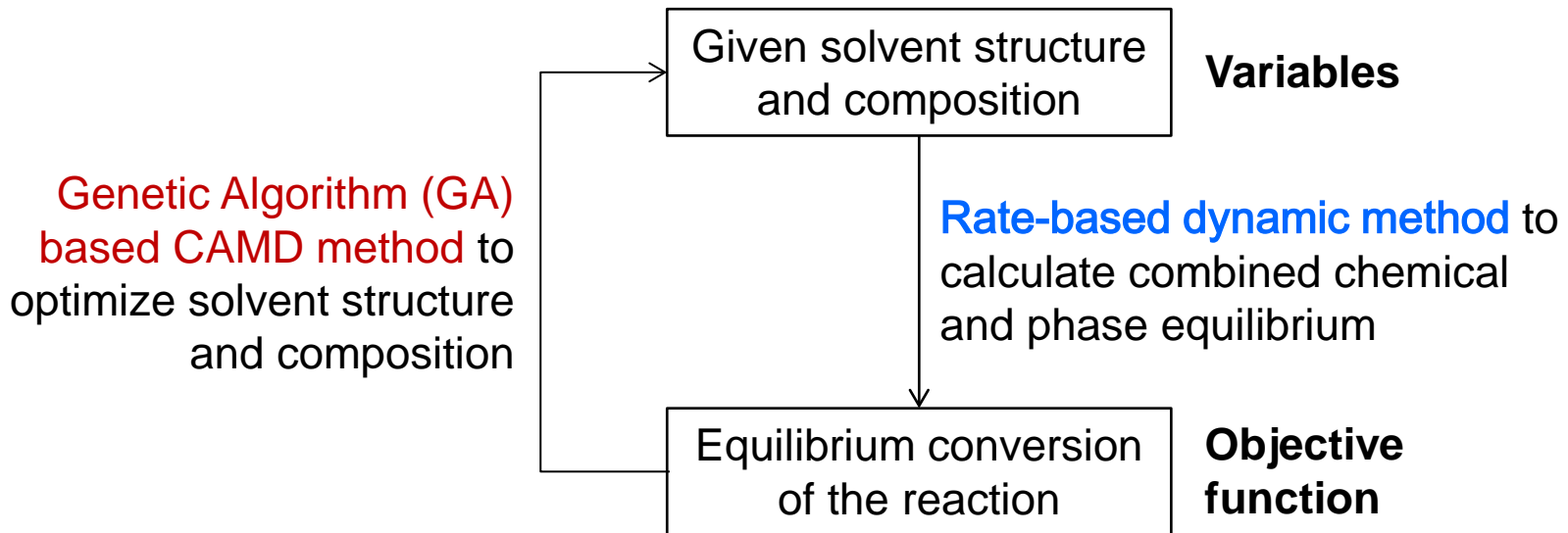
**Design Task:** Given a liquid reaction mixture under a specified  $T$  and  $P$ , determine **which solvent** and **by which amount** it should be added to the mixture in order to achieve **a maximum equilibrium conversion** of the reaction.



# Solution Methods

To design solvents for extractive reaction, we need:

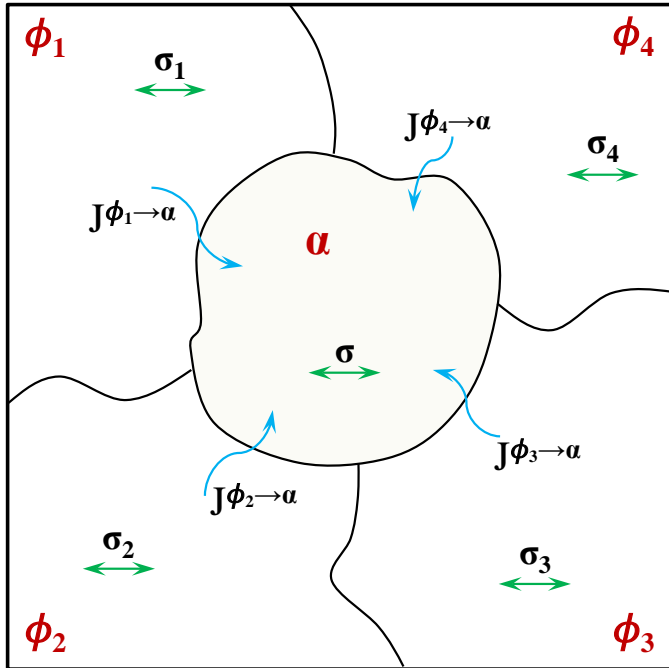
- (1) A **thermodynamic method** to determine combined chemical and phase equilibrium under specified solvents
- (2) A **CAMD method** to design solvents to maximize reaction equilibrium conversion determined by the thermodynamic method







# Rate-based Dynamic Method



Mass transfer between phases:

$$J_i^{k,\alpha} = k_{trans,i} (x_i^k \gamma_i^k - x_i^\alpha \gamma_i^\alpha)$$

Reaction rate of the  $m^{\text{th}}$  reaction in phase  $\alpha$ :

$$r_m^\alpha = k_{reac,m} \left[ \prod_{\substack{i \in NC \\ v_{i,m} < 0}} (x_i^\alpha \gamma_i^\alpha)^{-v_{i,m}} - \frac{1}{K_{th,m}^\alpha} \prod_{\substack{i \in NC \\ v_{i,m} > 0}} (x_i^\alpha \gamma_i^\alpha)^{v_{i,m}} \right]$$

Sources/sinks of component  $i$  in phase  $\alpha$  induced by the  $m^{\text{th}}$  reaction:

$$\sigma_{i,m}^\alpha = v_{i,m} r_m^\alpha$$

Mass balance of component  $i$  in phase  $\alpha$ :

$$\frac{dn_i^\alpha}{dt} = \sum_{k=1}^{NP} J_i^{k,\alpha} + \sum_{m=1}^{NR} \sigma_{i,m}^\alpha \quad (i = 1, 2, \dots, N_C, \alpha = 1, 2, \dots, N_P)$$

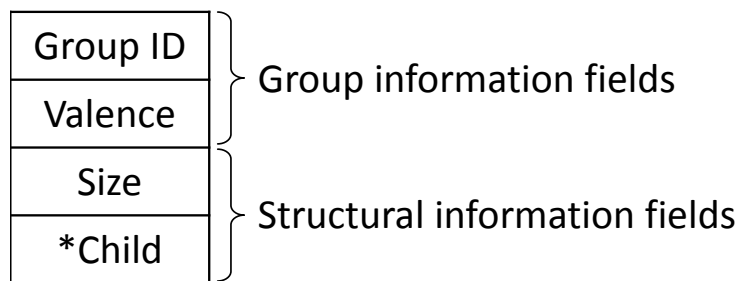
The steady state of the  $(N_C \times N_P)$  ODEs indicates the equilibrium state of the multiphase reactive system.



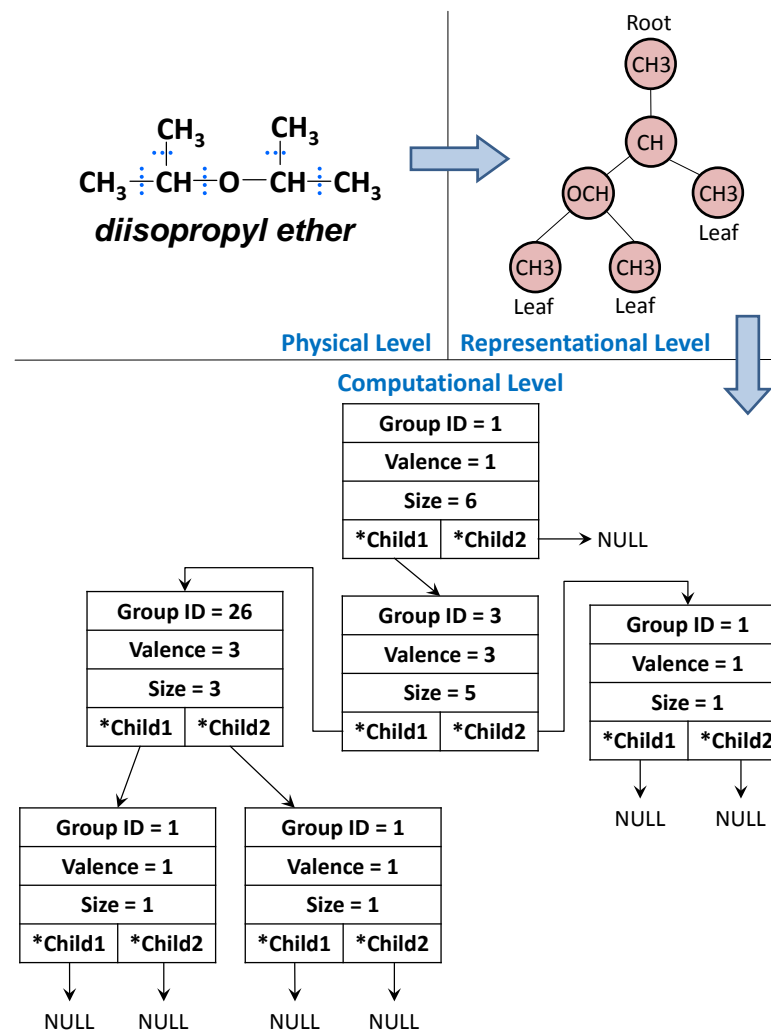
# GA-based solvent design – molecular encoding

Each GA individual includes a solvent initial composition and a solvent molecular structure

- ✓ Solvent initial composition, a continuous variable, is encoded as a binary array
- ✓ Solvent molecules are encoded as tree structures with UNIFAC groups as the tree nodes



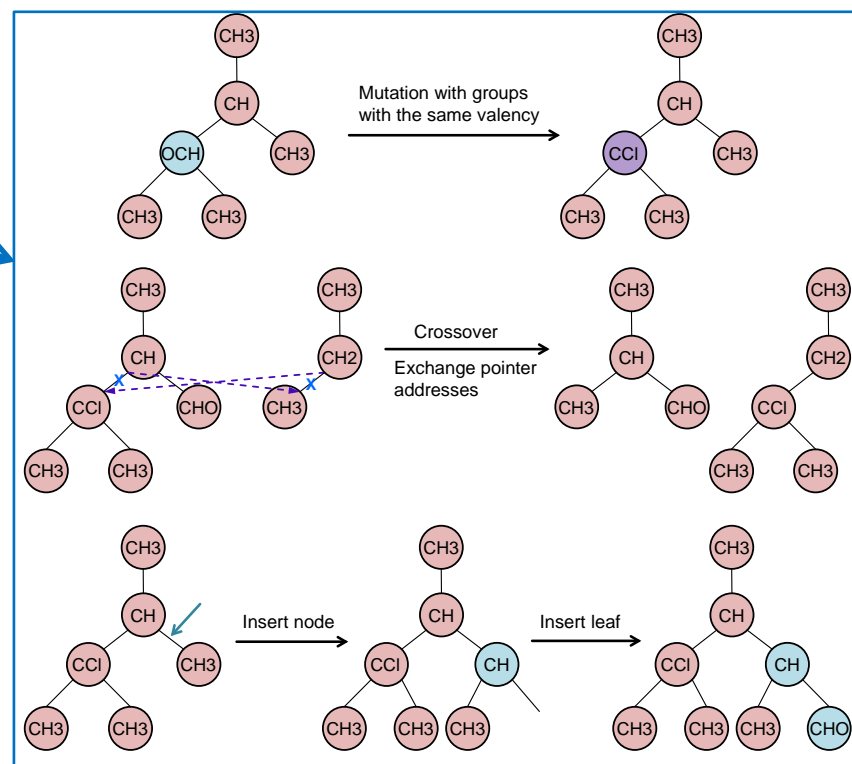
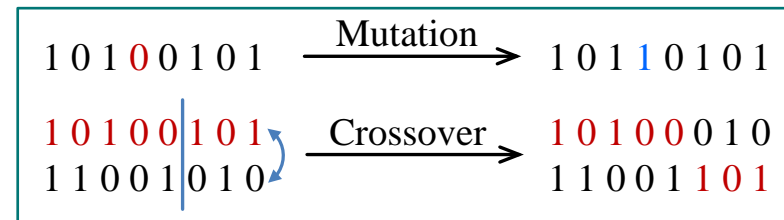
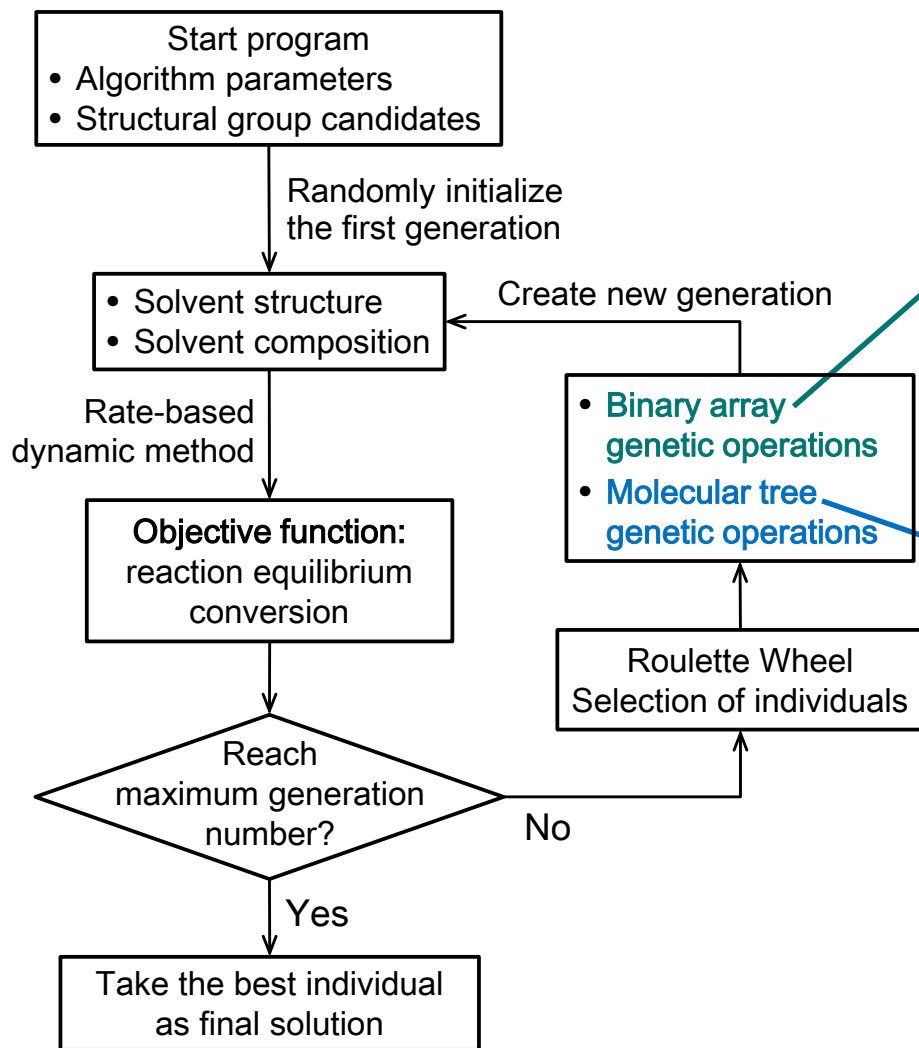
Structure of a group node



Zhou T, Wang J, McBride K, Sundmacher K. AIChE Journal. 2016, 62, 3238–3249.



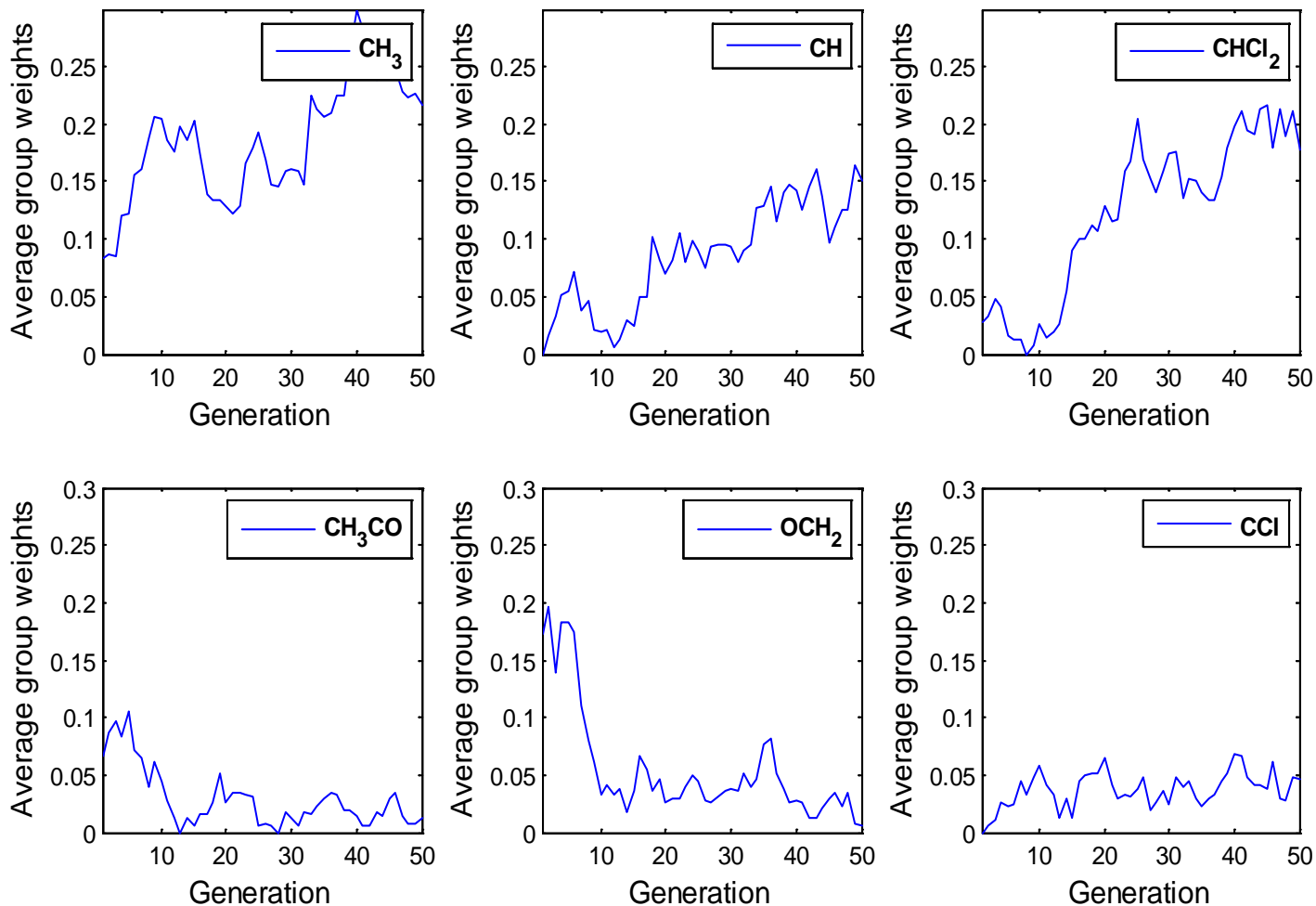
# Overall Design Framework





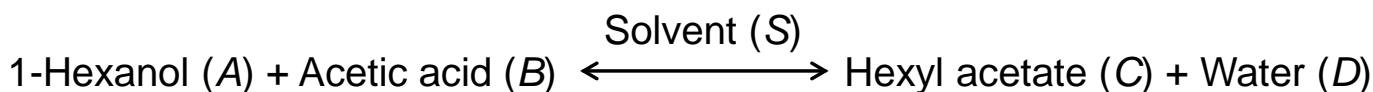
# Case study on an esterification reaction

## Evolution of average group weights in a generation





# Results of 10 optimization runs



No. of run	Optimal solvent structure	Optimal solvent initial composition	Reaction equilibrium conversion
1	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> CHCl <sub>2</sub>	0.5524	0.918000
2	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> CHCl <sub>2</sub>	0.5714	0.918019
3	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> CHCl <sub>2</sub>	0.5619	0.918025
4	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> CHCl <sub>2</sub>	0.5619	0.918025
5	(CH <sub>3</sub> ) <sub>2</sub> CHCHCl <sub>2</sub>	0.5524	0.918042
6	(CH <sub>3</sub> ) <sub>2</sub> CHCHCl <sub>2</sub>	0.5810	0.918043
7	(CH <sub>3</sub> ) <sub>2</sub> CHCHCl <sub>2</sub>	0.5714	0.918066
8	(CH <sub>3</sub> ) <sub>2</sub> CHCHCl <sub>2</sub>	0.5619	0.918068
9	(CH <sub>3</sub> ) <sub>2</sub> CHCHCl <sub>2</sub>	0.5619	0.918068
10	(CH <sub>3</sub> ) <sub>2</sub> CHCHCl <sub>2</sub>	0.5619	0.918068

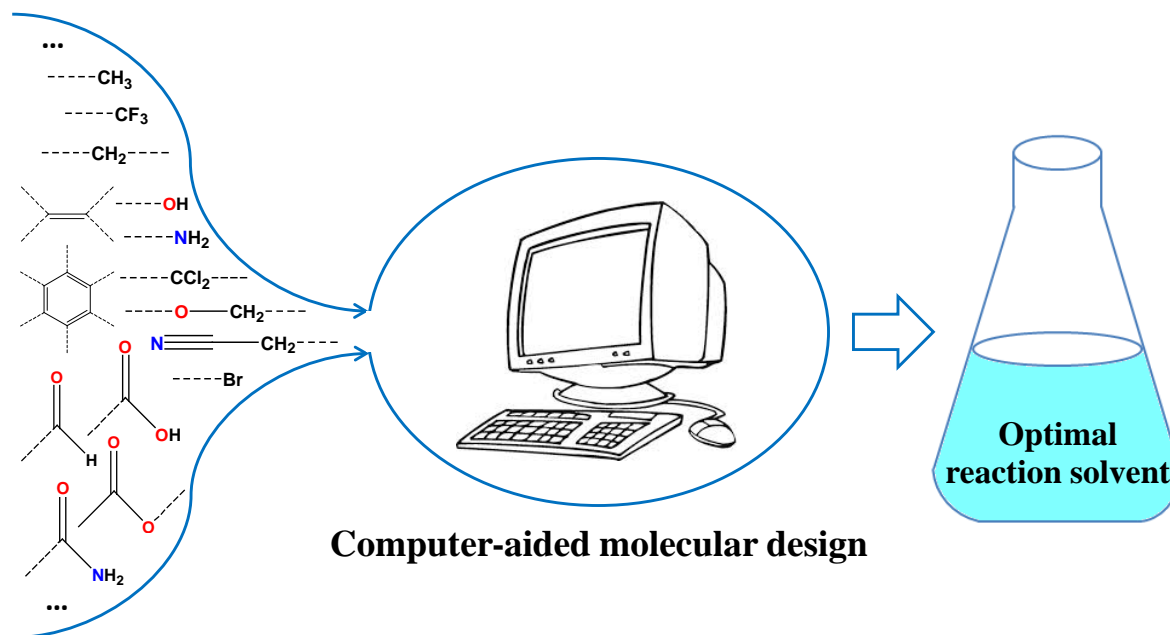
**Small deviation** in the reaction conversions obtained from 10 random optimization runs



**Near-global solutions**



# Summary



- ❑ Solvents can influence both reaction kinetics and thermodynamics, CAMD methods are developed for finding optimal solvents to increase reaction rates and equilibrium conversions.
- ❑ When designing solvents for chemical reactions, the subsequent separation cost should also be considered. For that reason, integrated solvent and process design is necessary.



**Thank you for your attention!**