Chemical product centric sustainable process design: Computer aided product (molecules, polymers & mixtures) design

Rafiqul Gani
PSE for SPEED
Skyttemosen 6, DK-3450 Allerod, Denmark
rgani2018@gmail.com

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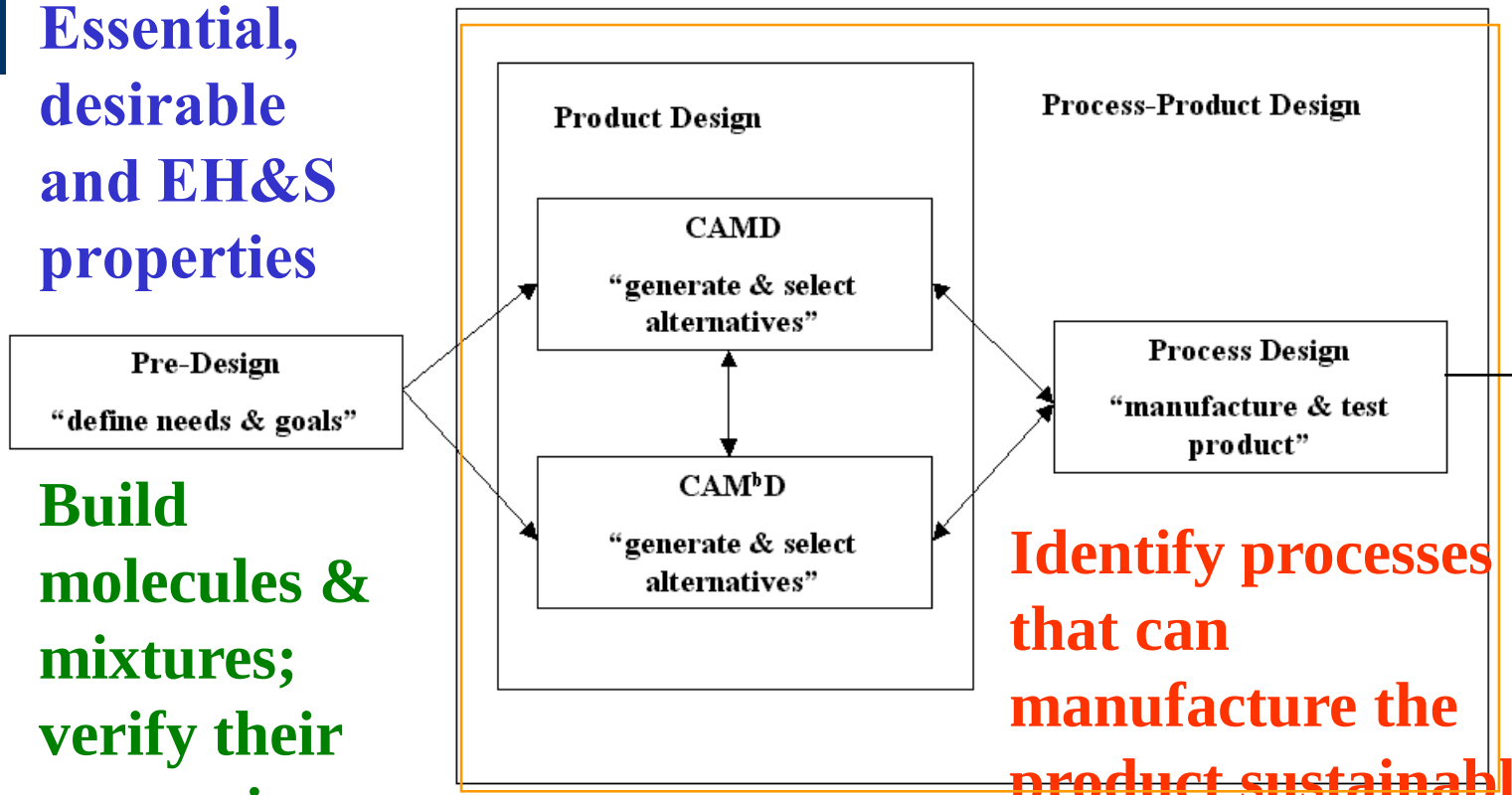
SPEED Chemical product classification

Product Type / Issues	Single species		Multiple species		Devices
	Small	Large	Formulated		
Examples	Solvents, refrigerants	APIs, surfactants, membranes	Blended fuels, solvents, lubricants	Functional Detergents, personal care, healthcare, medicinal	Fuel-cells, microcapsules, hemodialysis device
Key factors in design	Cost of production		Cost and product functions	Product functions	
	N.A		Time to market (speed)		
Basis of design	Process flowsheet (unit operations)	Synthesis routes (chemistry)	Blend properties	Microstructure and stability	Device form and constituent materials
Measure of performance	Closely related to process	Closely related to application	Closely related to application	Consumer satisfaction	Consumer satisfaction
Challenges in design	Translation of needs to molecular structure	Translation of needs to properties	Delivering product functions defined by needs		Translation of needs to product material properties and configuration
	Large number of product alternatives		Trial & error approach (non-optimal product)		
Risks	Feedstock availability science			Absence of engineering knowledge	
	Environmental impact and sustainability				

Chemical product design framework

Essential, desirable and EH&S properties



Product & process evaluation

Build molecules & mixtures; verify their properties

Identify processes that can manufacture the product sustainably

1. Define needs; 2. Design products; 3. Design processes; 4. Evaluate process-product

An example of product design

.

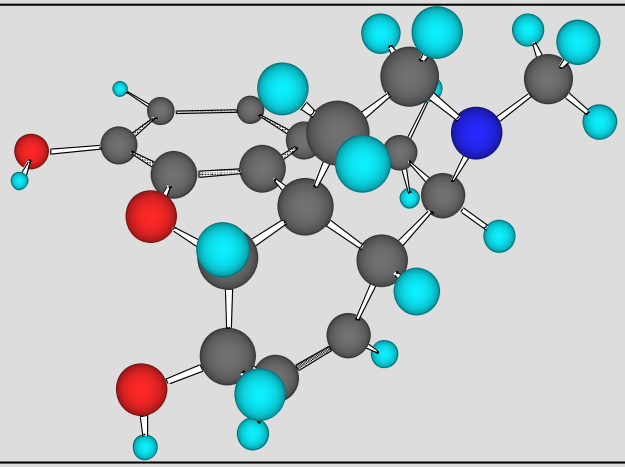
Structure	
Name	Morphine
T_m (K)	528
δ (MPa)^{½}	26.3

Figure 1: Molecular structure and properties of morphine

Can we "design" drugs/pesticides/chemical products with desirable properties?

Can we "design" additives that must be added to obtain the final (formulated) product?

Define the product/additive needs and then identify the molecules/mixtures that match these needs!

Steps 1&3. Define needs - Product analysis

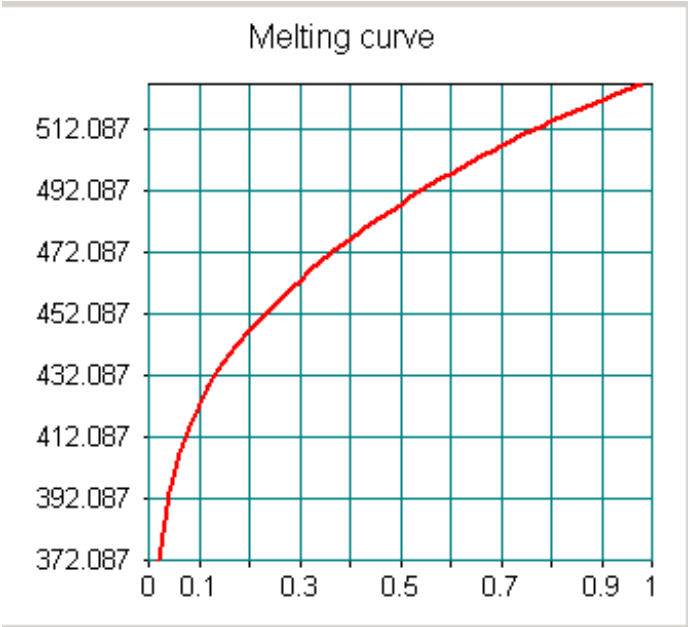
Compound Name : Morphine
Compound CAS : 000057-27-2
Compound Smiles : Oc1ccc2CC3N(C)CCC45C3C=CC(O)C4Oc1c25
Compound Formula : C17H19NO3
Mw (g/mol) : 285.34

Best estimates are suggested for each property according developers' criteria. See detailed estimates through each in the corresponding pages

WARNING:
Accuracy of some estimated properties (e.g. Hansen parame might be poor if the melting point is far above 298 K

Property	Method	Unit	Est.Value	Exp.V
Tm	MG	K	493.59	528.1
Tb	MG	K	697.94	N/A
Tc	MG	K	926.95	N/A
Pc	MG	bar	29.96	N/A
Vc	MG	cm³/mol	848.93	N/A
Zc	MG		0.330	N/A
Gf[298K]	MG	kJ/mol	65.33	N/A
Hf[298K]	MG	kJ/mol	-319.10	N/A
omega	CG		0.917	N/A
Hv[298K]	******	kJ/mol	N/A	N/A
Hv[Tb]	MG	kJ/mol	98.06	N/A
Hfus	MG	kJ/mol	37.97	N/A
Sfus	MG	J/(mol*K)	71.90	N/A
Vm[298K]	******	cm³/mol	N/A	N/A
Vm[Tb]	MG	cm³/mol	334.43	N/A
Sol. Par.[298K]	MG	MPa½	35.32	N/A
Refractive Index	MG		2.39	N/A
Molar Refraction	******		N/A	N/A
Surf.Tens.[298K]	******	dyn/cm	N/A	N/A
G.T. Temp.	******	K	N/A	N/A
Log(Kow)	MG		3.35	N/A
Log(Ws)	MG	Log(mg/L)	1.99	2.30
Closed Flash Temp.	CG	K	537.20	N/A
Open Flash Temp.	CG	K	650.99	N/A
Hansen Disp. sol.	CG	MPa½	17.67	N/A
Hansen Polar sol.	CG	MPa½	6.06	N/A
Hansen Hydr. sol.	CG	MPa½	15.49	N/A

Analyze solubility to estimate partition coefficients (logP): Ethanol, 1-butanol, acetonitrile, water, amines, chlorides, ….. hexane, benzene



Partition coefficients are correlated to Product Activity during application

Step 2: CAMD for product design

CAMD can be described as “Reverse Property Prediction”

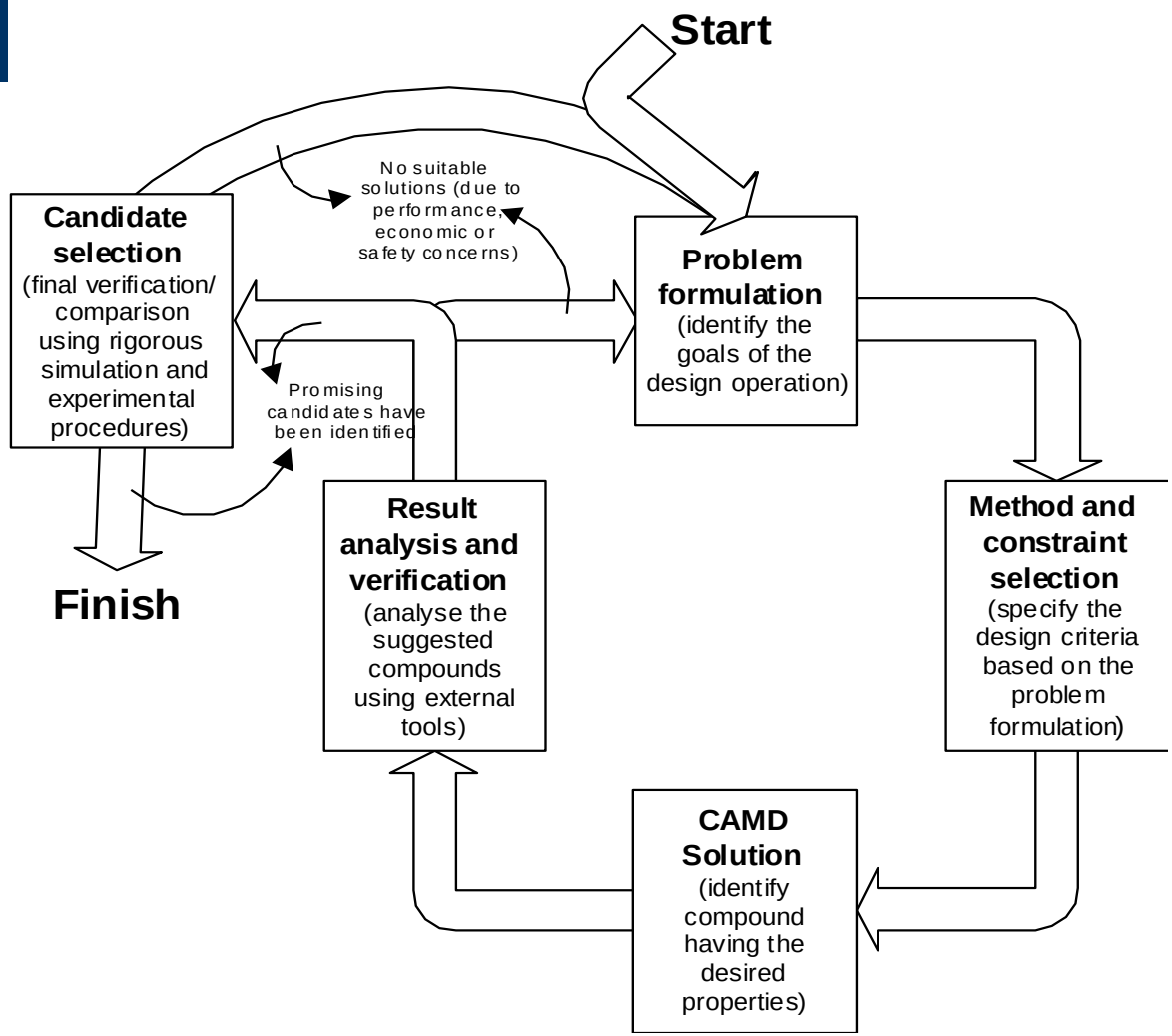
Property prediction:

Given:	**Obtained:**
Information on compound structure.	Properties of the compound.

CAMD:

Given:	**Obtained:**
Information on desired properties & type of compound.	Compound structures having the desired properties.

CAMD Framework



- Solutions of CAMD problems are iterative.
- Problem formulation controls the success.
- Essential qualities vs. (un)desirable qualities.
- Connectivity with external tools, data and methods.

A 3-stage Iterative Solution Approach

1. **Set Goals (Pre-Design Stage) – Define Needs**
   - Essential properties
   - Desirable properties
   - Safety, Environmental, etc.
2. **Design/Selection (Design Stage) – Generate Alternatives**
   - Search through database
   - Iteratively build molecules/mixtures, comparing to goals
     - Generate set of feasible molecules/mixtures
   - Simultaneously build and evaluate molecules/mixtures
     - Identify optimal molecule/mixture
     - Identify feasible set
3. **Analyze, verify and select (Post-Design Stage) - Final Selection (process/operation constraints)**

CAMD problem solution: Database search

View Compound | Plot Results

Found Compounds:

casno	Chemname	mw	SolPar
000075-07-0	ACETALDEHYDE	44.053	19.9094
000074-87-3	METHYL-CHLORIDE	50.487	19.7197
000067-64-1	ACETONE	58.08	19.7297
000107-31-3	METHYL-FORMATE	60.053	20.4951
000110-02-1	THIOPHENE	84.142	20.1206
000075-09-2	DICHLOROMETHANE	84.932	20.3726
000107-92-6	n-BUTYRIC-ACID	88.106	20.2368
000100-66-3	ANISOLE	108.14	20.1055
000095-50-1	o-DICHLOROBENZENE	147.003	20.3107
000541-73-1	Benzene,1,3-dichloro-	147.003	19.5744

Record 10

Problem: Find solvents that have

19.5 > Sol Par < 20.5

Solution: Use a search engine within a database to identify the set of feasible molecules

What do we need to solve CAMD problems?

Necessary Methods & Tools

Method to generate candidates

- Molecules and/or mixtures

Method to evaluate candidates

- Predictive property models
- Process/operation model

Method to select the best candidates

- Criteria for selection

Descriptors represent molecules & contribute to properties

Represent molecules with groups

Groups are the molecular descriptors

CH3- , -CH2- , -OH, CH3CO-, CH3O-, -CH2CO-, -CH2O-

How many compounds can be formed by joining these groups?

Examples:

CH3-CH2-CH2-CH2-CH2-CH3

CH3-CH2-OH ; CH3-COCH3

CH3-COCH2-CH3 ; CH3-CH2-CH2-OH

Group classification & combination rules

Class	Category				
	1	2	3	4	5
1	CH3	CH2NO2	CH3CO	OH	CH2=CH
2	CH2				
3	CH				

Class Number: Defines the number of free attachments

-CH3; -CH2-; -CH(-)-; -C(-)(-)-

Category Number: Defines degree of restriction to joining with other groups. Examples -

1: no restrictions; 2-4: cannot join with each other; 5: only one per molecule of specified size

Group classification & combination rules

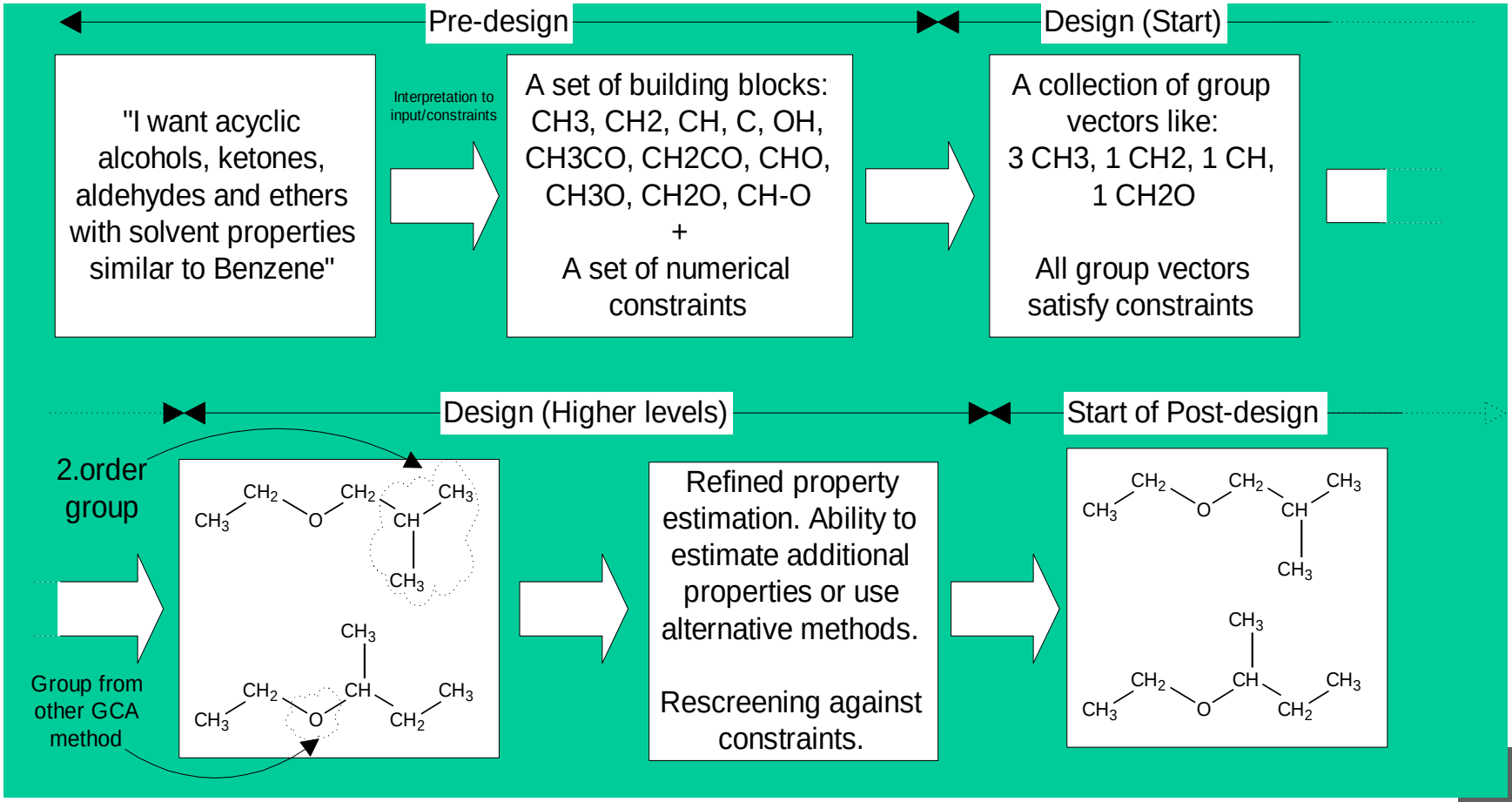
Class	Category				
	1	2	3	4	5
1	CH3	CH2NO2	CH3CO	OH	CH2=CH
2	CH2				
3	CH				

Examples of rules to join groups to form feasible molecules

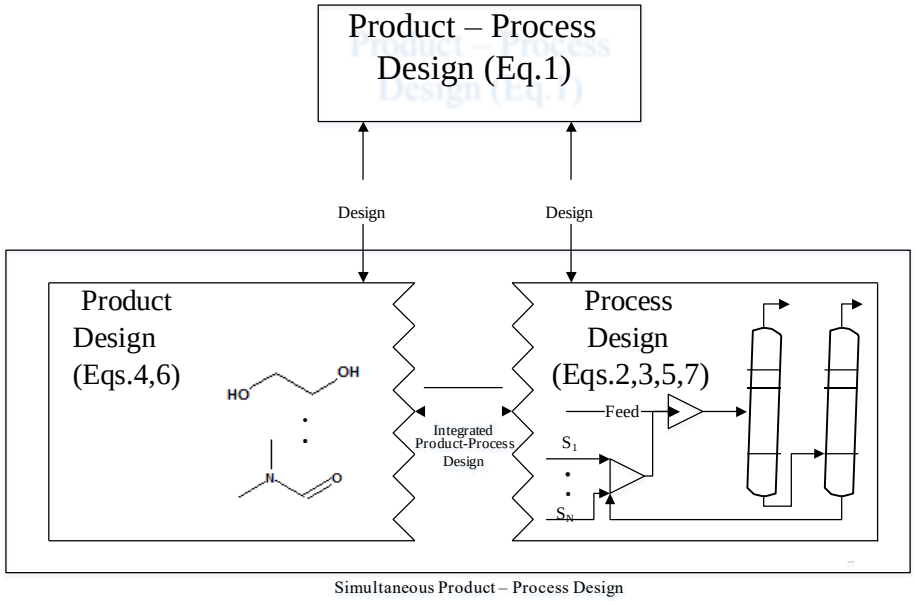
- A complete structure cannot have free attachments
- Groups from category 2-4 cannot join with each other
- Groups from category 5 can appear only once

CAMD group based method: Overview

Multi-level generate & test according to a predefined sequence



CAMD: Application examples



Simultaneous Product – Process Design

Molecular design (single molecular products)

- **Solvents**
- **Process fluids**
- **Surfactants**
- **Active ingredients**
- **Polymer repeat units**
- **…..**

Eqs. 4, 6 with or without Eq. 1 (product design and implicit performance verification)

Example - 1: CAMD problem formulation

Given: A set of descriptors (groups) and target values for a set of properties.

Find all feasible chemical molecules that satisfy the target properties

Given, descriptors CH3-; -CH2-; -OH

Target properties: $345 > T_b > 355$

Solution: Join descriptors to form molecules, for example, CH3-CH2-OH (one likely candidate?)

Estimate property: $\exp(T_b/T_{b0}) = A_{CH3} + A_{CH2} + A_{OH}$

$T_b = 351.44$ K

Example - 2: CAMD problem formulation

Given, descriptors CH3-; -CH2-; -OH

Target properties: $345 > T_b > 355$

Dissolves Vanillin (000121-33-5)

Solution: Join descriptors to form molecules, for example, CH3-CH2-OH (one likely candidate?)

Estimate T_b (351.44 K) & Solubility (mutually miscible)

Solubility $\approx 1/(\gamma_i^{\infty})$; γ_i^{∞} is infinite dilution activity coefficient of Vanillin (solute) in Ethanol (solvent)

γ_i^{∞} = f(T, $\underline{x}$, group contributions & interactions) = UNIFAC

Example - 3: CAMD problem formulation

Example: Given, descriptors CH3-; -CH2-; -OH

Target properties: $345 > T_b > 355$

Dissolves Vanillin (000121-33-5) & select the best temperature of operation

Solution: Join descriptors to form molecules, for example, CH3-CH2-OH (one likely candidate?)

Estimate T_b (351.44 K) & Solubility (mutually miscible)

Solubility $\approx 1/(\gamma_i^{\infty})$

γ_i^{∞} = f(T, $\underline{x}$, group contributions & interactions) = UNIFAC

Compute a phase diagram (T versus x); select T; verify operation through a process model (process simulation)

Example - 4: CAMD problem formulation

Example: Given, descriptors CH3-; -CH2-; -OH

Target properties: $345 > T_b > 355$

Dissolves Vanillin (000121-33-5) & select the best temperature of operation

Given: y_i, i = 1, NG (NG= number of groups)

$g_j(\underline{y}) = 0$, j = 1,NR (NR= number of rules to join groups)

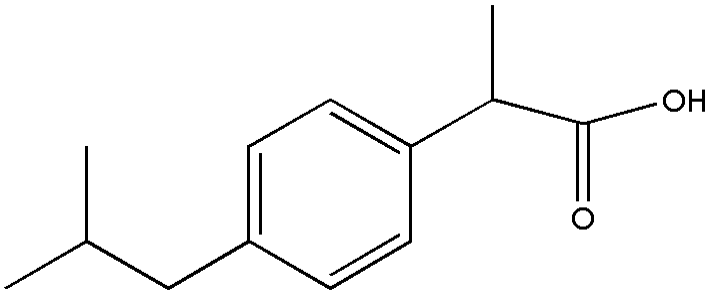
$L_2 > h_{1,k1}(\underline{y}, \underline{\theta}) > U_2$, $k_1 = 1,NP_1$ (NP_1 = number of pure component properties)

$L_3 > h_{2,k2}(\underline{y}, \underline{x}, \underline{\varphi}) > U_3$, $k_2 = 1,NP_2$ (NP_2 = number of secondary & mixture properties)

$\underline{f}_{k3}(\underline{x}, \underline{h}_1, \underline{h}_2, \underline{z}) = 0$

$\underline{y}$: vector of group identifiers; $\underline{\theta}$: vector of group contributions; $\underline{x}$: vector of compositions; $\underline{\varphi}$: vector of property model parameters; $\underline{z}$: vector of process parameters; $\underline{g}$: constraints for feasible molecules; $\underline{h}_1$ & $\underline{h}_2$: constraints for properties; $\underline{f}$: process constraints (mass and/or energy balance)

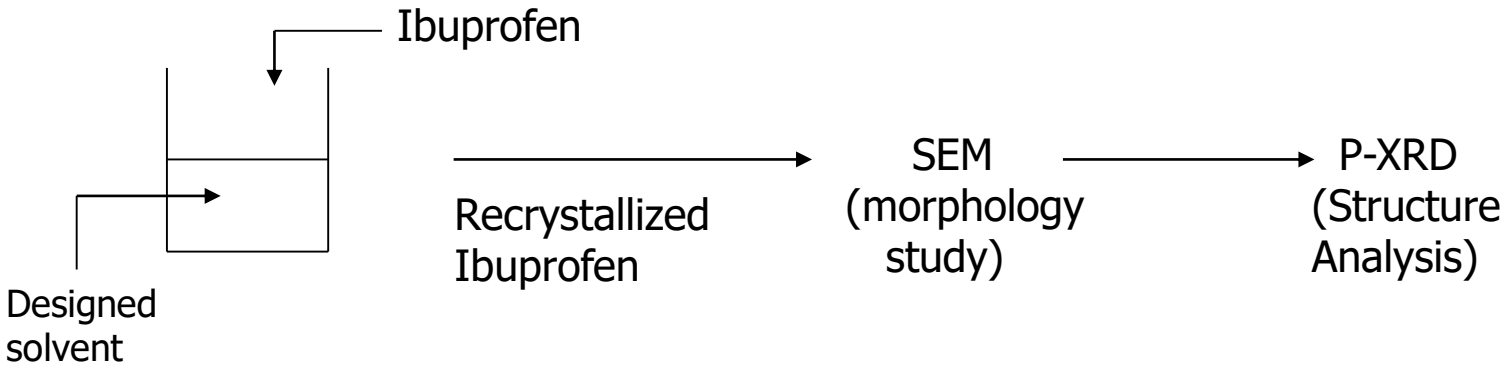
Product Recovery: Crystallization



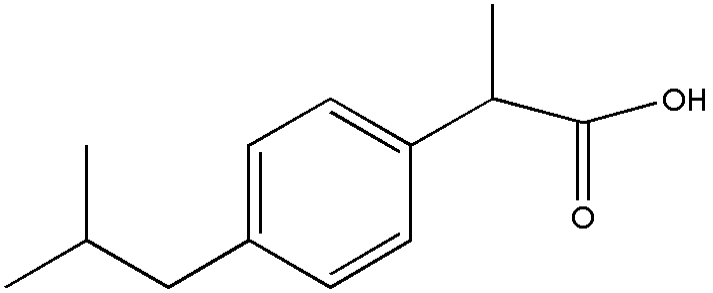
Chemical product: Ibuprofen

Consider cooling as well as drowning-out crystallization

Find solvents, anti-solvents & their mixture that makes the following process feasible:



Product Recovery: Crystallization



Chemical product: Ibuprofen

Consider cooling as well as drowning-out crystallization

Find solvents, anti-solvents & their mixture that satisfy the following:

Potential recovery > 80%

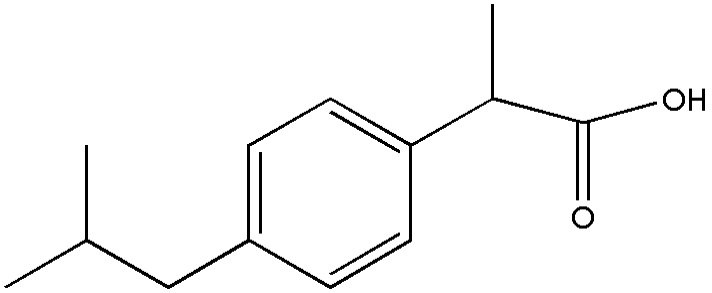
Solubility parameter > 18 $MPA^{1/2}$ (or > 30)

Hydrogen bonding solubility parameter > 9 $MPA^{1/2}$ (or > 24)

Tm < 270 K; Tb > 400 K; -log (LC50) < 3.5

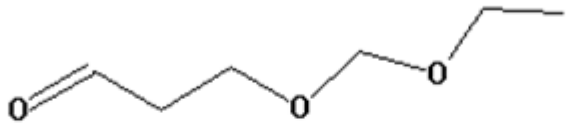
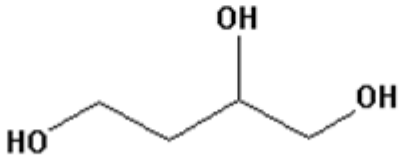
Solution strategy: Define CAMD problem to generate solvent candidates; verify performance through solubility calculations; check database to verify predictions

Product Recovery: Crystallization



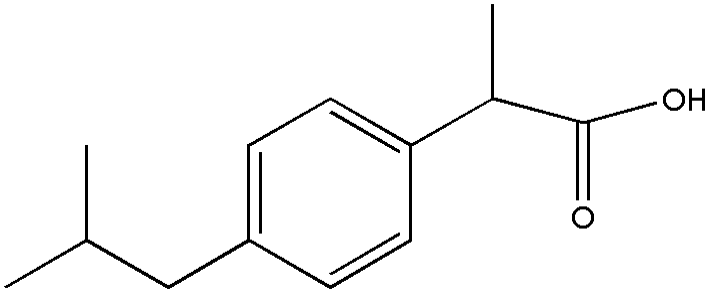
Chemical product: Ibuprofen

Consider cooling as well as drowning-out crystallization

Component	*Structure*	*Compositions*
Solvent		**0.21**
Anti-solvent		**0.79**

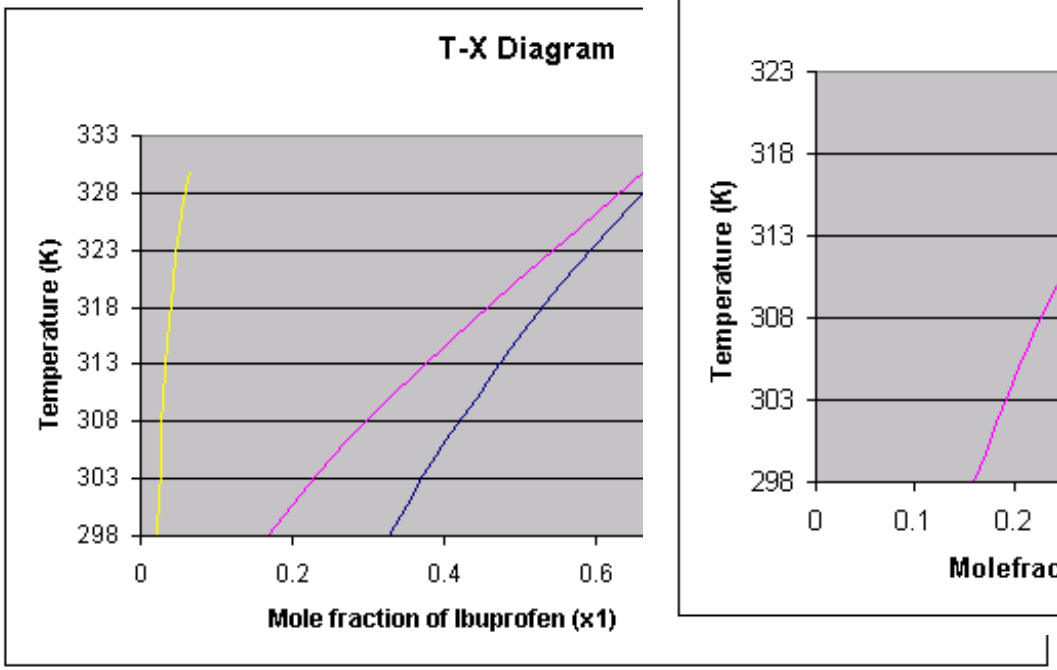
A computer aided-molecular design framework for crystallization solvent design. *Karunanithi, A.T; Achenie, L.E.K; Gani, R.* *Chemical Engineering Science, 2006, 61, 1243-1256.*

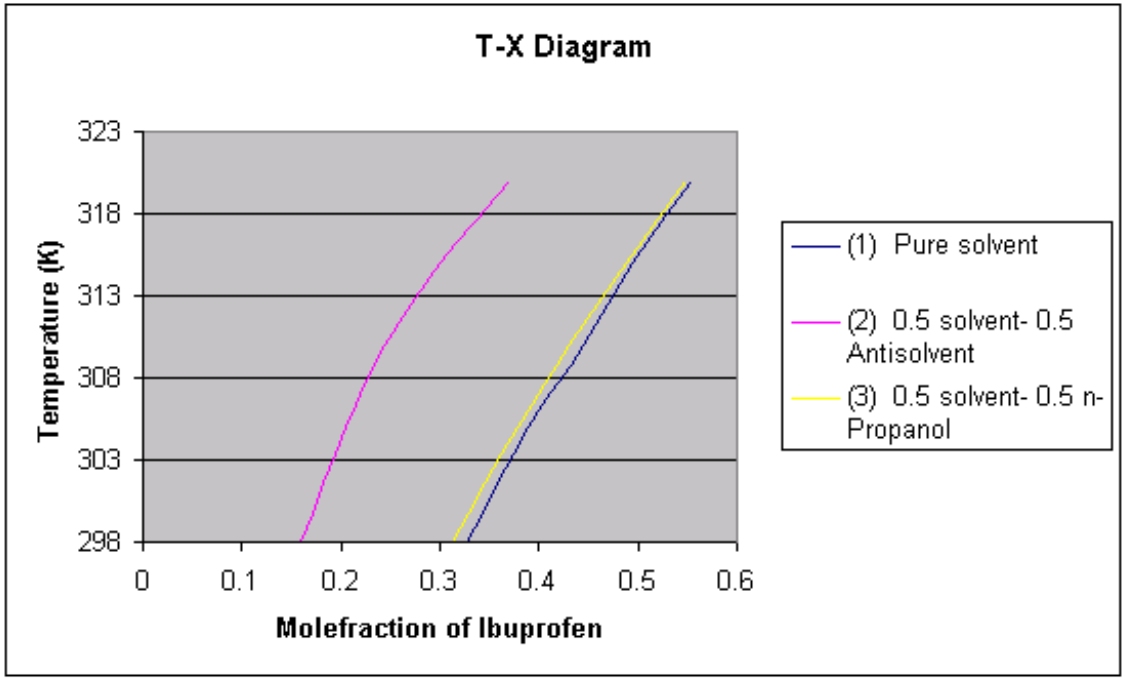
Product Recovery: Crystallization



Chemical product: Ibuprofen

Consider cooling as well as drowning-out crystallization





Polymer Design: MINLP applied to CAMD

Polymer design problem where polymer repeat units with 2-4 different groups and 2-9 total number of groups in the repeat unit structure are being sought

$$Fobj = \Sigma [(P_i - P_i^*)/P_i^*]^2$$

s.t.

$$T_g \cong 373 \text{ K}$$

$$\text{Density} \cong 1.5 \text{ g/cm}^3$$

Water absorption = 0.005 g H_2O/g polymer)

-CH2- ; -CO- ; -COO- ; -O- ; -CONH- ; -CHOH-; -CHCL-

Polymer Design: MINLP applied to CAMD

$$Fobj = \Sigma [(P_i - P_i^*)/P_i^*]^2$$

select property models

s.t.

$$T_g = [\Sigma (Y_k n_k)]/ [\Sigma (M_k n_k)] \cong (373 \pm 20)\ K$$

$$Density = [\Sigma (M_k n_k)]/ [\Sigma (V_k n_k)] \cong (1.5 \pm 0.1)\ g/cm^3$$

$$Water\ absorption = [\Sigma (H_k n_k)]/ [\Sigma (M_k n_k)]$$

$$\cong (0.005 \pm 0.0005)\ g\ H_2O/g\ polymer)$$

-CH2- ; -CO- ; -COO- ; -O- ; -CONH- ; -CHOH-; -CHCL-

Note: objective function and constraints are non linear; n_k, the optimization variables are integer (0-9)

Polymer Design: MINLP applied to CAMD

$$Fobj = \Sigma [(P_i - P_i^*)/P_i^*]^2$$

s.t.

$$353\ K < T_g = [\Sigma (Y_k n_k)]/ [\Sigma (M_k n_k)] < 393\ K$$

$$1.4 < \rho = [\Sigma (M_k n_k)]/ [\Sigma (V_k n_k)] < 1.5\ g/cm^3$$

$$0.0045 < W = [\Sigma (H_k n_k)]/ [\Sigma (M_k n_k)] < 0.0055)\ g\ H_2O/g\ polymer)$$

$$2 \leq \Sigma y_j \leq 3 \quad ; \quad y_j : 0 \text{ or } 1 \text{ for } j=1,7$$

$$2 \leq \Sigma y_k n_k \leq 9$$

add structural constraints

-CH2- ; -CO- ; -COO- ; -O- ; -CONH- ; -CHOH-; -CHCL-

Note: objective function and constraints are non linear; n_k, the optimization variables are integer (0-9)

Polymer Design: Reformulate - I

$$Fobj = \Sigma [(P_i - P_i^*)/P_i^*]^2$$

s.t.

$$353\ K < T_g = [\Sigma (Y_k n_k)]/ [\Sigma (M_k n_k)] < 393\ K$$

$$1.4 < \rho = [\Sigma (M_k n_k)]/ [\Sigma (V_k n_k)] < 1.5\ g/cm^3$$

$$0.0045 < W = [\Sigma (H_k n_k)]/ [\Sigma (M_k n_k)] < 0.0055)\ g\ H_2O/g\ polymer)$$

$$50 < \Sigma (M_k n_k) < 100$$ ← add a new constraint

$$2 \leq \Sigma y_j \leq 3 \quad ; \quad y_j : 0 \text{ or } 1 \text{ for } j=1,7$$

$$2 \leq \Sigma y_k n_k \leq 9$$

-CH2- ; -CO- ; -COO- ; -O- ; -CONH- ; -CHOH-; -CHCL-

Polymer Design: Reformulate – II (MILP)

Min Fobj = M

reformulate Fobj & constraints

s.t.

$$18.7 < T_gM = [\Sigma (Y_k n_k)] < 37.3 \text{ K g/mol}$$

$$50/1.4 < M/\rho = [\Sigma (V_k n_k)] < 100/1.5 \text{ g/cm}^3$$

$$0.0045*50 < W\,M = [\Sigma (H_k n_k)] < 0.0055*100 \text{ g } H_2O/\text{g polymer})$$

$$LB_1 \leq \Sigma y_j \leq UB_1 \quad ; \quad y_j : 0 \text{ or } 1 \text{ for } j=1,7$$

$$LB_2 \leq \Sigma y_k n_k \leq UB_2$$

-CH2-	-CO-	-COO-	-O-	-CONH-	-CHOH-	-CHCL-
14	28	44	16	43	30	48.5

Polymer Design: Problem solution

Min Fobj = M

s.t.

reformulate Fobj & constraints

$LB_1 \leq \Sigma y_j \leq UB_1$; y_j : 0 or 1 for j=1,7

$LB_2 \leq \Sigma y_k n_k \leq UB_2$

-CH2-	-CO-	-COO-	-O-	-CONH-	-CHOH-	-CHCL-
14	28	44	16	43	30	48.5

Generate & test (all these polymers satisfy the structural constraints but not necessarily the property constraints)

[-CH2 – COO-]; M = 58

[-CH2 – CH2 – CH2 – CH2-]; M = 56

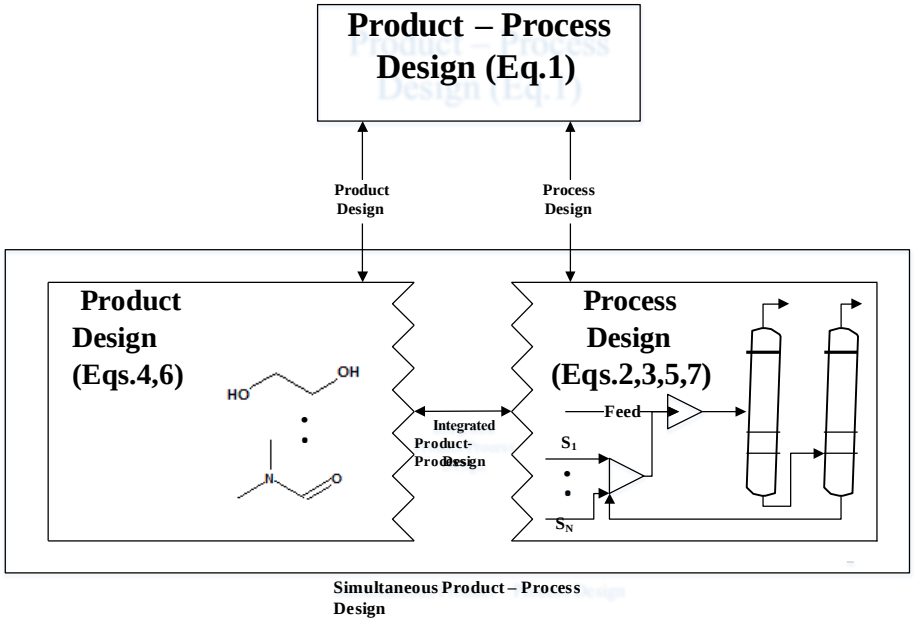
[-CH2 – CHCL- CH2-]; M = 76.5

[-CH2 – CHOH –CH2-]; M = 58

.....

Formulation Design: Mixtures, blends, ...

Computer Aided Mixture^{blend} Design



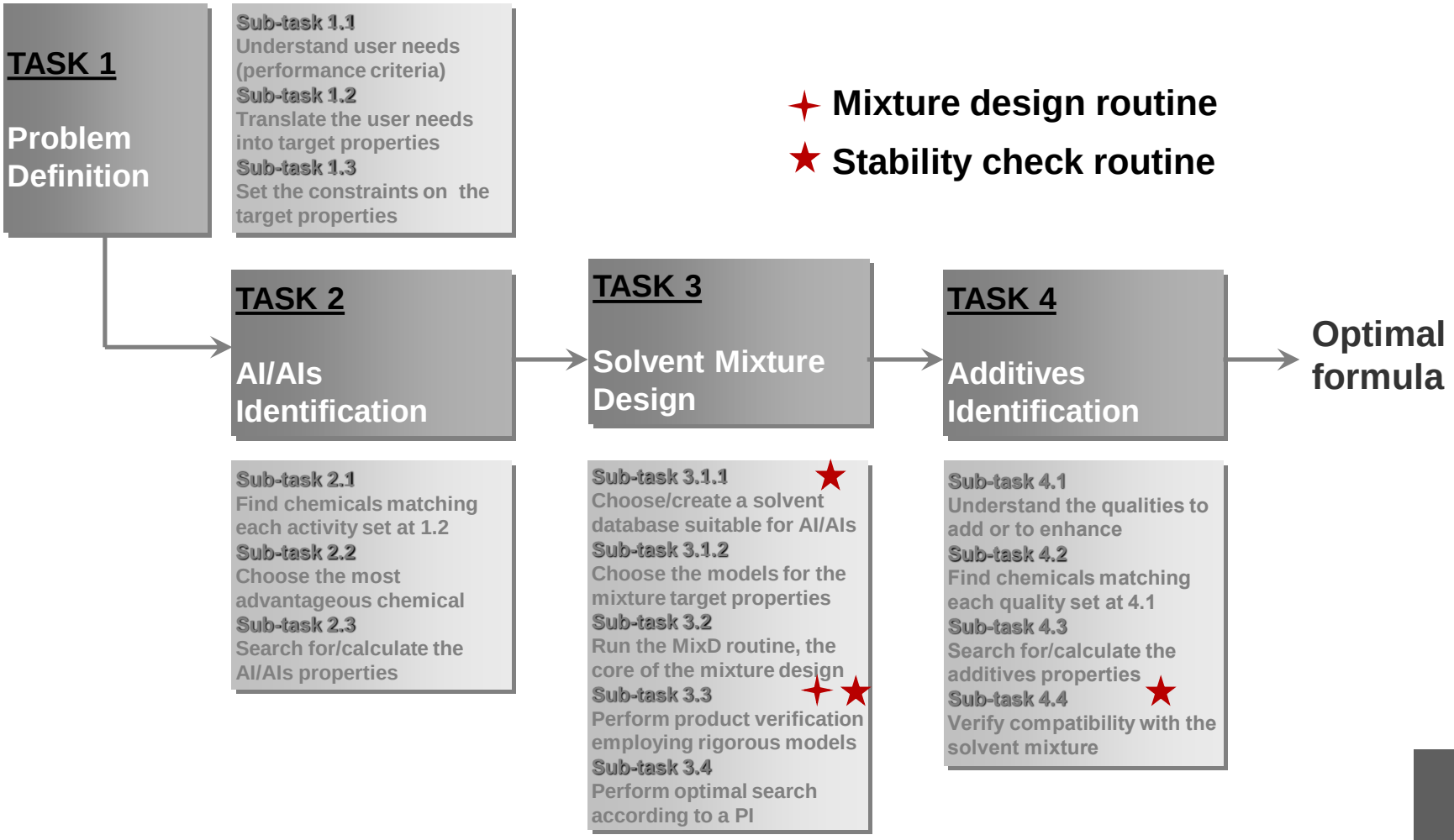
Simultaneous Product – Process Design

- Liquid formulated products
- Tailor-made blends
- Emulsified products
- .....

Eqs. 1, 4 & 6: mixture-blend design

Formulation Design: Mixtures, blends, ...

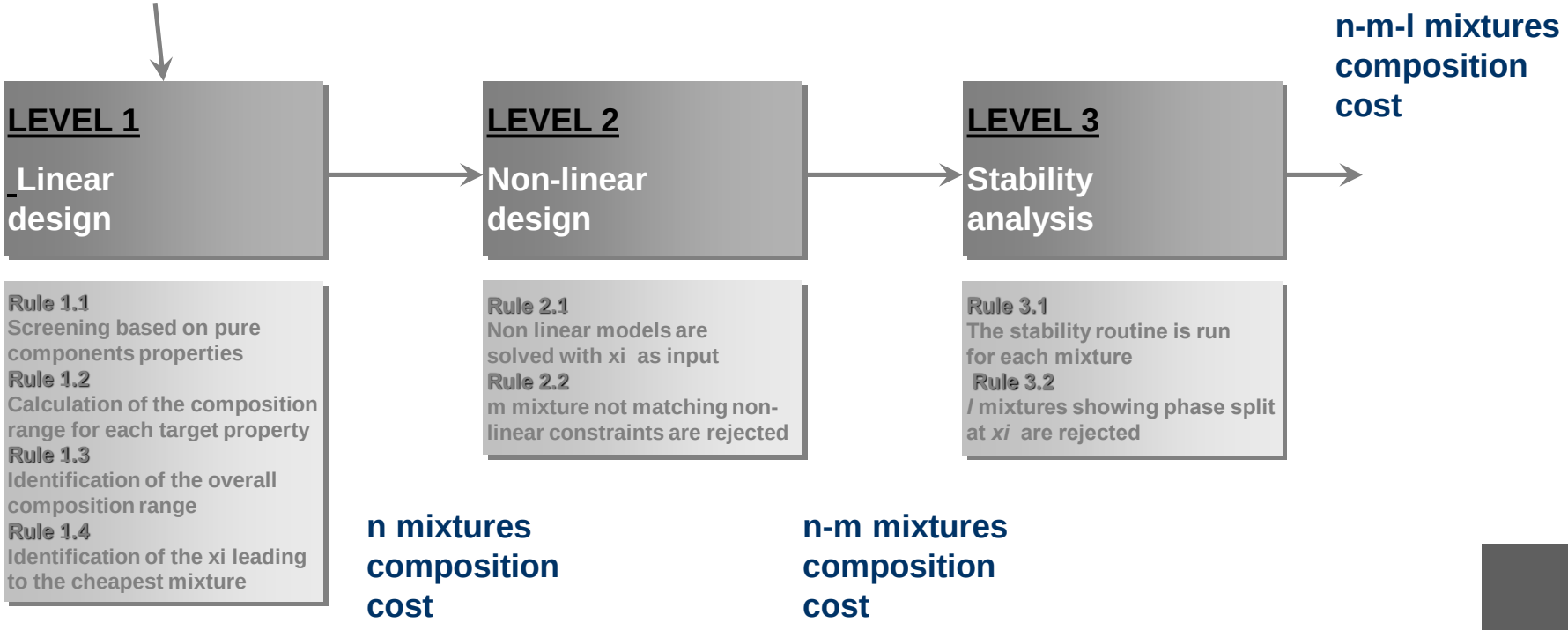
Algorithm: Work-flow



Algorithm: Mixture design

INPUTS:

1. Database of solvents properties (sub-task 3.1.1)
2. Mixture property models (sub-task 3.1.2)
3. Number of target properties
4. Temperature (K)
5. Information for non-linear models



Formulation Design: Mixtures, blends, ...

Four case studies have been developed:

- Design of a white paint for house interiors
- Design of an alcohol based insect repellent (spray lotion)
- Design of an water based insect repellent (spray lotion)
- Design of a water resistant sunscreen (spray lotion)

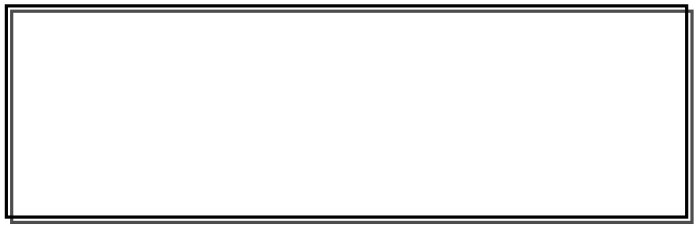
Formulation Design: Mixtures, blends, ...

Performance criteria:

what do consumers want?

- protection from sunburns
- protection from skin cancer
- prevention of skin aging
- easy and fast applicability
- high durability
- good stability
- water resistance
- low toxicity
- good material compatibility
- pleasant skin feel
- low price
- pleasant color
- pleasant scent

main activities → Active Ingredients



qualities to enhance → Additives

Formulation Design: Mixtures, blends, ...

Performance criteria:
what do consumers want?

- **easy and fast applicability**
- **high durability**
- **good stability**
- **water resistance**
- **low toxicity**
- **good material compatibility**
- **pleasant skin feel**
- **low price**

Target properties:
which are the related chemical properties?

- **form: viscosity** v**, density** ρ**, solubility** δ
- **solvents evaporation rate** T_{90}
- **phase equilibrium: 1 phase system**
- **solvents: oil soluble chemicals**
- **lethal concentration** LC_{50}
- suitable database of solvents
- **solvents with good cosmetic properties**
- **cost** C

Formulation Design: Mixtures, blends, ...

Target properties:

- **viscosity** v
- **density** ρ $(\tilde{V})$
- **solubility** δ
- **lethal concentration** LC_{50}
- **evaporation time** T_{90}

Constraints:

0.0	<	v	<	75.0	cS
100.0	<	$\tilde{V}$	<	150.0	l/kmol
$0.85 \cdot \delta_{AI}$	<	δ	<	$1.15 \cdot \delta_{AI}$	MPa½
3.16	<	LC_{50}	<	+∞	mol/m³
700	<	T_{90}	<	1300	s

- **one phase system**
- **solvent type**
- **cost**

→ **Considered later in the design**

Formulation Design: Mixtures, blends, ...

Main product activities:

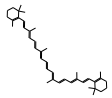
- protection from sunburns
- protection from skin cancer
- prevention of skin aging

AIs needed:

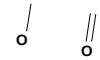
- UV-A blocker
- UV-B blocker
- antioxidant
- inorganic pigment

AIs chosen:

- avobenzone
- octyl salicylate
- α-carotene, β-carotene, vitamin A
- TiO_2

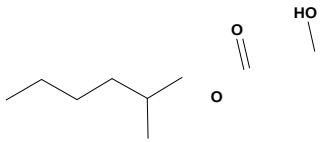


β-carotene



avobenzone

octyl salicylate



Formulation Design: Mixtures, blends, ...

AIs properties:

Kind of AI	AI	δ [MPa^{½}]	solubility
UV filters	avobenzone	23.44	oil-soluble
	octyl salicylate	21.50	oil-soluble
antioxidants	α-carotene	17.71	oil-soluble
	β-carotene	17.92	oil-soluble
	vitamin A	20.69	oil-soluble
inorganic pigments	TiO_2	34.4	insoluble

$$\delta_{AI} = 20.3$$

Therefore, the constraint on the solubility parameter becomes:

$$0.85 \cdot \delta_{AI} < \delta < 1.15 \cdot \delta_{AI} \quad \text{MPa}^{½}$$

$$\downarrow$$

$$17.3 < \delta < 23.3 \quad \text{MPa}^{½}$$

Formulation Design: Mixtures, blends, ...

The solvent database has to contain:

- oil soluble chemicals
- with good cosmetic properties
- with good material compatibility
- giving one phase system

Database: 97 esters

The properties to control are:

- **kinematic viscosity** ν
- **density** ρ $(\tilde{V})$
- **solubility parameter** δ
- **lethal concentration** LC_{50}
- **evaporation time** T_{90}

All the models are linear except for T_{90} for which a rigorous model is chosen

Formulation Design: Mixtures, blends, ...

One phase systems matching the targets (results from MiXD routine):

nº	Compounds	x_1	δ	ν	LC_{50}	T_{90}	Cost
			MPa^{½}	cS	mol/m^3	s	$/kg
1	MAcAl + 2,2-dimethylpropyl butanoate	0.89	18.95	0.53	3.63	1017.8	1.40
2	MAcAl + tert-butyl pentanoate	0.89	18.95	0.53	3.63	1017.8	1.40
3	MAcAl + isobutyl isopentanoate	0.89	18.93	0.48	3.65	878.7	1.40
4	MAcAl + 1,1-dimethylpropyl 3-methylbutanoate	0.91	18.91	0.52	3.86	846.7	1.41
5	MAcAl + 2,2-dimethylpropyl 3-methylbutanoate	0.91	18.92	0.53	3.80	940.2	1.41
6	MAcAl + isobutylene 3,3-dimethylbutanoate	0.91	18.92	0.53	3.80	940.2	1.41

Property verification:

nº	H-B	x_1	ν -linear	ν -Cao (1992)	R^2	RD (%)
			cS	cS		
1	PNA-PNA	0.89	0.533	0.537	0.00	0.75
2	PNA-PNA	0.89	0.533	0.537	0.00	0.75
3	PNA-PNA	0.89	0.480	0.482	0.00	0.37
4	PNA-PNA	0.91	0.517	0.495	0.00	4.52
5	PNA-PNA	0.91	0.529	0.533	0.00	0.73
6	PNA-PNA	0.91	0.529	0.533	0.00	0.73
RSME/AAD (%)					0.01	1.31

$$R^2 = \left(P_i^{rig} - P_i^{lin}\right)^2$$

$$RD(\%) = \frac{\left|P_i^{rig} - P_i^{lin}\right|}{P_i^{rig}} \cdot 100$$

$$SD = \sqrt{\frac{\sum\left(P_i^{rig} - P_i^{lin}\right)^2}{N}}$$

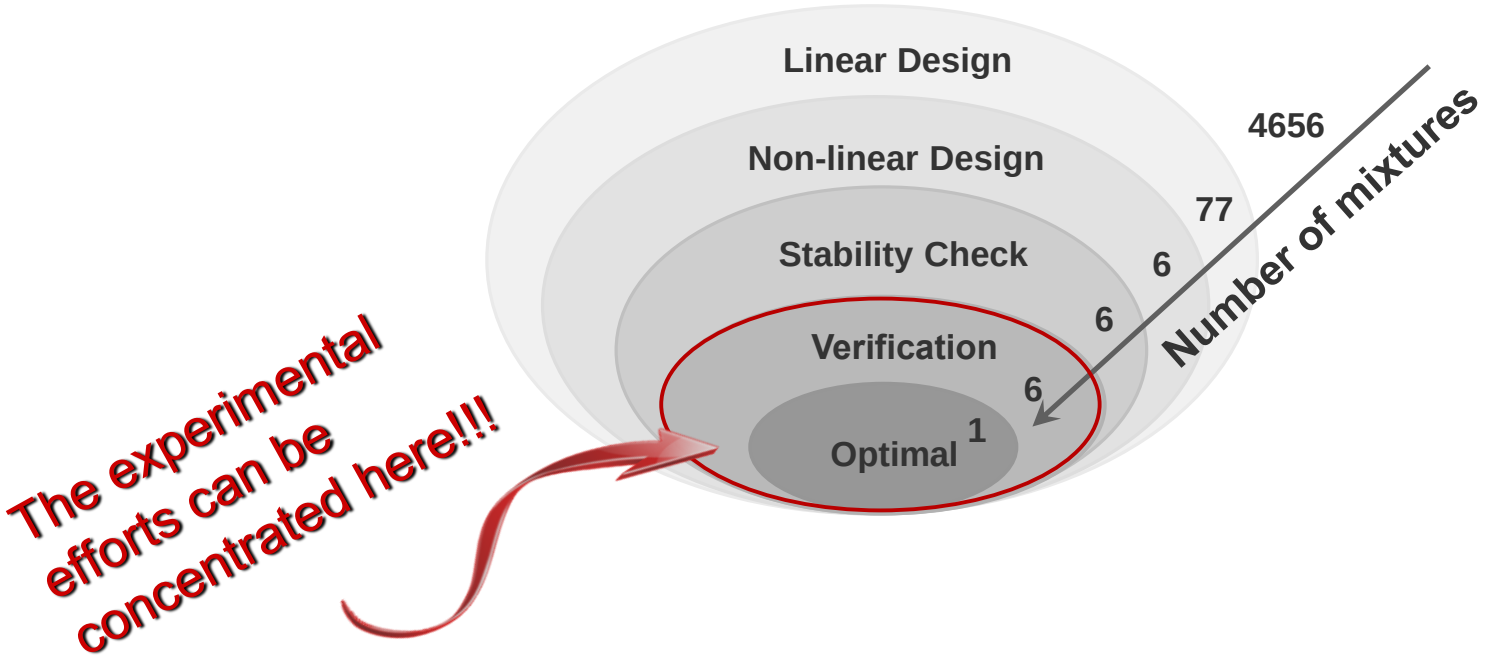
$$AARD(\%) = \frac{\sum\left|P_i^{rig} - P_i^{lin}\right|}{N}$$

Optimal search:

- The PI chosen is toxicity (LC_{50})
- The optimal mixture is mixture nº 4

Formulation Design: Mixtures, blends, ...

Summary of all the actions performed during the mixture design task:



Formulation Design: Mixtures, blends, ...

Qualities to enhance:

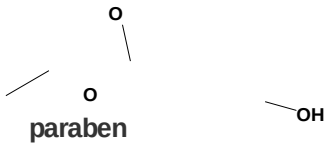
- augmentation of UV protection
- enhancement of stability
- prevention of microbial growth
- pleasant scent

Feasible Additives:

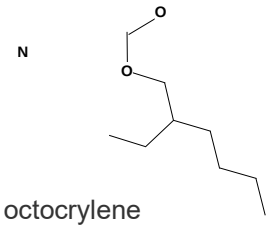
- octocrylene
- octocrylene
- parabens
- para-menth-3-yl phenylacetate

Additives properties:

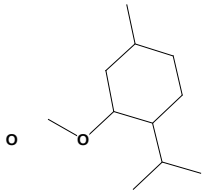
- esters
- oil soluble
- solubility parameter compatible



paraben



octocrylene



para-menth-3-yl phenylacetate

Formulation Design: Mixtures, blends, ...

Final result - optimal formulation:

Family	Chemical	x_i	w_i
AIs	avobenzone	0.010	0.0325
	octyl salicycate	0.013	0.0325
	α-Carotene	0.003	0.0163
	β-Carotene	0.003	0.0161
	vitamin A	0.011	0.0325
	TiO_2	0.025	0.0325
Solvent mixture	methoxyacetaldehyde	0.789	0.593
	2,2-dimethylpropylbutanoate	0.098	0.157
Additives	octorylene	0.009	0.034
	parabens	0.021	0.033
	iso-propyl salicylate	0.018	0.033

Tailor-made fuel blends - 1

The main challenge involves how to identify the blends that satisfy the blend target properties with various types of additives

Problems solved: Tailor made design of gasoline blends, diesel blends, jet-fuel blends and lubricant blends.

Example: Blending gasoline with different **additives:**

- ✓impact of fuel consumption on the environment.
- ✓performances can be retained and improved.

Blend templates help to efficiently narrow down the search space of feasible chemicals to be added and obtain improved tailor-made blends in a faster, reliable and robut manner

* Collaboration with Texas A&M in Qatar.

Tailor-made fuels - 2

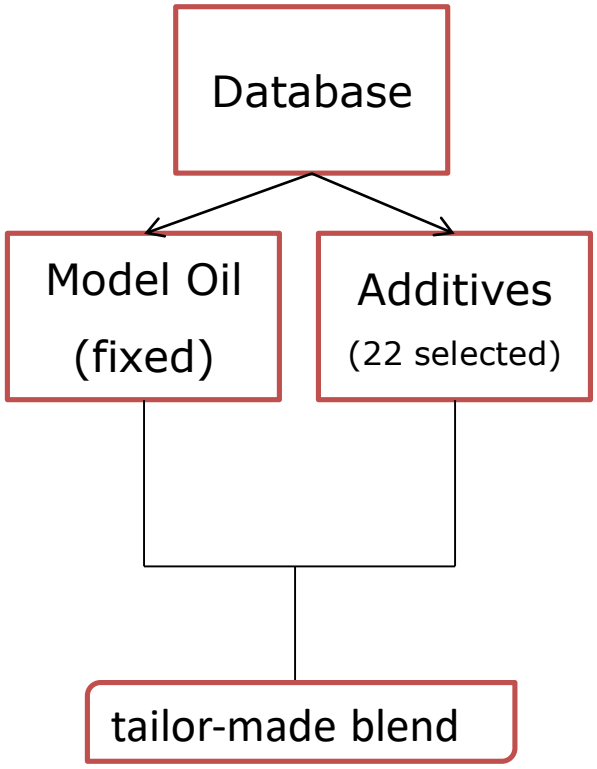
Task 1 Problem Defintion

1.1 Identify product needs

1.2 Translate needs into physico-chemical properties

1.3 Set target values

Need	Target property	Target value
Ability to be burned	RVP	$45 \leq RVP \leq 60$
Engine efficiency	RON	$RON \geq 92$
	HHV	$HHV \geq 40$
Consistency of fuel flow	η	$0.30 \leq \eta \leq 0.60$
	ρ	$0.720 \leq \rho \leq 0.775$
Flammability	T_f	$T_f \leq 300$
Toxicity	LC_{50}	$-logLC_{50} < 3.08$
Stability	ΔG^{mix}	$\Delta G^{mix} < 0$
Environmental aspect	Wt_{O2}	$2 \leq Wt_{O2} \leq 20$
Low oxidation	Choice of chemicals	



Tailor-made fuels

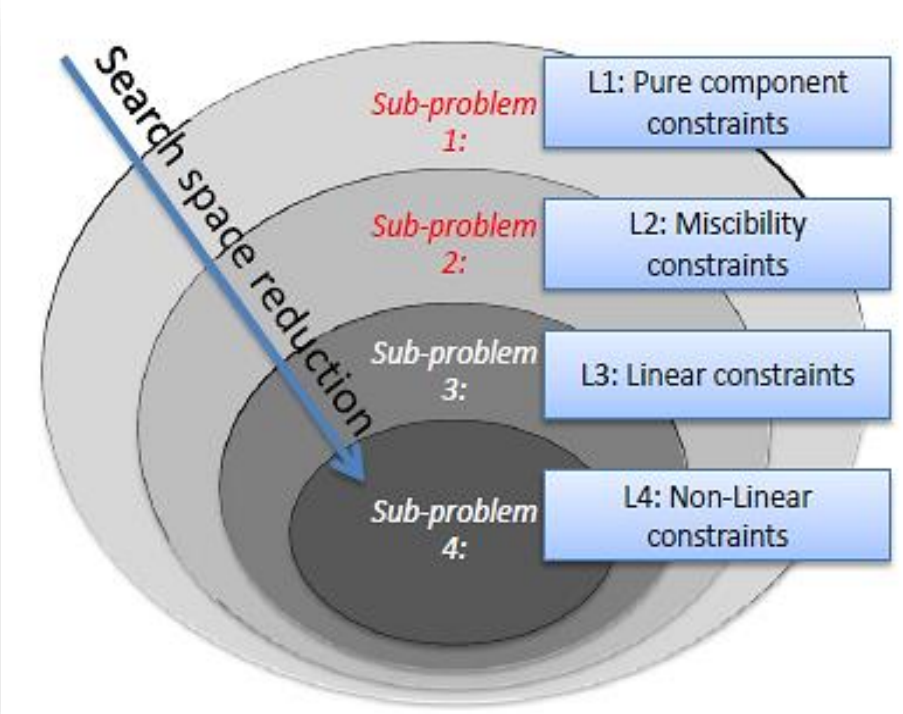
Task 2 Mixture/blend design

2.1 Pure component constraints (HHV, ρ, *η, LC50, WtO2*)

2.2 Miscibility constraint (ΔG^{mix})

2.3 Linear constraints (HHV, ρ, *η, LC50, WtO2*)

2.4 Non-linear constraints (RVP, Tf)



Miscibility test: $\Delta G^{Mix} < 0$

Linear Program

$$\min \text{ or } \max \quad f_{obj}(x)$$

$$s.t.$$

$$\zeta_{LB}^k \le \sum_i^{NC} x_i \zeta_i^k \le \zeta_{UB}^k$$

(5 Eqs. One for each prop-erty)

$$\sum_{i=1}^{NC} x_i - 1 = 0$$

$$0 < x_i < 1$$

Nonlinear Program

$$\min \text{ or } \max \quad f_{obj}(x)$$

$$s.t.$$

$$\sum_{i=1}^{NC} \frac{x_i \gamma_i P_i^{sat}(310.95\ \text{K})}{RVP_B} = 1$$

$$\sum_{i=1}^{NC} x_i \gamma_i T_{f,i} = T_{f,mix}$$

$$\sum_{i=1}^{NC} x_i - 1 = 0$$

$$x_{LB} < x_i < x_{UB}$$

Tailor-made fuels

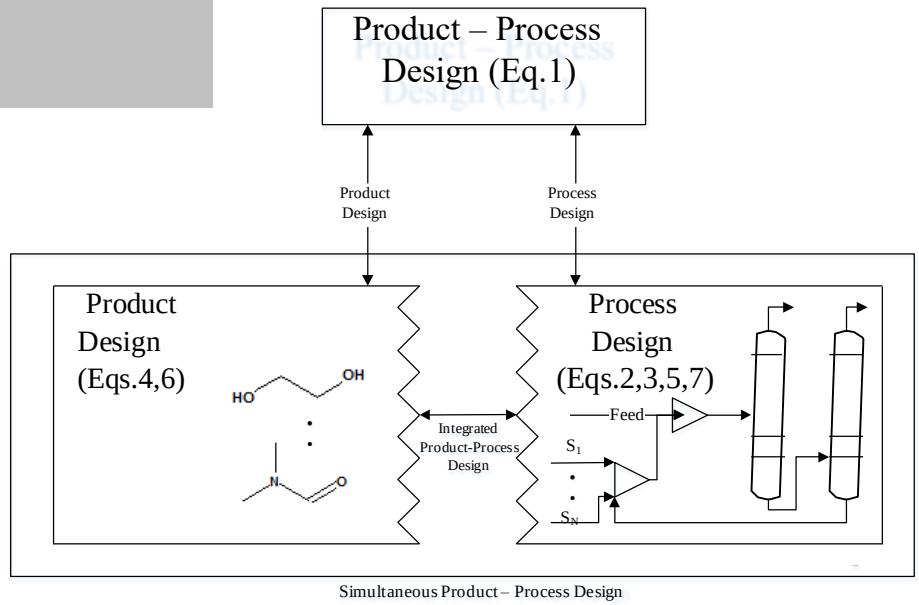
Task 3 Rank blend candidates according to a selection criterion

Blend	Composition (vol%)
Blend 1	MI (69), Tetrahydrofuran (11), 2-Methyl Tetrahydrofuran (20)
Blend 2	MI (67), Acetone (13), 2-Methyl Tetrahydrofuran (20)
Blend 3	MI (72), Acetone (10), 2-Butanone (18)
Blend 4	MI (75), 2-Butanone (13), 2-Methyl Tetrahydrofuran (12)
Blend 5	MI (77), Ethanol (12), 2-Methyl Tetrahydrofuran (11)

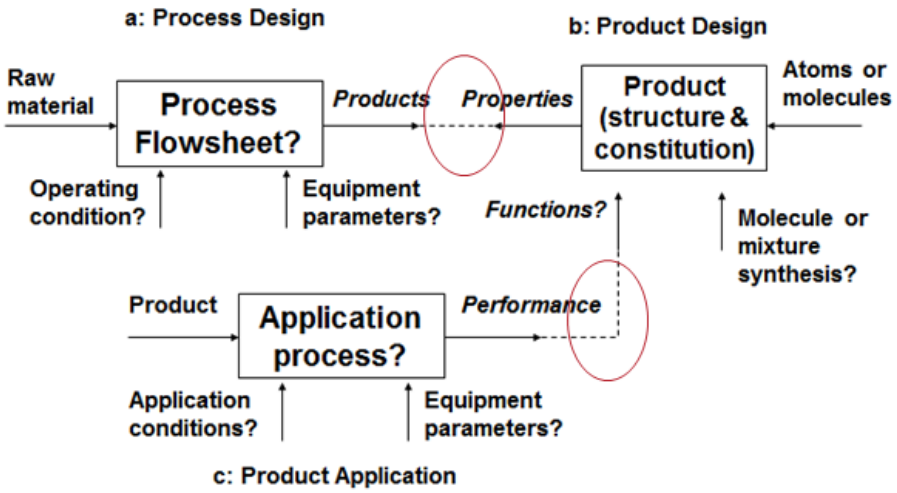
Task 4 Experimental verification

Sample	Density at 15°C (g/⟦cm⟧^3)		Dynamic Viscosity(mPa.s)		Vapor Pressure at 37.8°C (kPa)	
Target Values	0.720 – 0.775		0.3 – 0.6		45 - 60	
	Experimental	Model	Experimental	Model	Experimental	Model
Main Ingredient	0.71	0.73	0.50	0.51	51.0	54.0
Blend 1	0.76	0.76	0.54	0.46	46.2	50.8
Blend 2	0.75	0.74	0.46	0.43	60.4	64.5
Blend 3	0.73	0.74	0.45	0.43	58.9	63.7
Blend 4	0.74	0.73	0.46	0.45	50.1	53.5
Blend 5	0.74	0.74	0.61	0.58	55.1	58.9

What next? SPEED



Simultaneous Product – Process Design

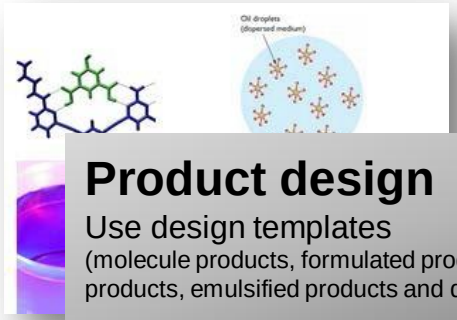


Some interesting developments:

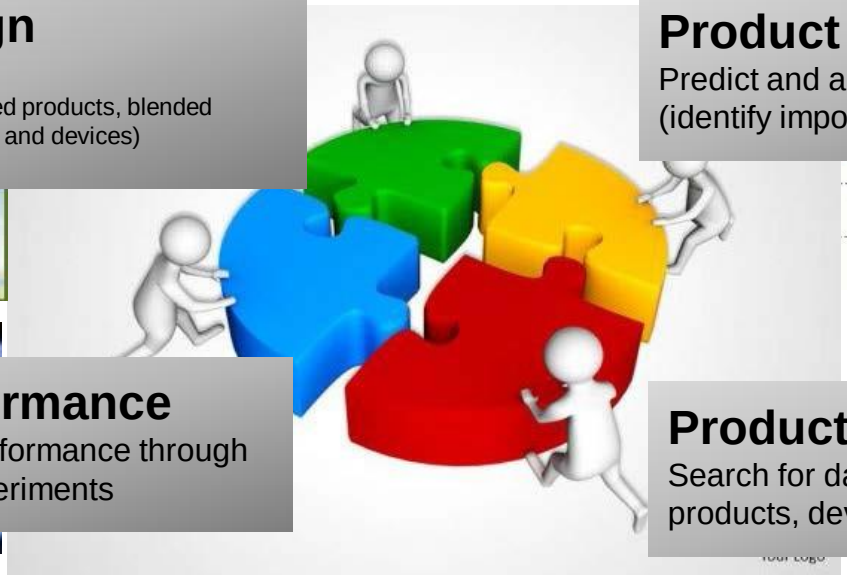
- **The chemical product simulator**
- **Product-process development**
- **…..**

Chemical product design simulator

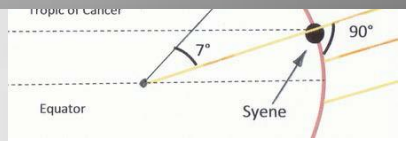
There is a need for a product simulator with the same and more useful features than a typical process simulator. Based on available data, models, methods and analysis tools, the first chemical product simulator has been developed: ***ProCAPD***



Product design
Use design templates
(molecule products, formulated products, blended products, emulsified products and devices)



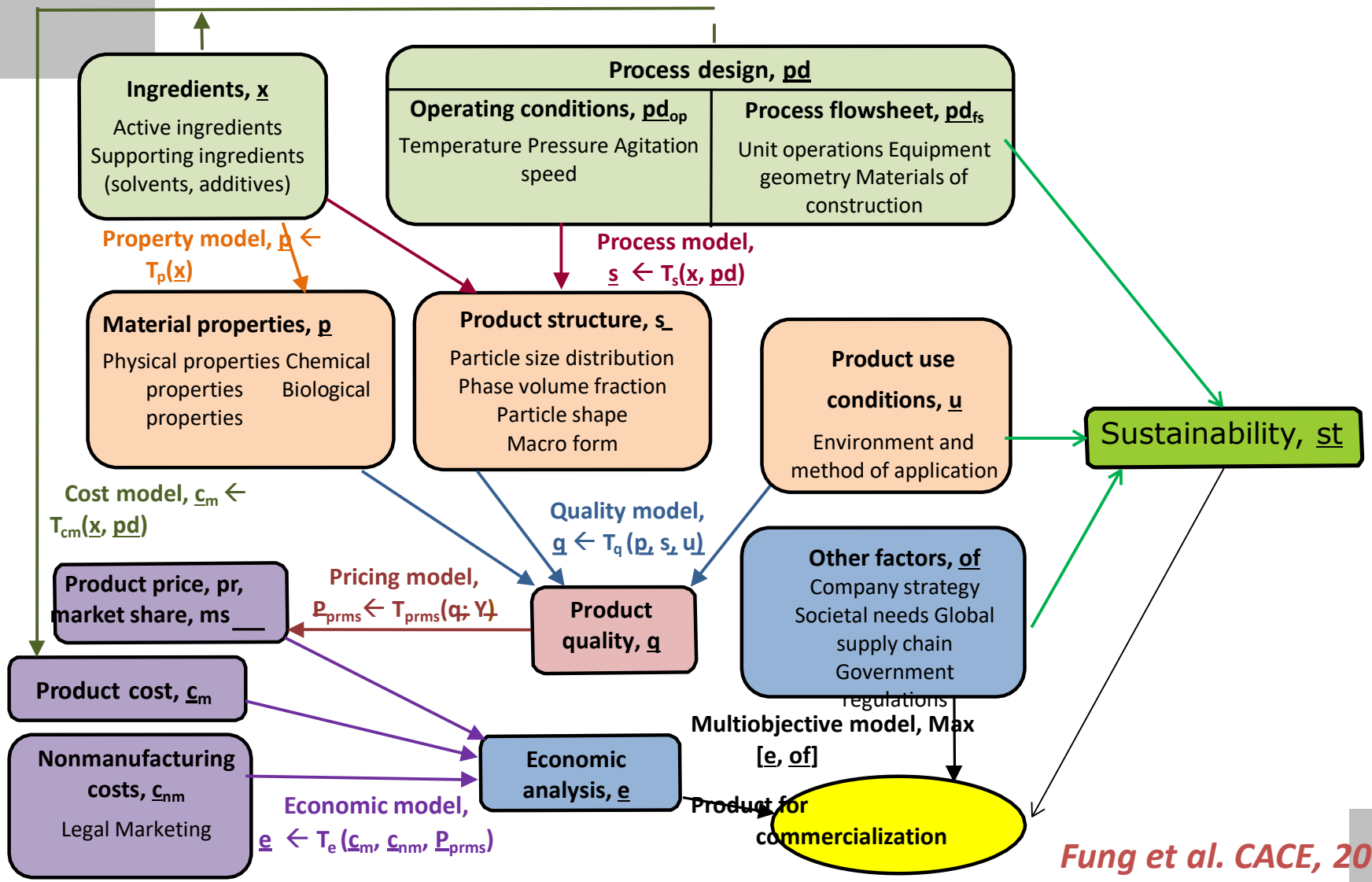
Product analysis
Predict and analyze product behavior (identify important product properties)



Product performance
Simulated product performance through virtual application experiments

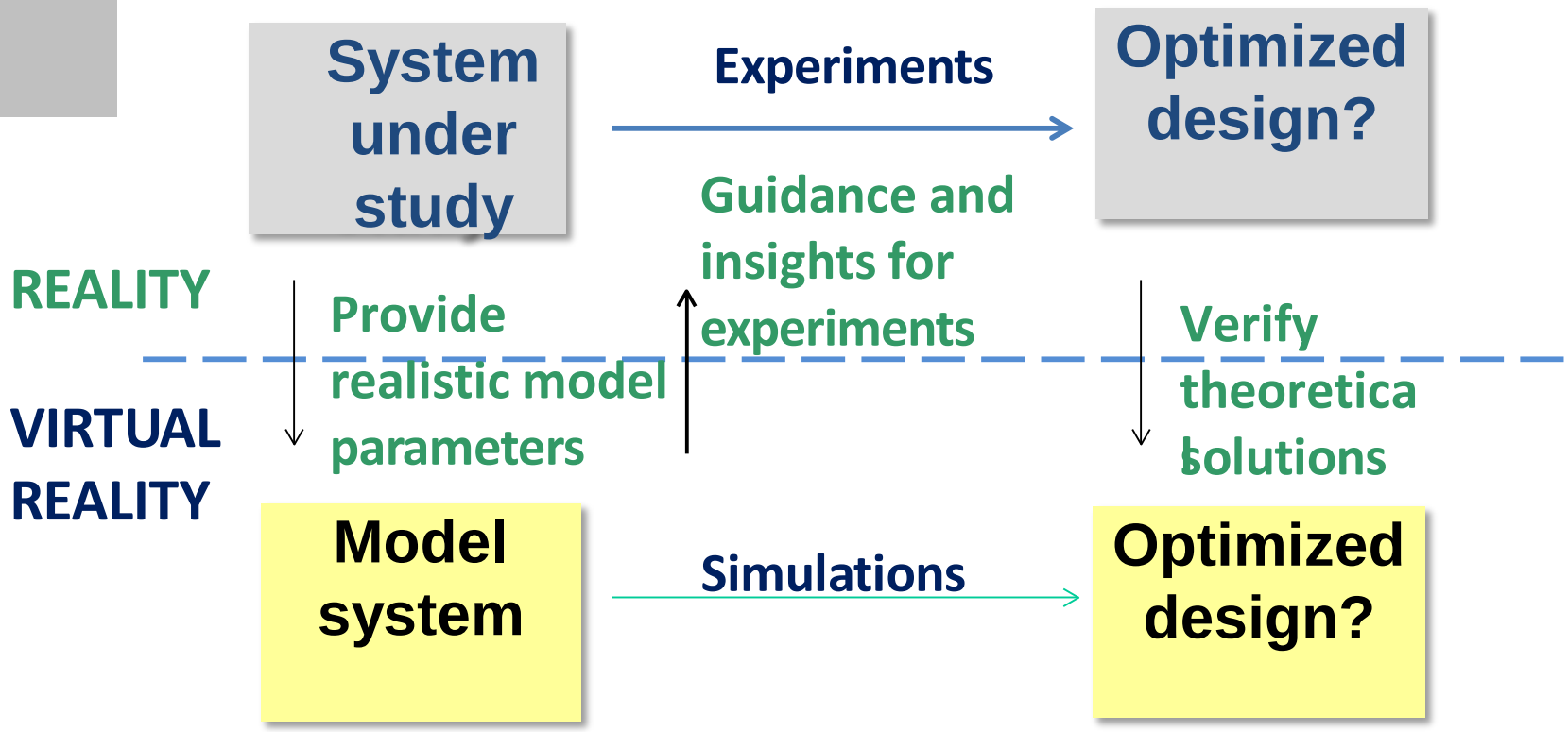
Product search
Search for data, models, properties, products, devices, etc.

The grand chemical product design model

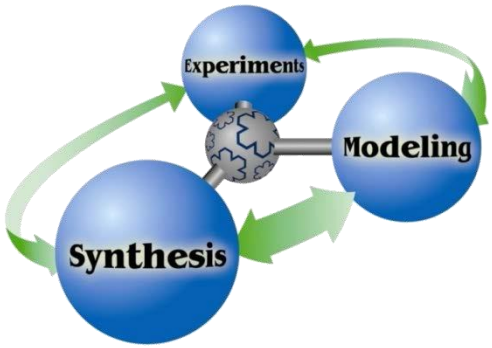


Fung et al. CACE, 2015

Collaborative effort needed!



- Solution approaches
  - Integrated multiscale modeling, experiments and synthesis
  - Ability to find predictive-innovative solutions



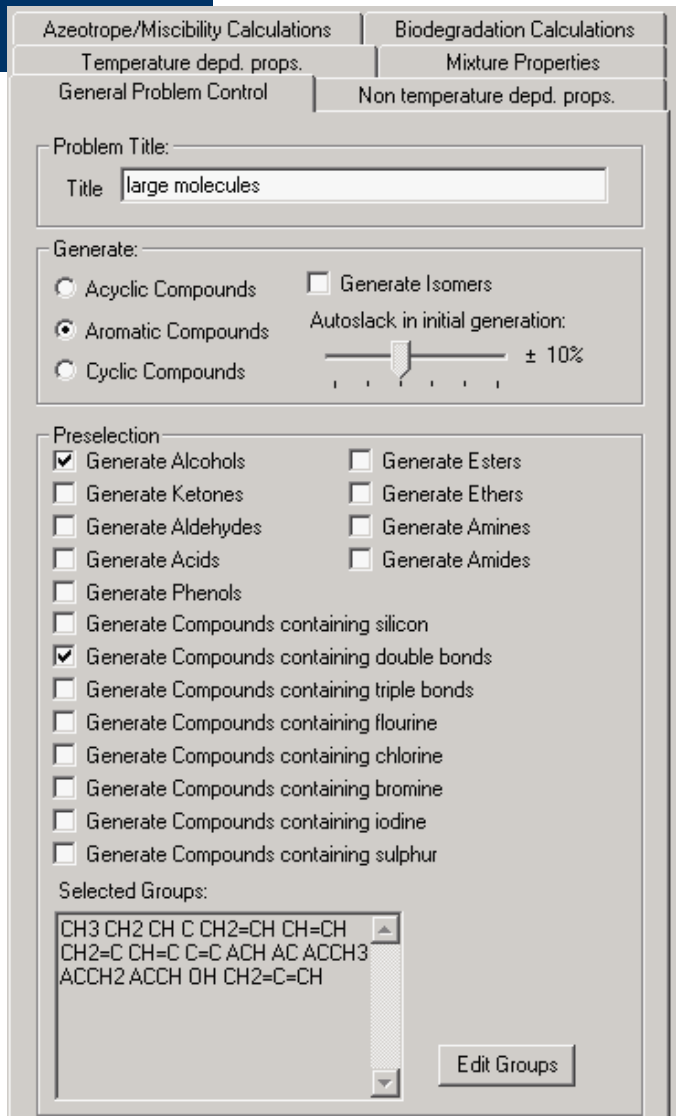
Design Problem from 60 Years Ago

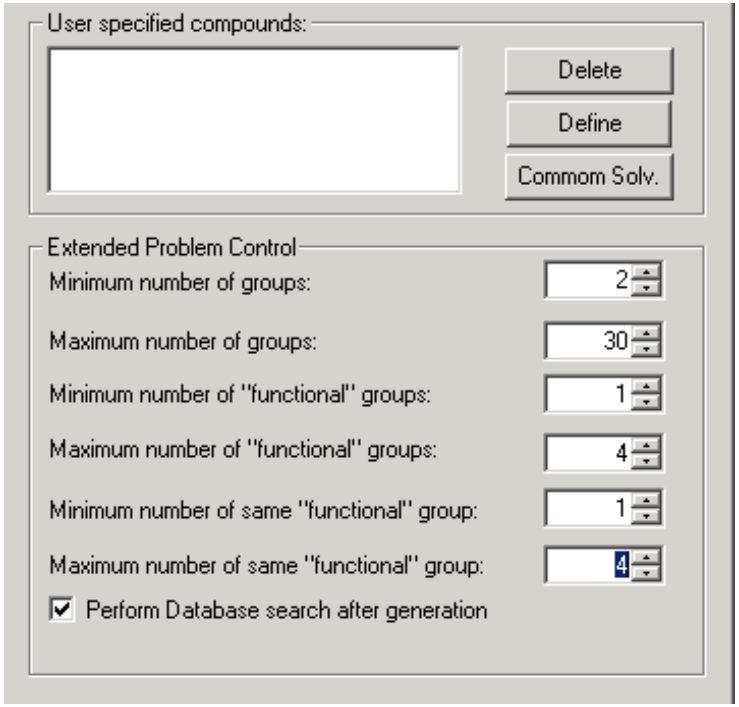
- **Non-scumming "soap bar" (world's best-selling soap bar) – Launched by Lever Bros (US division of Unilever) in 1955**
- **Attributes comparable to ordinary soap bars**
  - **Firmness**
  - **Lather**
  - **Rate of wear**
  - **Slipperiness**
  - **Mildness**
  - **No unpleasant odors**
  - **No "cracking" from wet/dry cycles**

Michael Hill
M Hill & Associates
Mahwah, NJ

- **Processable on ordinary soap bar line: model-based system yet to be developed**

Example of problem solution with ProCAMD - 1

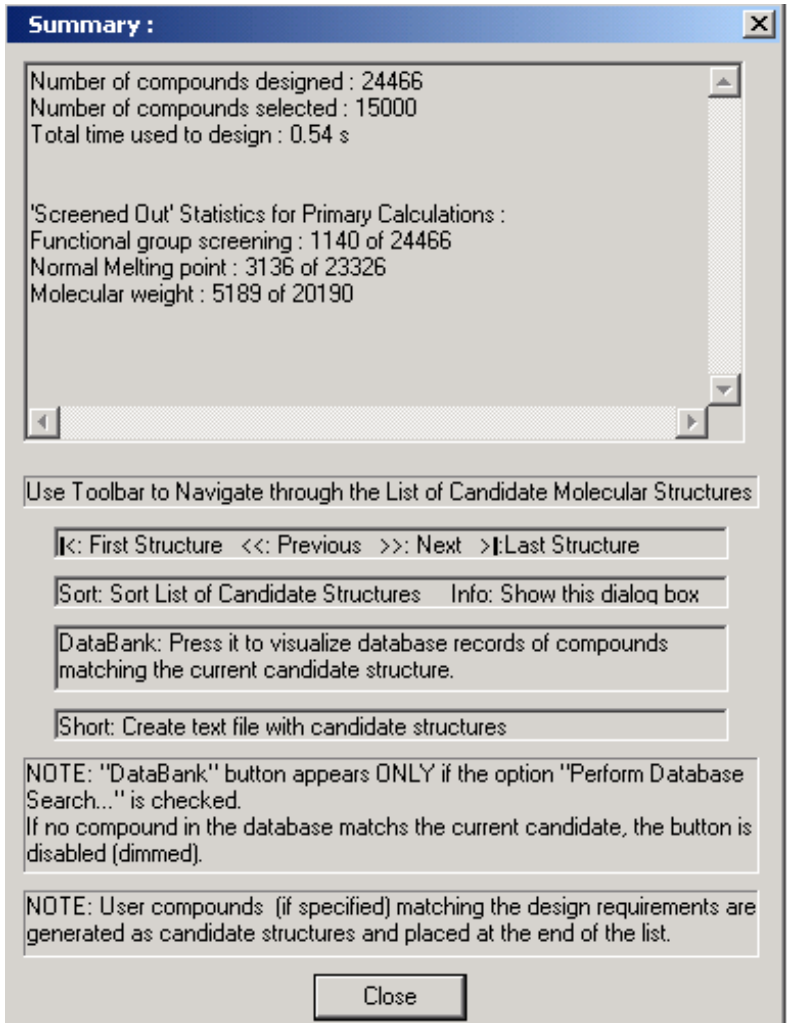




General problem control

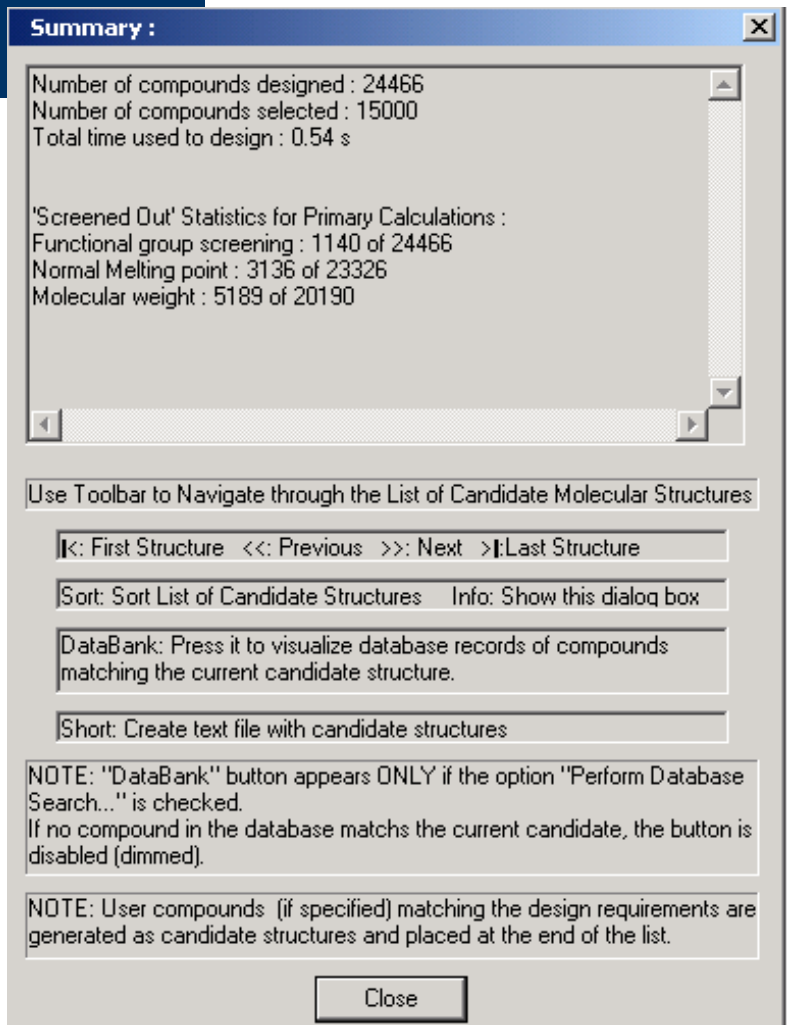
Fill out also the non-temperature depd props (Mw > 400 ; Tb > 500; Tm > 350)

Example of problem solution with ProCAMD - 2



Solution statistics

Example of problem solution with ProCAMD - 3



Compound 1 :

Description :	
No	Groupname
8	CH2
3	CH
5	ACCH3
1	ACCH2
3	OH
1	CH2=C=CH

Properties :		
Property	Value	Unit
Normal Melting point	356.05	K
Normal Boiling point	719.09	K
Molecular weight	402.60	g/mol

Details of generated compound

Solution statistics

Example of problem solution with ProCAMD - 4

ProPred - Untitled

File Edit View Tools Help

Summary | Marrero and Gani | Constantinou and Gani | Joback and

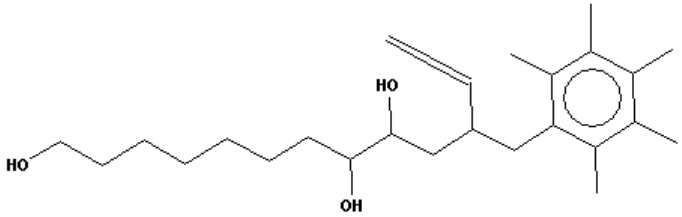
Property Values estimated by using methods
included in ProPred

Compound Name : unknown
Compound CAS : unknown
Compound Smiles : OCCCCCCCC(O)C(O)CC(C=C=C)Cc1c(C)c(C)c(
Compound Formula : C26H42O3
Mw (g/mol) : 402.61

Best estimates are suggested for each property according
developers' criteria. See detailed estimates through each
in the corresponding pages

WARNING:
Accuracy of some estimated properties (e.g. Hansen parame
might be poor if the melting point is far above 298 K

Property	Method	Unit	Est.Value	Exp.V
Tm	MG	K	413.64	N/A
Tb	MG	K	737.07	N/A
Tc	MG	K	929.51	N/A
Pc	MG	bar	13.04	N/A
Vc	MG	cm³/mol	1387.47	N/A
Zc	MG		0.234	N/A
Gf[298K]	MG	kJ/mol	7.27	N/A
Hf[298K]	MG	kJ/mol	-611.19	N/A
omega	CG		1.988	N/A
Hv[298K]	******	kJ/mol	N/A	N/A
Hv[Tb]	MG	kJ/mol	121.13	N/A
Hfus	MG	kJ/mol	55.63	N/A
Sfus	MG	J/(mol*K)	134.49	N/A
Vm[298K]	******	cm³/mol	N/A	N/A
Vm[Tb]	MG	cm³/mol	559.62	N/A
Sol. Par.[298K]	MG	MPa½	24.82	N/A
Refractive Index	MG		1.85	N/A
Molar Refraction	******		N/A	N/A
Surf.Tens.[298K]	******	dyn/cm	N/A	N/A
G.T. Temp.	******	K	N/A	N/A
Log(Kow)	******		N/A	N/A
Log(Ws)	******	Log(mg/L)	N/A	N/A
Closed Flash Temp.	CG	K	586.82	N/A
Open Flash Temp.	CG	K	658.92	N/A



Launch ProPred from ProCAMD for further analysis

Tutorial exercise - I

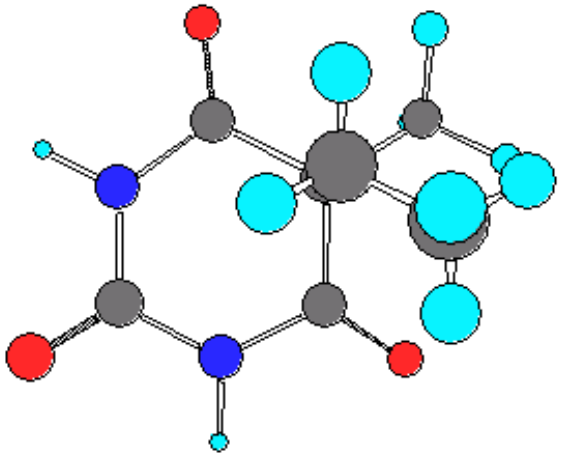
- **Analyze the drug Ibuprofen (define the needs for improving process efficiency in extracting the product from solution in the reactor) – use ProPred**
  - **Search compound in database**
    - **start ICAS**
    - **click on M, select basic search, search with CAS-number (015687-27-1), copy SMILES**
  - **Start ProPred**
    - **import SMILES, analyze properties**

Tutorial exercise - I

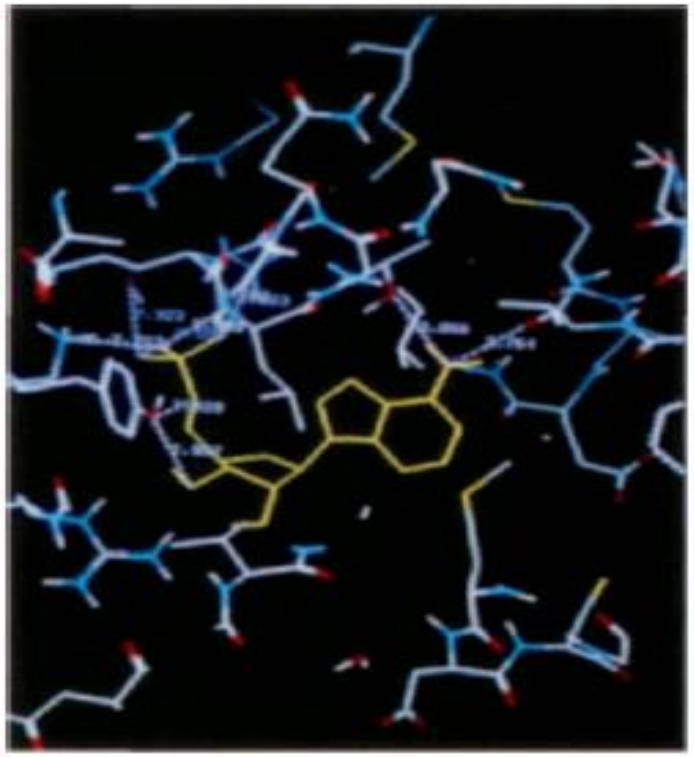
- **Use ProCamd to match the list of solvents and anti-solvents for Ibuprofen**
  - **Formulate problems (solvent & anti-solvent) see slide 19)**
    - **Start ProCamd**
      - **Specify problem (ProCamd manual)**
      - **Start execution**
      - **Analyze results**

Tutorial exercise -II

Problem Statement-1: **From the derivatives of Barbituric acid, identify the candidate that is required in the smallest amount (C) to produce a 1:1 complex with protein (binding to bovine serum albumin)**

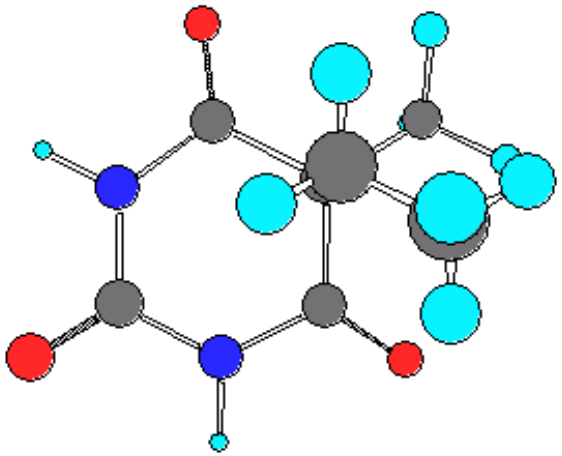


Barbituric Acid (000077-02-1)

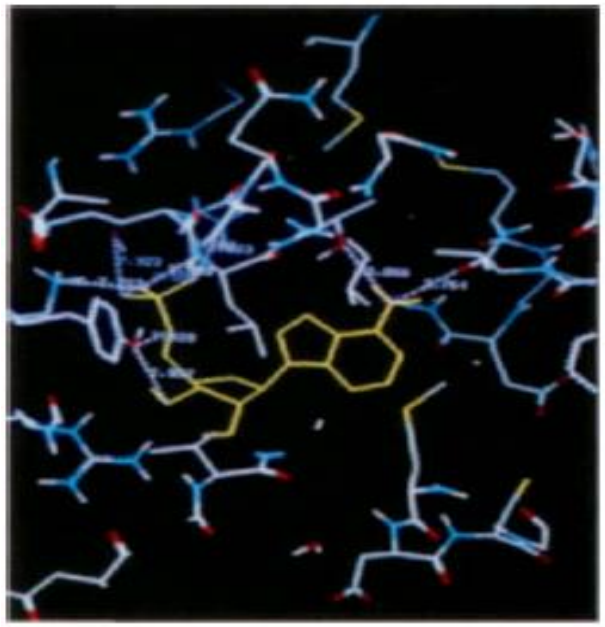


Tutorial exercise - II

Problem Statement-1: From the derivatives of Barbituric acid, identify the candidate that is required in the smallest amount (C) to produce a 1:1 complex with protein (binding to bovine serum albumin)



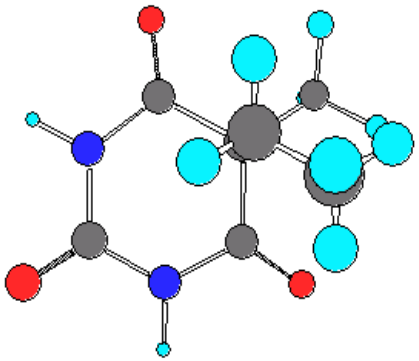
Barbituric Acid (000077-02-1)



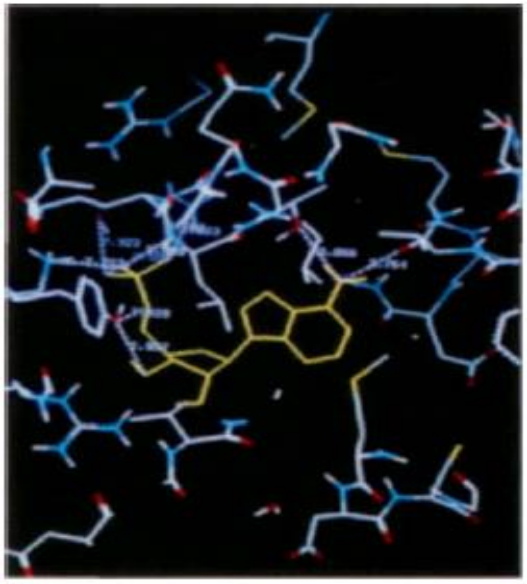
Calculate C as a function of octanol-water partition coefficient of the candidate compounds: $Log_{10}(1/C) = 0.58\ log_{10}P + 0.239$

Tutorial exercise - II

Problem Statement-1: From the derivatives of Barbituric acid, identify the candidate that is required in the smallest amount (C) to produce a 1:1 complex with protein (binding to bovine serum albumin)



Barbituric Acid
(000077-02-1)

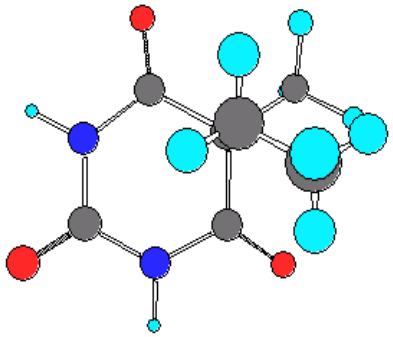


Calculate C as a function of octanol-water partition coefficient of the candidate compounds: $Log_{10}(1/C) = 0.58\ log_{10}P + 0.239$

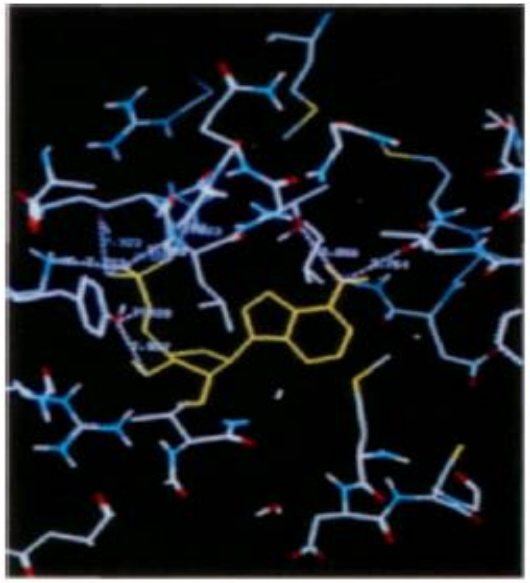
Question: How is the backbone (barbituric acid) identified and how is the relation (drug activity) between C vs $log_{10}P$ found?

Tutorial exercise - II

Problem Statement-1: From the derivatives of Barbituric acid, identify the candidate that is required in the smallest amount (C) to produce a 1:1 complex with protein (binding to bovine serum albumin)



Barbituric Acid
(000077-02-1)

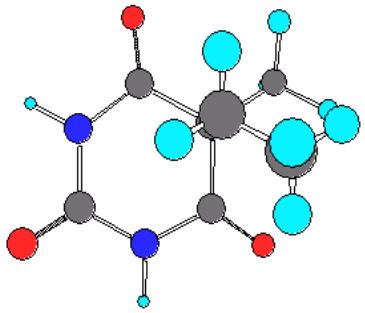


Calculate C as a function of octanol-water partition coefficient of the candidate compounds: $Log_{10}(1/C) = 0.58\ log_{10}P + 0.239$

***Solution Steps**: Generate candidates; calculate LogP; calculate C; order solutions w.r.t. C to identify the best candidate; check for solubility in water*

Tutorial exercise - II

Problem Statement-1: From the derivatives of Barbituric acid, identify the candidate that is required in the smallest amount (C) to produce a 1:1 complex with protein (binding to bovine serum albumin)



Barbituric Acid (000077-02-1)

Solution Steps

- Generate candidates (check database)
- Use ProPred to calc LogP and LogWs
- Calculate C
- Order solutions with respect to C

Calculate C as a function of octanol-water partition coefficient of the candidate compounds: $Log_{10}(1/C) = 0.58\ log_{10}P + 0.239$

Candidates (CAS Numbers) : 061346-87-0; 000076-94-8; 091430-64-7; 001953-33-9; 007391-69-7; 090197-63-0; 017013-41-1; 027653-63-0

Other Applications of CAMD

- Drug design
- Specialty chemicals design
- Lubricant design
- Refrigerant design
- Solvents for reaction synthesis
- Formulation design
- Polymer design
- ……

Summary

- **Scope of CAMD is very large but application is limited by availability of suitable property models**
- **Extension to mixture (blend) design is simple and easy**
- **Integration of process and product design is possible (covered in lecture 3)**
- **Available software: ICAS-ProCAMD**