Chemical Product Design How is it done?

Dr. Kevin G. Joback

Molecular Knowledge Systems, Inc.

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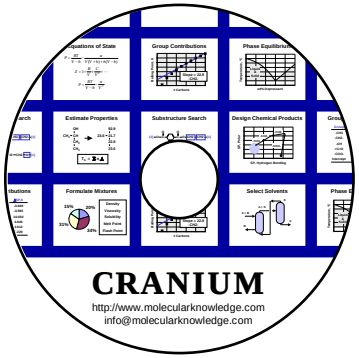
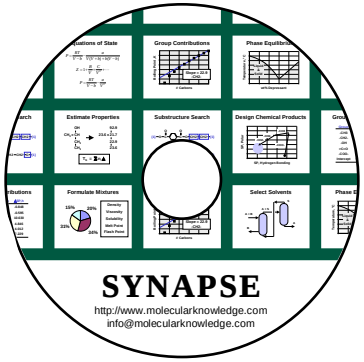
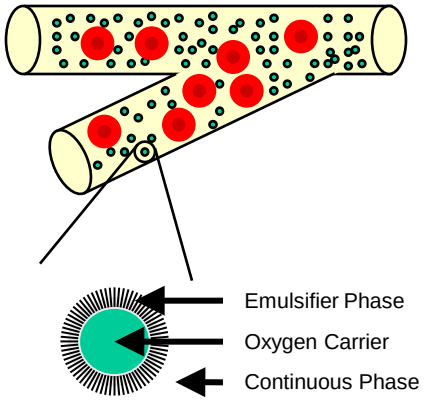
Molecular Knowledge Systems

- Located in Bedford, New Hampshire
- Company Started in 1989
- Computer Software
- Consulting







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How is it Done?

How did they choose these chemicals?

Shaving Cream

Sodium lauryl sulfate
Propylene glycol
Diazolidinyl urea
Triethanolamine
Methylparaben
Propylparaben
Stearic acid
Laureth-23
Fragrance
Isobutane
Propane
Water
Aloe

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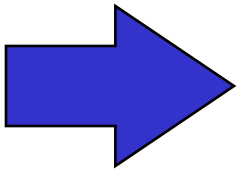
How is it Done?

Goal

*"The goal of chemical product design is to create chemical structures and mixtures that possess those chemical and physical **properties** desired by customers."*

Environmental friendly
Skin lubrication
Water solubility
Pleasant aroma
Hair softening
Moisturizing
Foaminess



Shaving Cream

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Laureth-23

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Chemical Product Design (3 Steps)

1. **Compile Property Constraints:** analysis
2. **Generate Candidates:** combination
3. **Evaluate Properties:** estimation

(refrigerants, solvents, anti-icing fluids)

Chemical Product Design (3 Steps)

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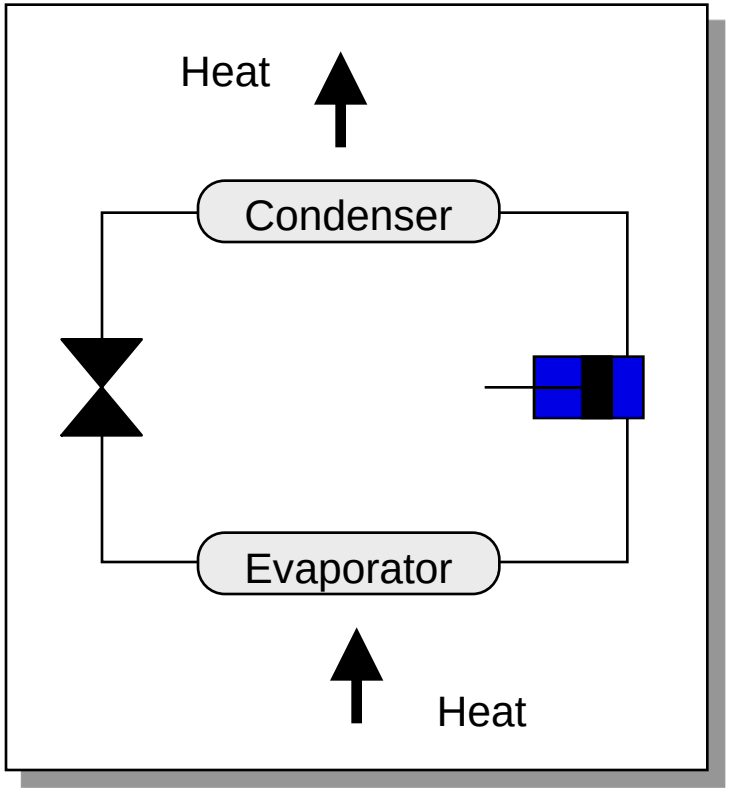
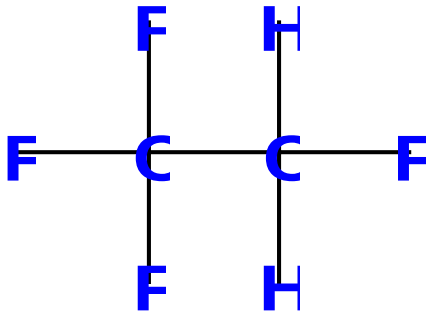
Designing New Refrigerants

Next Generation Refrigerants



Single Component



Replace R134a

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Chemical Product Design (3 Steps)

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(refrigerants, solvents, anti-icing fluids)

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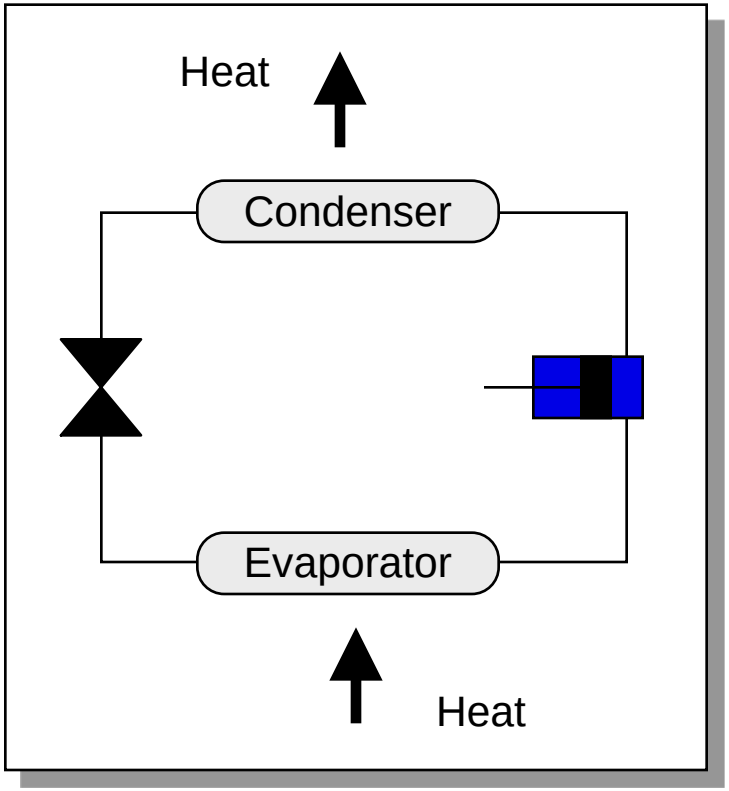
Step 1: Property Constraints

Next Generation Refrigerants



R134a Replacement

- ❑ Vapor Pressures Match
- ❑ Low Global Warming
- ❑ Not Ozone Depleting
- ❑ P-H Diagrams Match
- ❑ High Oil Solubility
- ❑ Low Flammability
- ❑ Low Toxicity

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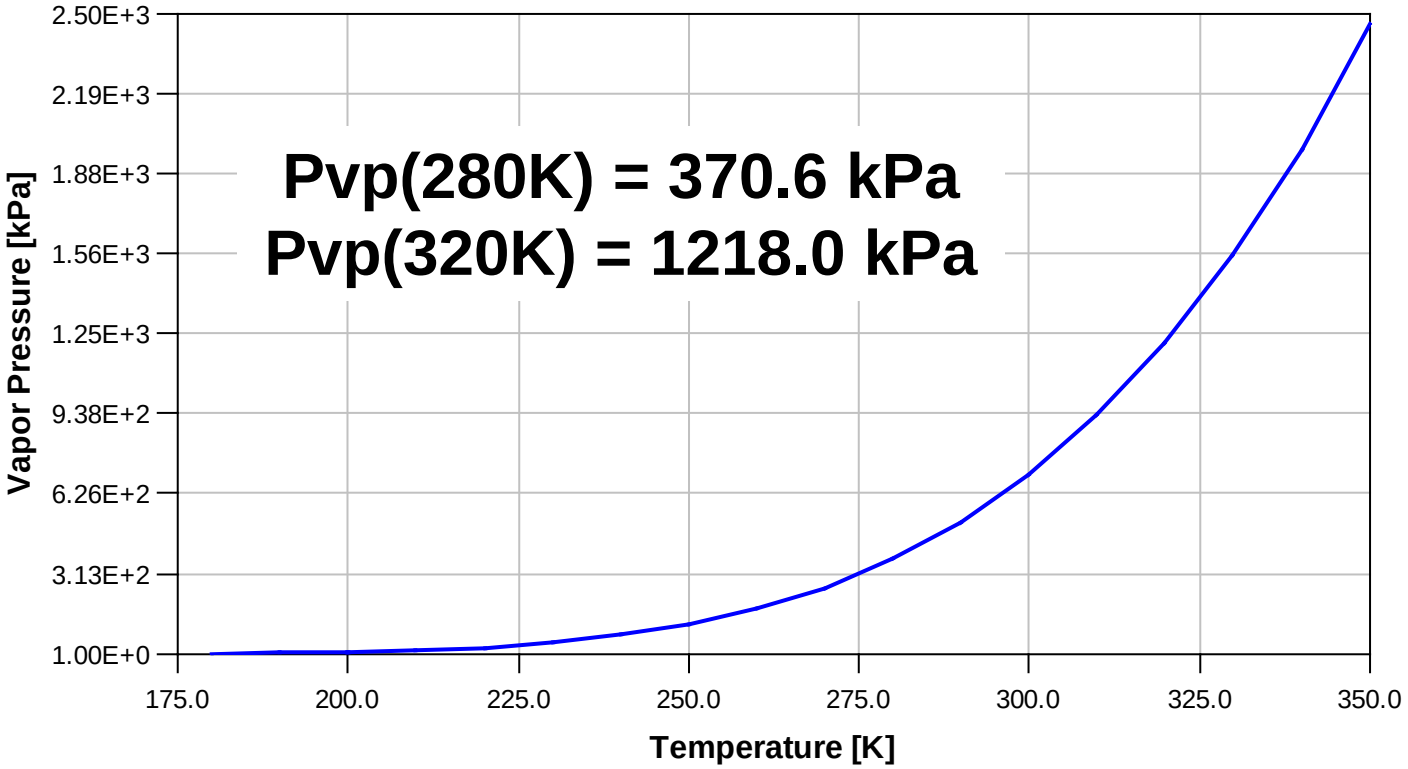
Step 1: Property Constraints

Which chemicals match R134a Vapor Pressures ?



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Chemical Product Design (3 Steps)

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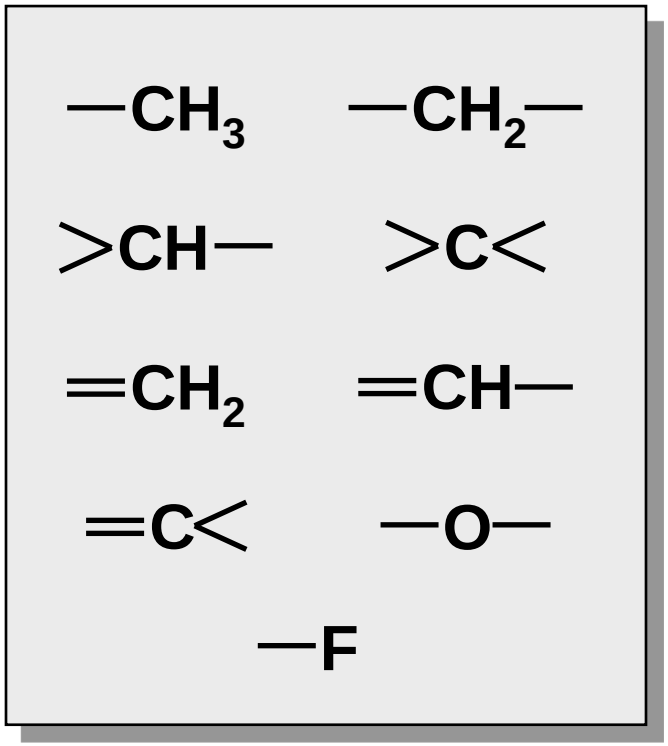
Step 2: Generate Candidates

Group Basis



Combinations of 2

- (-CH3 -CH3)
- (-CH3 -CH2-)
- (-CH3 >CH-)
- (-CH3 =CH2)
- . . .

Combinations of 3

- (-CH3 -CH3 -CH3)
- (-CH3 -CH3 -CH2-)
- (-CH3 -CH3 >CH-)
- . . .

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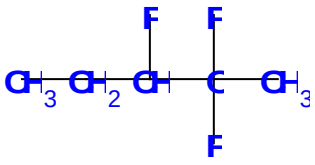
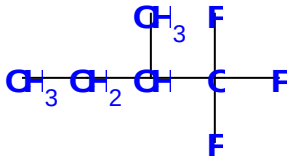
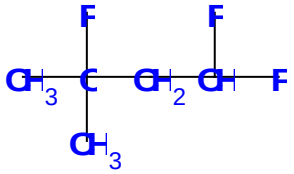
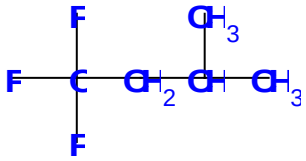
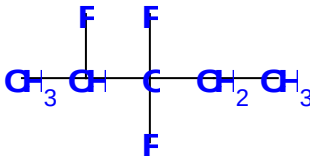
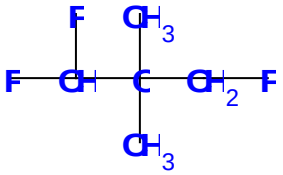
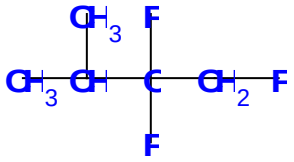
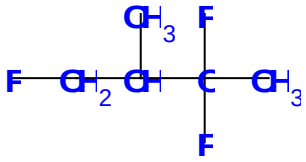
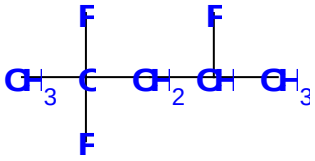
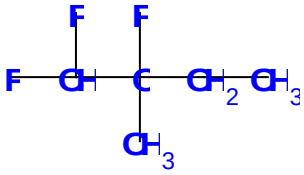
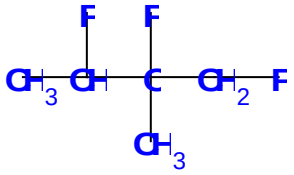
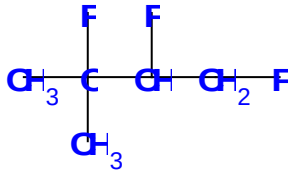
Step 2: Generate Candidates

Structure Enumeration

(-CH3 -CH3 -CH2- >C< >CH- -F -F -F)

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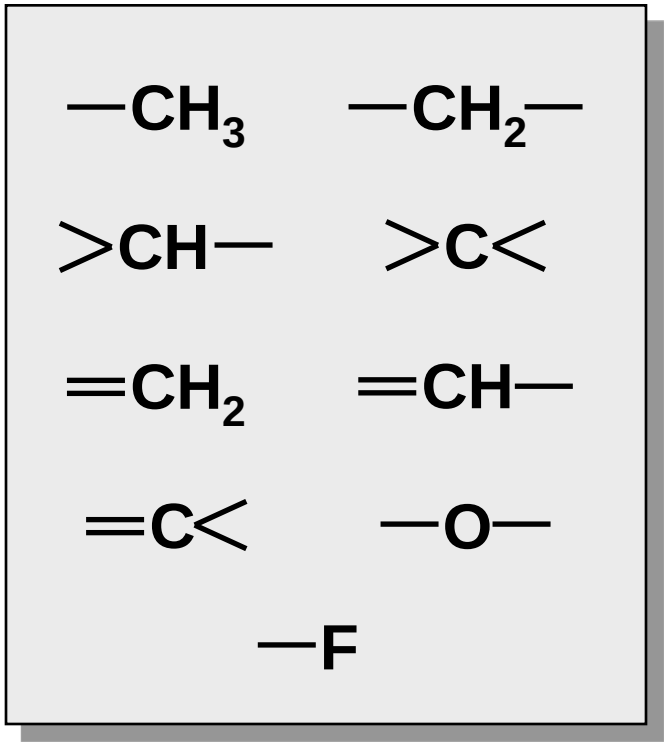
Step 2: Generate Candidates

Possible Candidate Structures

Groups to Choose From	Groups in Molecule	Feasible Candidates
9	4	24
9	6	261
9	8	3,992
9	10	72,214
9	12	many

Step 2: Generate Candidates

Group Basis



24 Valid Structures of 4 Groups

CH3-CH2-CH2-CH3	CH2=C(CH3)-F
CH3-CH(CH3)-CH3	CH3-CH2-O-F
CH3-CH2-CH=CH2	CH3-O-CH2-F
CH3-CH=CH-CH3	CH2=CH-O-F
CH2=CH-CH=CH2	CH3-O-O-F
CH2=C(CH3)-CH3	F-CH2-CH2-F
CH3-CH2-O-CH3	CH3-CH(F)-F
CH3-O-O-CH3	F-CH=CH-F
CH3-CH2-CH2-F	CH2=C(F)-F
CH3-CH(CH3)-F	F-CH2-O-F
CH2=CH-CH2-F	F-O-O-F
CH3-CH=CH-F	F-CH(F)-F

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Chemical Product Design (3 Steps)

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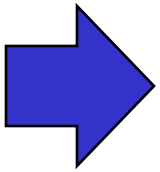
(refrigerants, solvents, anti-icing fluids)

Step 3: Evaluate Properties

Need to Screen Thousands of Candidates

CH3-CH2-CH2-CH3
CH3-CH(CH3)-CH3
CH3-CH2-CH=CH2
CH3-CH=CH-CH3
CH2=CH-CH=CH2
CH2=C(CH3)-CH3
CH3-CH2-O-CH3



- Ozone Depletion Potential
- Global Warming Potential
- Vapor Pressures – f(T)
- Flammability Limits
- Rat LC50 4 Hours
- Enthalpy – f(T,P)
- Oil Solubility

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Step 3: Evaluate Properties

Physical Property Estimation Techniques

- ❑ **Group Contribution Techniques**
- ❑ **Equation Oriented Techniques**
- ❑ **Force Field Techniques**
- ❑ **Connectivity Indices**
- ❑ **Parameter Fits**

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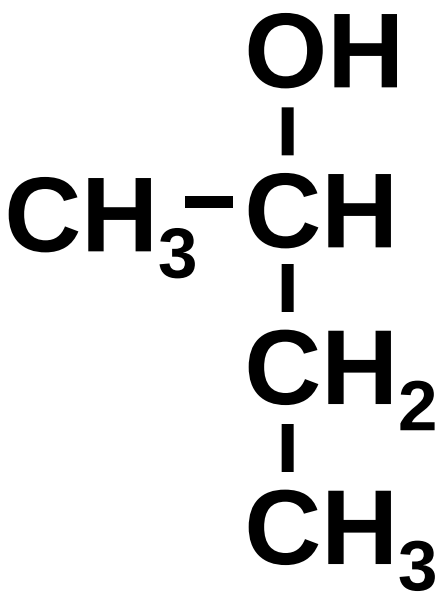
Group Contribution Techniques



1) Select Technique
2) Dissect Structure
3) Get Contributions
4) Insert into Model

Group	ΔTb
-CH3	23.6
-CH3	23.6
-CH2-	22.9
>CH-	21.7
-OH	92.9
Tb (est)	382.8 K
Tb (lit)	372.7 K

$$Tb = 198.1 + \Sigma\Delta_i$$

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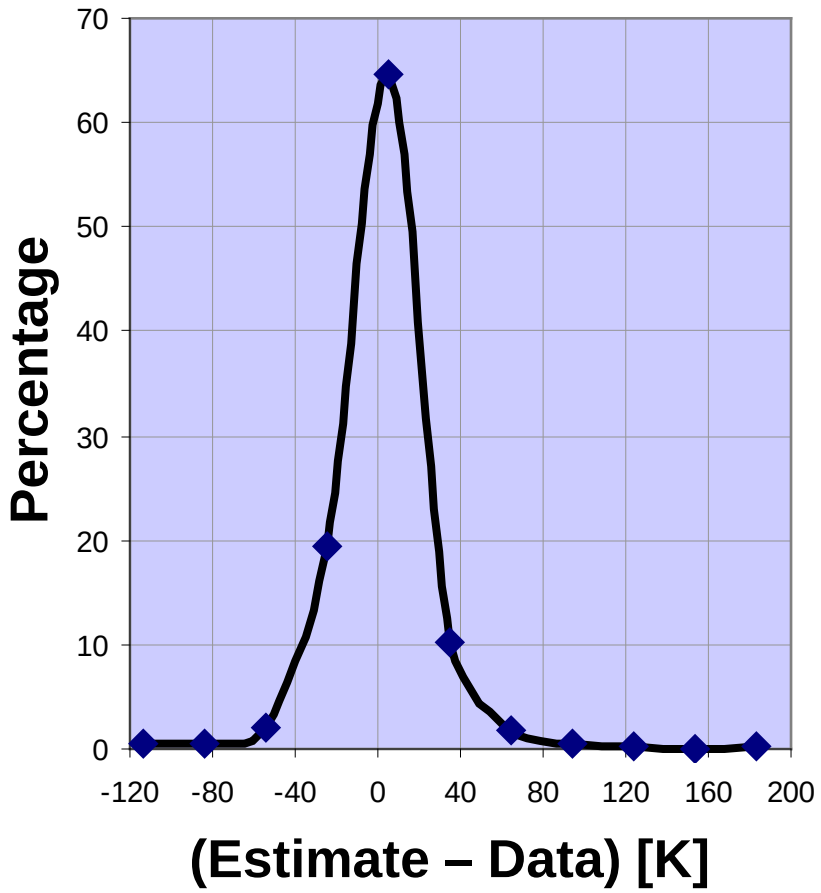
Boiling Point, Estimation Errors

Joback's Method



Statistics

Observations	559
Avg Error	0.97 K
Avg Abs Err	15.1 K
Avg % Error	4.8 %
Max Error	197.4 K

Outliers, Errors

N-Methylformamide	-128.5 K
Acetamide	-122.6 K
Fluorine	113.1 K
Cyanogen	197.4 K

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Equation Oriented Techniques

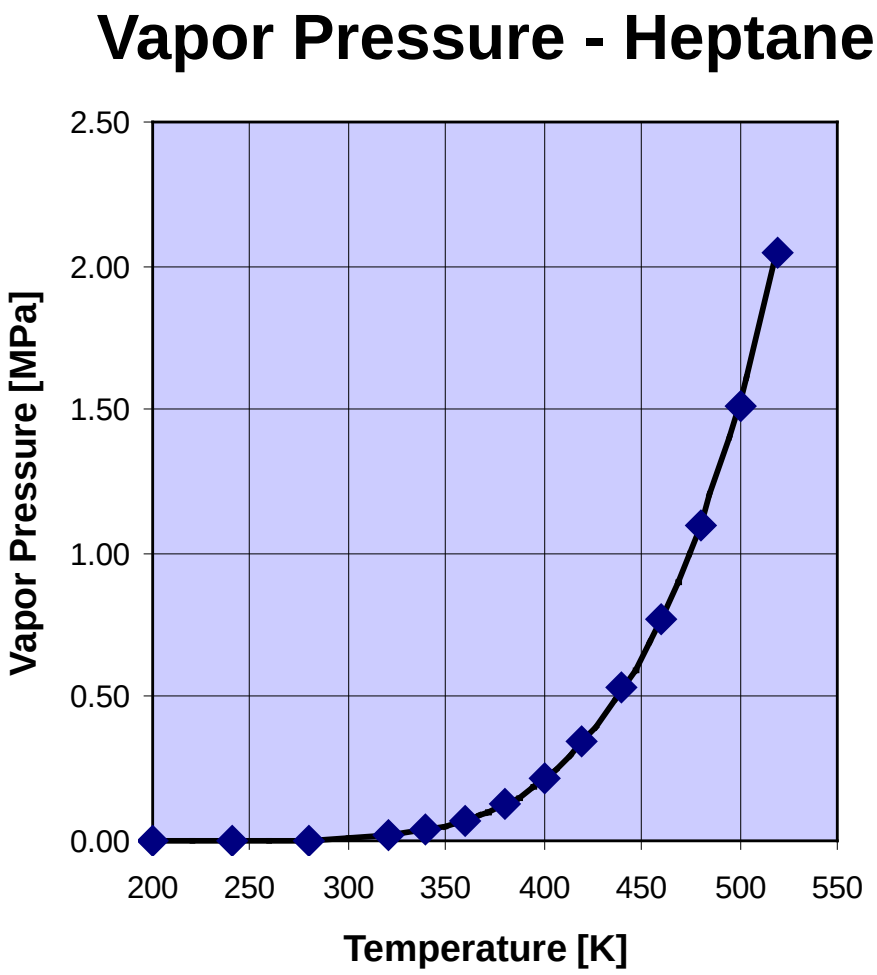
$$\ln\left(\frac{P_{vp}}{P_c}\right) = T_{br}\,\frac{\ln(P_c)}{1-T_{br}}\left(1-\frac{1}{T_r}\right)$$

Required Properties

Tc – Critical Temperature

Pc – Critical Pressure

Tb – Boiling point



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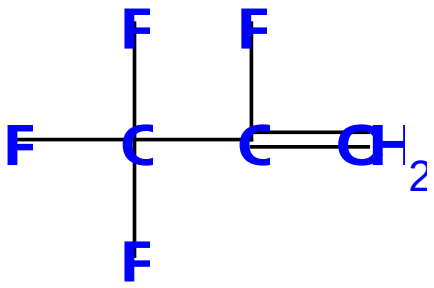
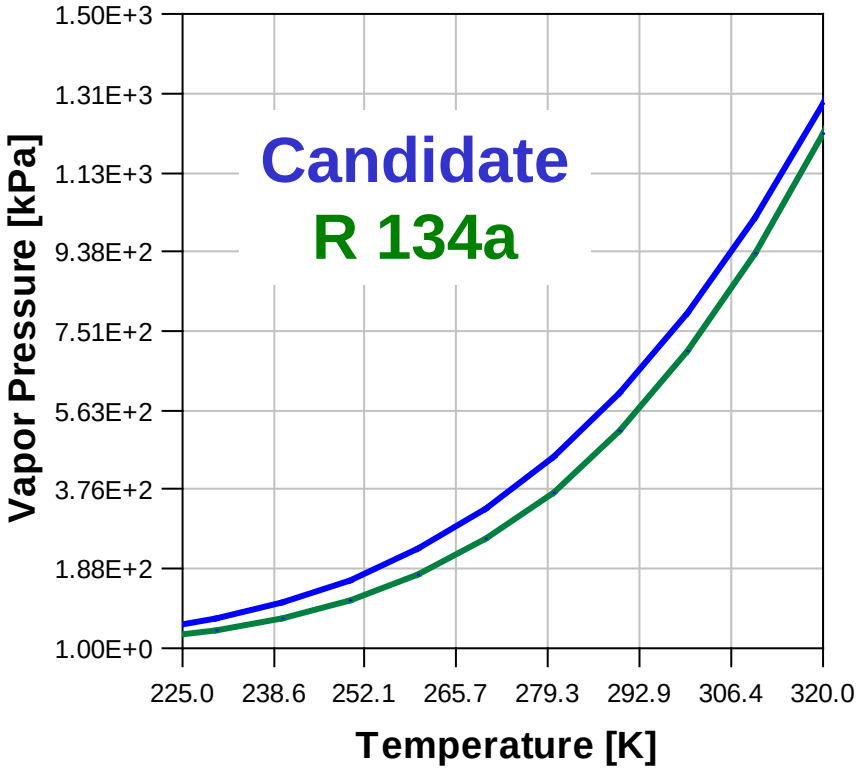
Step 3: Evaluate Properties



Property	Estimate
Tb	238.4 K
Tc	366.7 K
Pc	3406 kPa
Pvp (280 K)	452 kPa
Pvp (320 K)	1291 kPa



R134a Pvp(280K) = 370.6 kPa

R134a Pvp(320K) = 1218.0 kPa

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Step 3: Evaluate Properties

Candidate Refrigerants

Candidate	Pvp (280K)	Pvp (320K)
R 134a	370.6	1218
F-CHF-CHF-CH2-F	418.8	1275
F-CHF-O-CHF-F	414.8	1299
F-CF=CF-F	415.9	1223
F-CH2-CH2-F	409.2	1233
F-CHF-CH2-CHF-F	418.8	1275
CH3-CF2-CH3	385.3	1114
CH2=CF-CF3	452.5	1291

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Chemical Product Design (3 Steps)

1. **Compile Property Constraints:** analysis
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(refrigerants, solvents, anti-icing fluids)

Solvents in Chemical Products

Solvents Applications

Personal Care Products

Cosmetics / Fragrances

Pesticides / Herbicides

Cleaning / Degreasing

Adhesives / Sealants

Process Solvents

Paints / Coatings

Pharmaceuticals

Printing Inks

Detergents

Property Constraints

Evaporation rate

Solute solubility

Vapor pressure

Freezing point

Boiling point

Flammability

Recyclability

Viscosity

Irritancy

Toxicity

Listed

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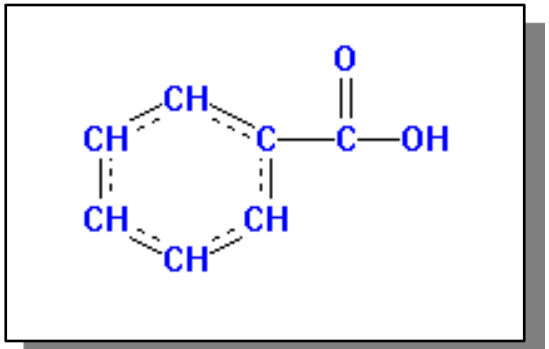
Step 1: Property Constraints

Solute = Benzoic Acid



Could solvent blends give higher solubility?

Solubility at 25°C

Solvent	wt %
Pyridine	64.0
Dimethyl sulfoxide	61.9
N,N-Dimethylformamide	61.7
N,N-Dimethylacetamide	60.7
N-Methylformamide	51.9
Methanol	42.6
Ethanol	36.6
2-Propanol	32.8

A. Beerbower, P. L. Wu and A. Martin. "Expanded Solubility Parameter Approach I: Naphthalene and Benzoic Acid in Individual Solvents." Journal of Pharmaceutical Sciences. Volume 73, number 2, page 179-188, 1984.

Step 1: Property Constraints

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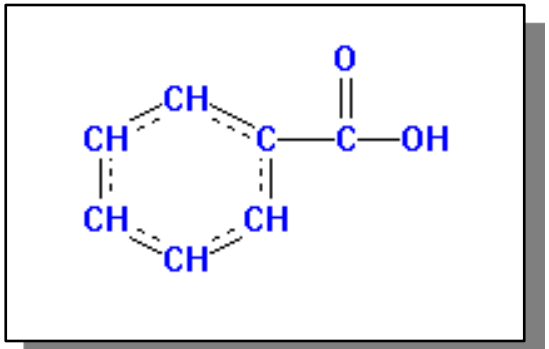

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Solvent	wt %
Pyridine	64.0
Dimethyl sulfoxide	61.9
N,N-Dimethylformamide	61.7
N,N-Dimethylacetamide	60.7
N-Methylformamide	51.9

Solubility > 50.0 wt%

A. Beerbower, P. L. Wu and A. Martin. "Expanded Solubility Parameter Approach I: Naphthalene and Benzoic Acid in Individual Solvents." Journal of Pharmaceutical Sciences. Volume 73, number 2, page 179-188, 1984.

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Step 2: Generate Candidates

62 Common Solvents
Generate all Combinations
1,891 Binary Solvent Blends

Solute + 1,1,1-Trichloroethane + 1,2-Dichloroethane

Solute + 1,1,1-Trichloroethane + 1,2-Propylene glycol

Solute + 1,1,1-Trichloroethane + 1,4-Dioxane

Solute + 1,1,1-Trichloroethane + 1-Butanol

• • • •

Solute + Water + n-Octane

Solute + Water + n-Pentane

Solute + Water + o-Xylene

Solute + Water + p-Xylene

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Step 2: Generate Candidates

34,596 compositions

Solute	Solvent1	Solvent2	
10.0	22.5	67.5	Solvent Ratio 1 : 3
20.0	20.0	60.0	
30.0	17.5	52.5	
. . .	. . .	. . .	
10.0	67.5	22.5	Solvent Ratio 3 : 1
20.0	60.0	20.0	
30.0	52.5	17.5	
. . .	. . .	. . .	

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(refrigerants, **solvents,** anti-icing fluids**)**

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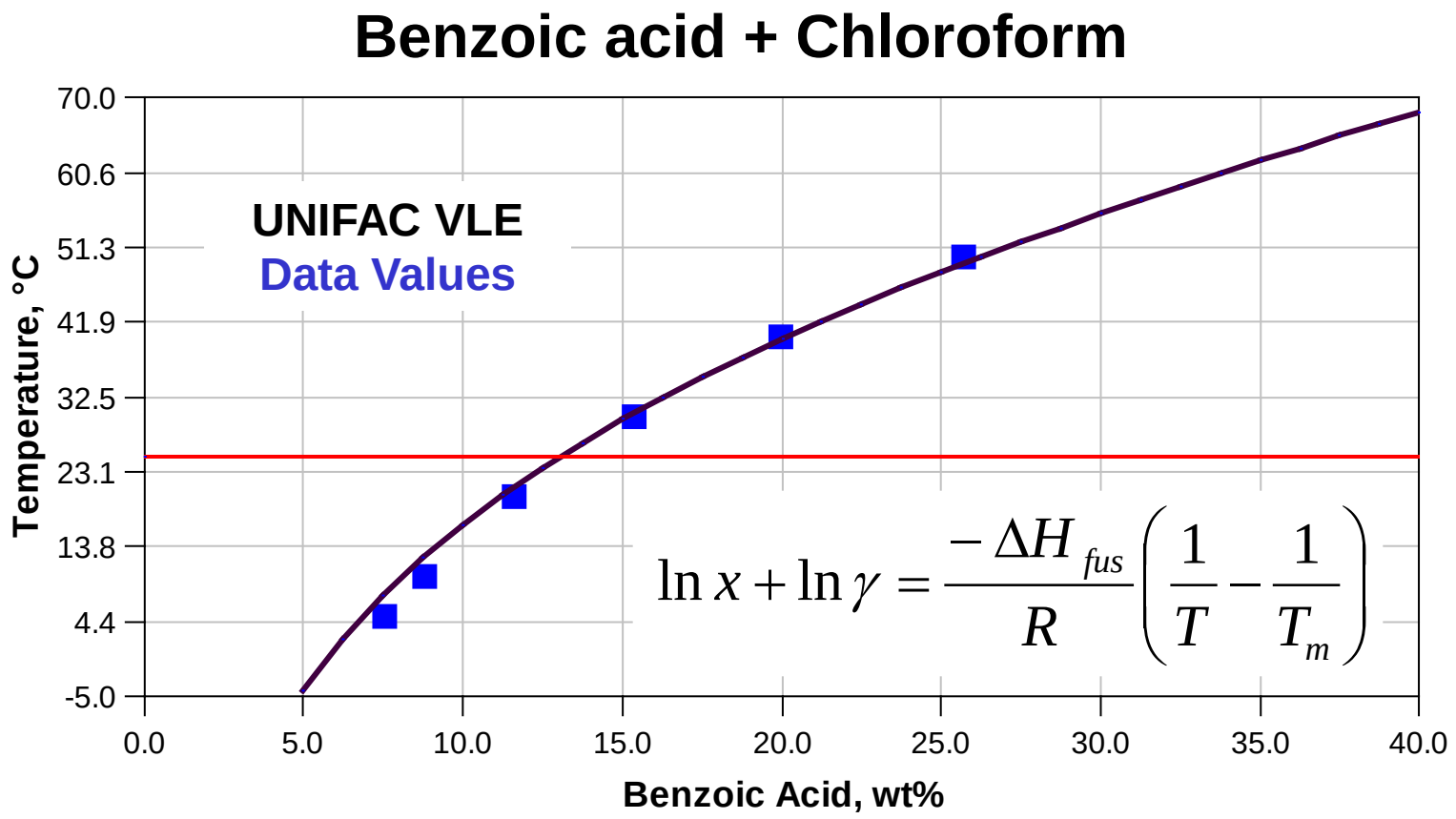
Step 3: Evaluate Properties



Data from: Thati, Nordström and Rasmuson. Journal of Chemical and Engineering Data. Volume 55, number 11, page 5124-5127, 2010.

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Step 3: Evaluate Properties

Candidate Binary Blends

Solvent 1	wt %	Solvent 2	wt %	BA wt %
Ethanol	15.0	Methanol	45.0	40.0
Ethylene glycol	54.4	Methyl acetate	18.1	27.5
2-Butanone	54.7	2-Propanol	18.3	27.0
Acetone	54.7	Butyl acetate	18.3	27.0

BA Solubility in Pure Solvents

Acetone (32.41 wt%) **Butyl acetate (17.7 wt%)**

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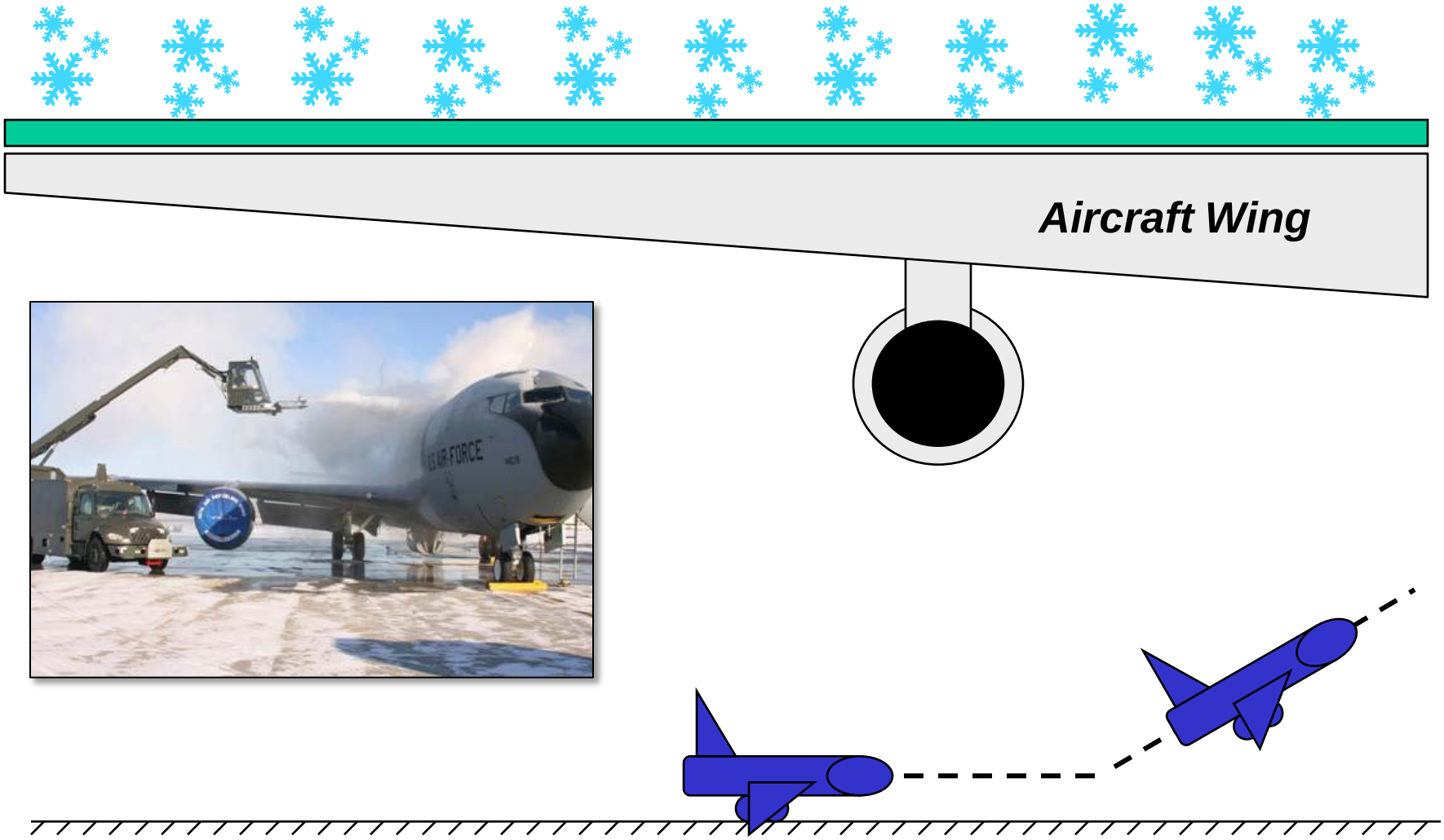
Designing an Anti-icing Fluid



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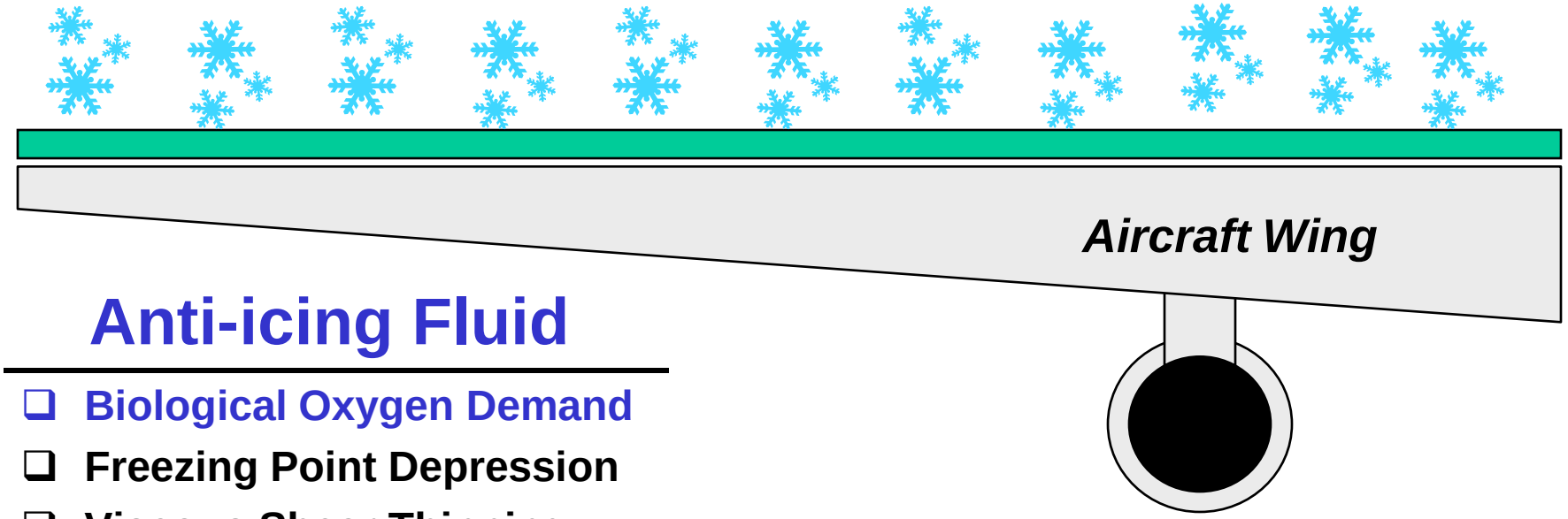
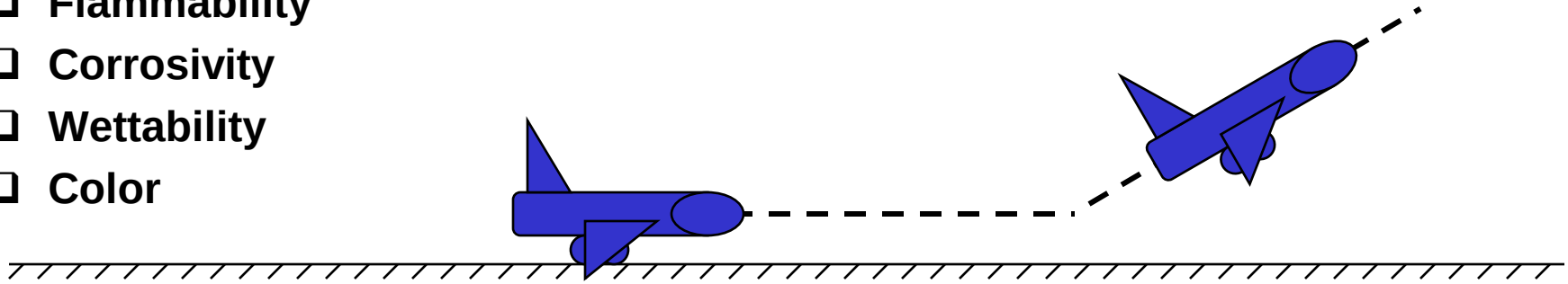
Anti-icing Fluid Design



Anti-icing Fluid

- Biological Oxygen Demand
- Freezing Point Depression
- Viscous Shear Thinning
- Aquatic Toxicity
- Flammability
- Corrosivity
- Wettability
- Color



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3. **Evaluate Properties:** estimation

(refrigerants, solvents, anti-icing fluids)

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Step 2: Generate Candidates

Aircraft Anti-icing Fluid

(after preliminary screening)

- Freezing Point Depressants: 419
- Corrosion Inhibitors: 17
- Surfactants: 19
- Thickeners: 5
- Antifoams: 2
- Dyes: 1
- Water

(generate independent sub-formulations)

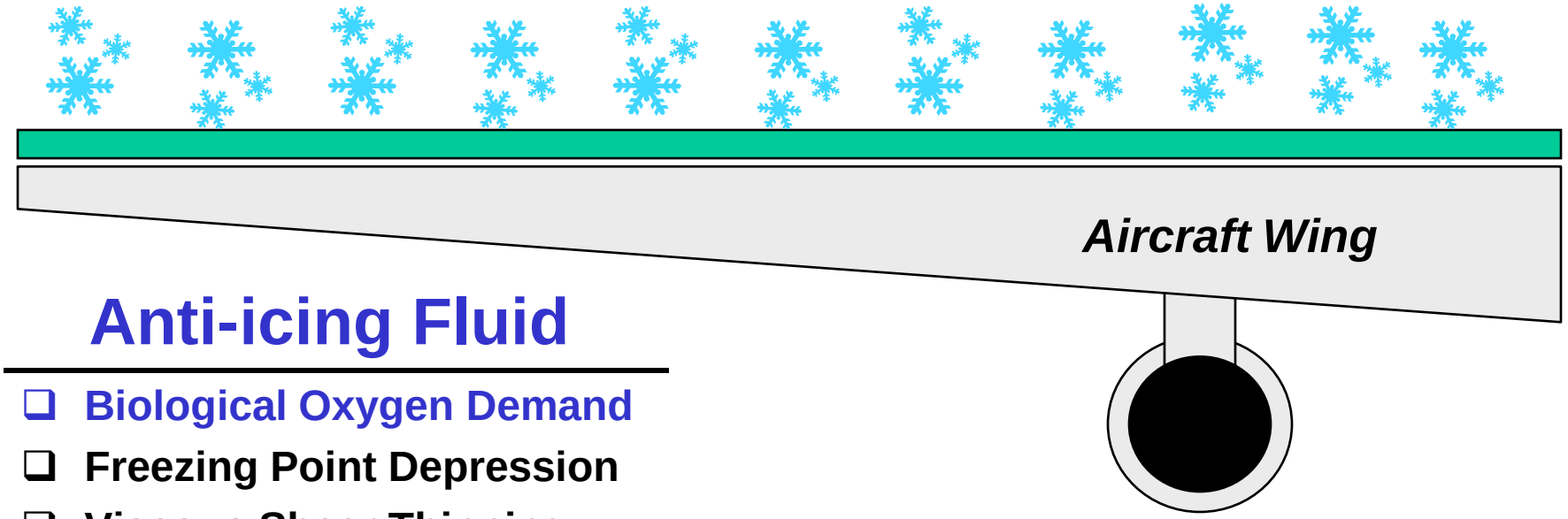
2000-11-15-01

Chemical Product Design (3 Steps)

1. **Compile Property Constraints:** analysis
2. **Generate Candidates:** combination
3. **Evaluate Properties:** estimation

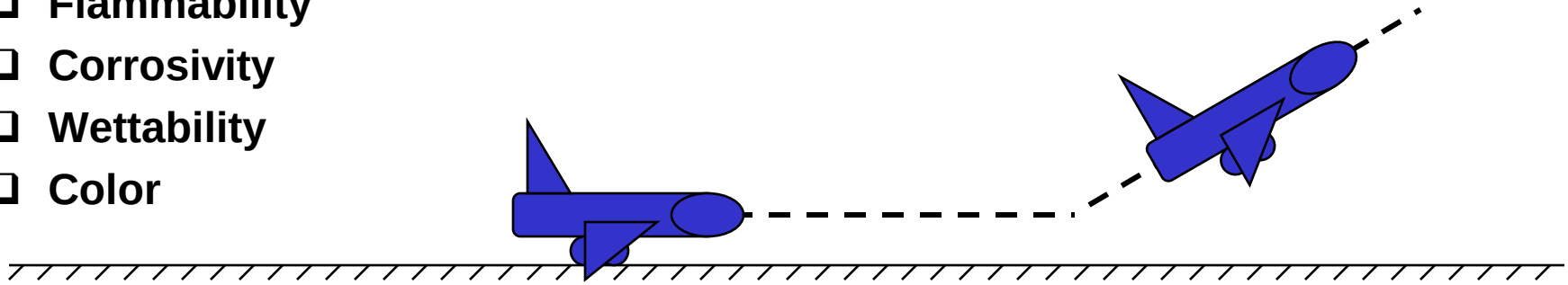
(refrigerants, solvents, anti-icing fluids)

Anti-icing Fluid Design



Anti-icing Fluid

- Biological Oxygen Demand
- Freezing Point Depression
- Viscous Shear Thinning
- Aquatic Toxicity
- Flammability
- Corrosivity
- Wettability
- Color



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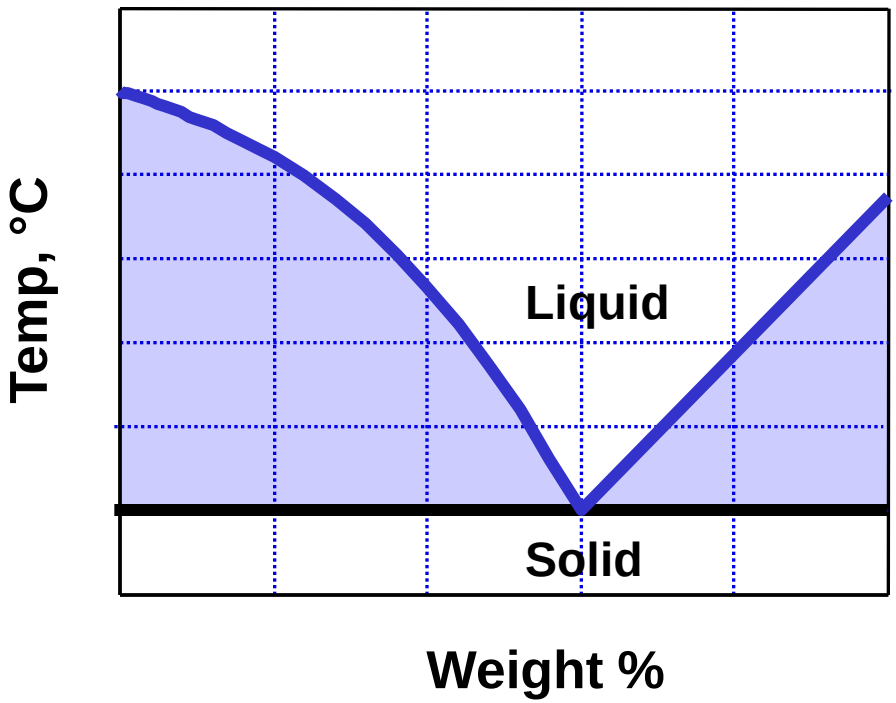
Step 3: Evaluate Properties

Estimate Freezing Point Depression

Assume a Simple Eutectic



Property Model

$$\ln x + \ln \gamma = \frac{-\Delta H_{fus}}{R}\left(\frac{1}{T} - \frac{1}{T_m}\right)$$

Need γ, ΔH_{fus}, T_m

for each candidate

2000-11-15-01

Step 3: Evaluate Properties

Estimate Mixture Flash Points

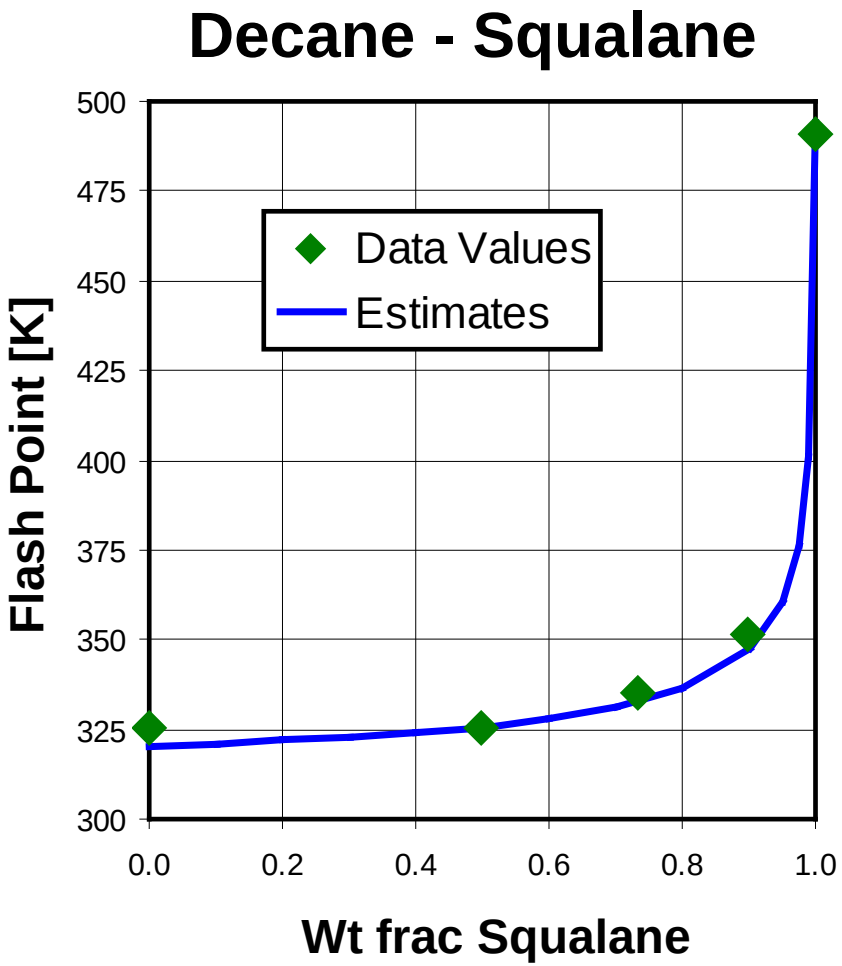
Le Chatelier's Method

$$LFL_{mix} = \frac{1}{\sum \frac{y_i}{LFL_i}}$$

VLE Calculation

$$LFL_{mix} = \sum y_i$$

$$y_i = x_i \gamma_i P_i^{vp}(T_f)$$



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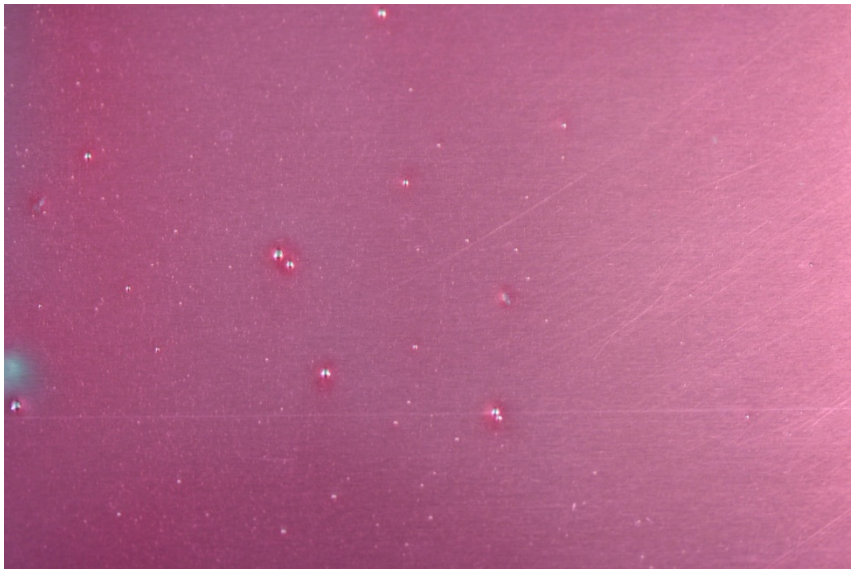
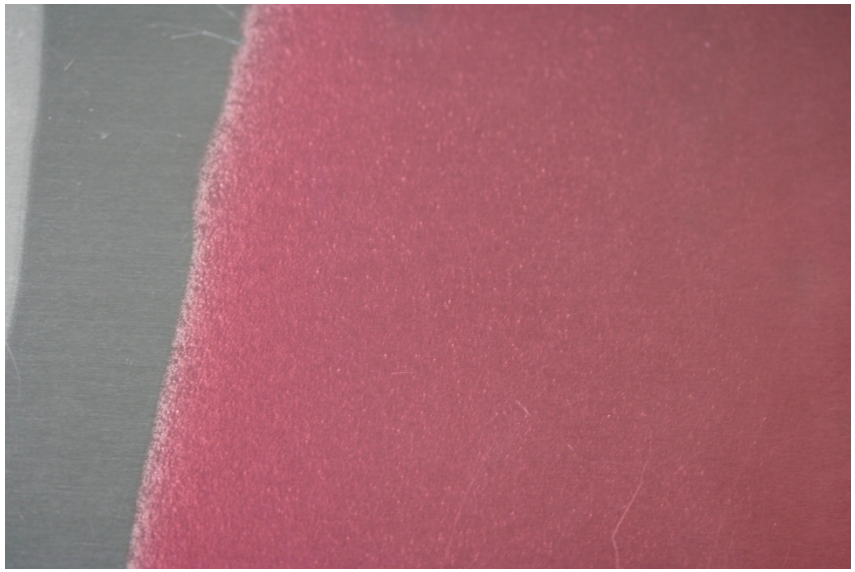
Step 3: Evaluate Properties



DEG without Antifoam



DEG with Antifoam

Formulation remained on surface for more than 30 minutes without draining

Step 3: Evaluate Properties

Niagara Falls, February 2006

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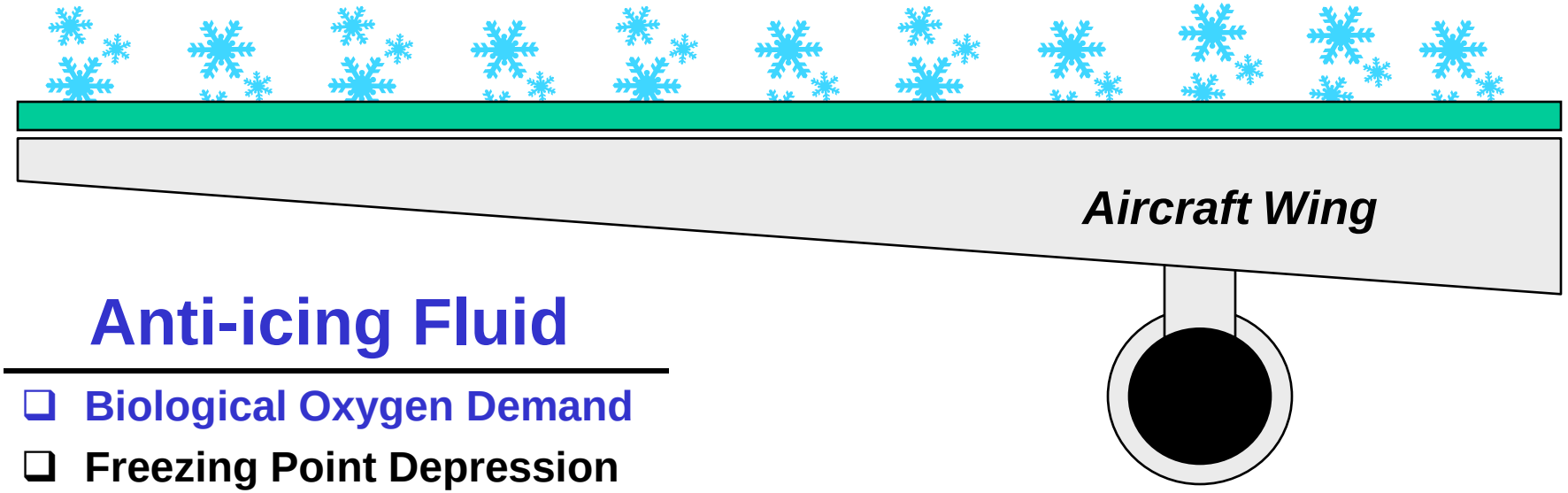
Anti-icing Fluid Design



Anti-icing Fluid

- ❑ Biological Oxygen Demand
- ❑ Freezing Point Depression
- ❑ Viscous Shear Thinning
- ❑ Aquatic Toxicity
- ❑ Flammability
- ❑ Corrosivity
- ❑ Wettability
- ❑ Color

Final Formulation

1. Diethylene glycol
2. Tergitol® TMN-10
3. Triethanolamine
4. Carbopol® 1610
5. Shilling Green
6. Water

2000-11-15-01

Chemical Product Design (3 Steps)

1. **Compile Property Constraints:** analysis
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(refrigerants, solvents, anti-icing fluids)

Questions?

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