



Live event
Consumer Safety & Cosmetics
Normandie, June 10, 2021

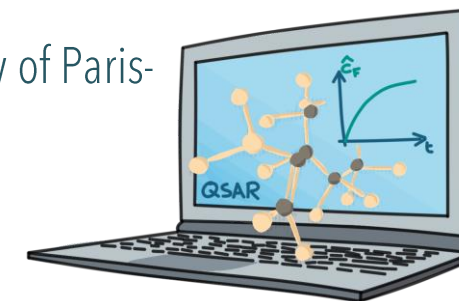
➤ Risk assessment and management of material in contact with cosmetic products

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> Content overview

> Comparison between cosmetic applications and food contact materials
 The EU regulation (EC) 1223/2009 of cosmetic products refers to the framework regulation (EC) 1935/2004 of food contact materials (FCM) to manage the risk of contamination of cosmetic contact materials (CCM)

FCM

inhalation
digestion

skin absorption

CCM

p. 3

Risk Assessment

Reviews:
 BOOK: Risk Assessment of Migration From Packaging Materials Into Food - <https://doi.org/10.1016/B978-0-08-100596-5.22501-8>
<https://fitness.asppattech.juhtimesoforum.com/>
<https://www.foodpackagingforum.org/food-packaging-health/migration-modeling>

p. 4

without contact

with more than two phases

NEW CONTAMINATION ROUTES

p. 5

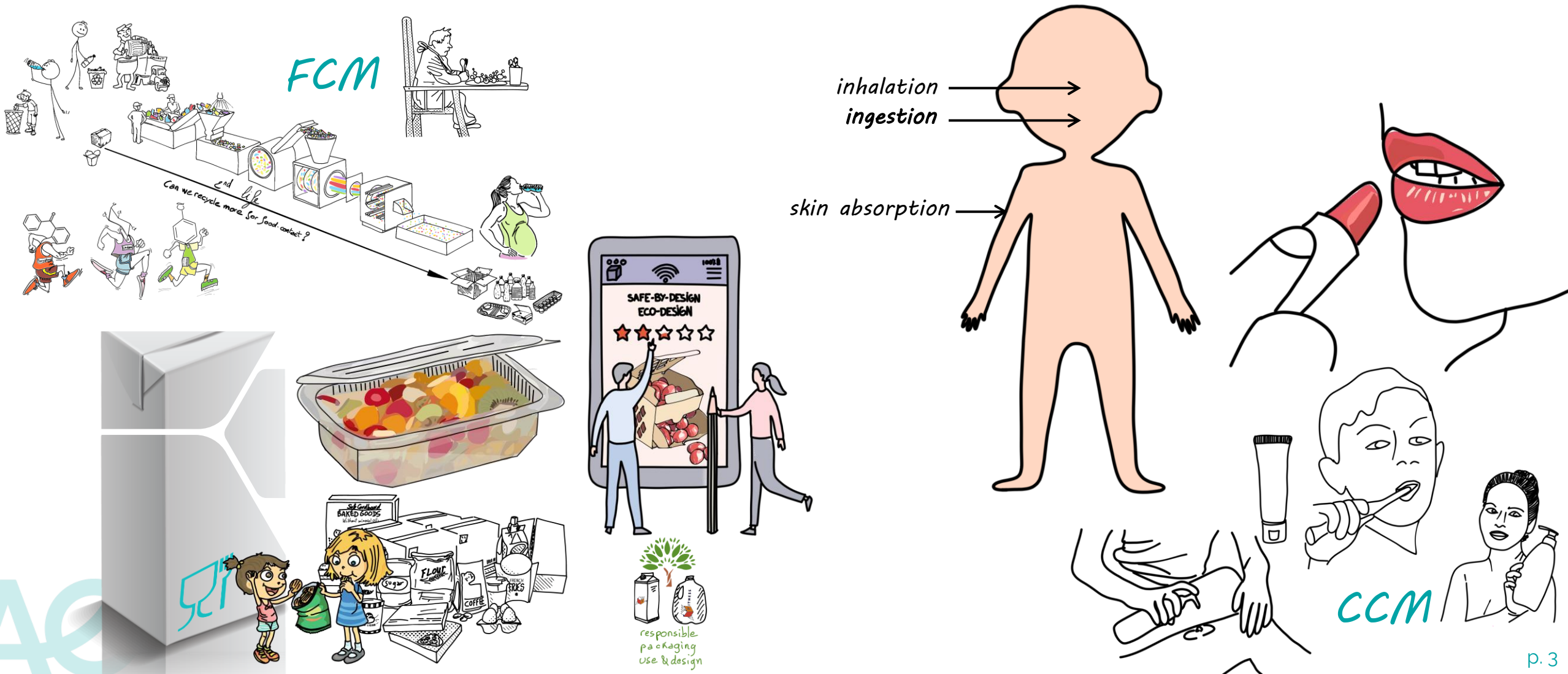
Preventive Approaches
 (Failure Mode Effects and Critical Analysis, Safe-by-design, Integrated engineering)

p. 6



➤ Comparison between cosmetic applications and food contact materials

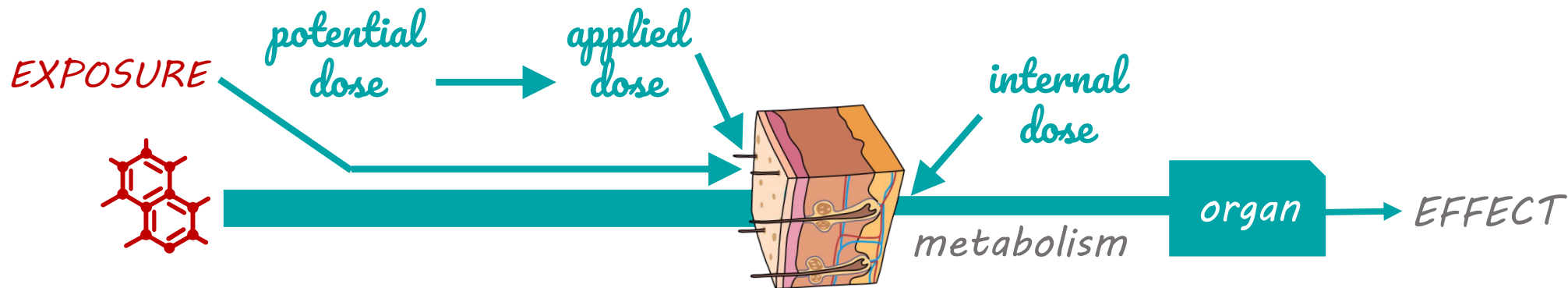
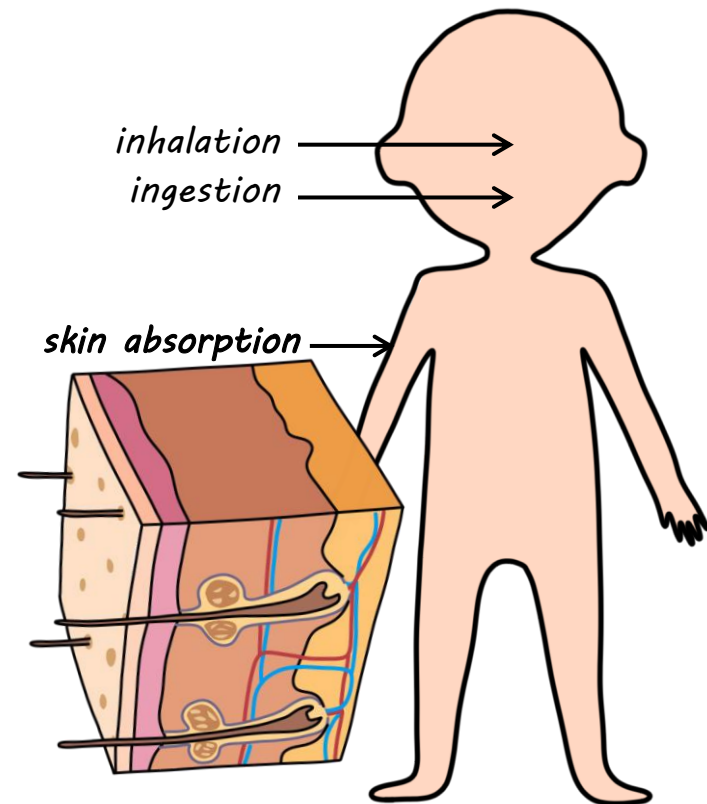
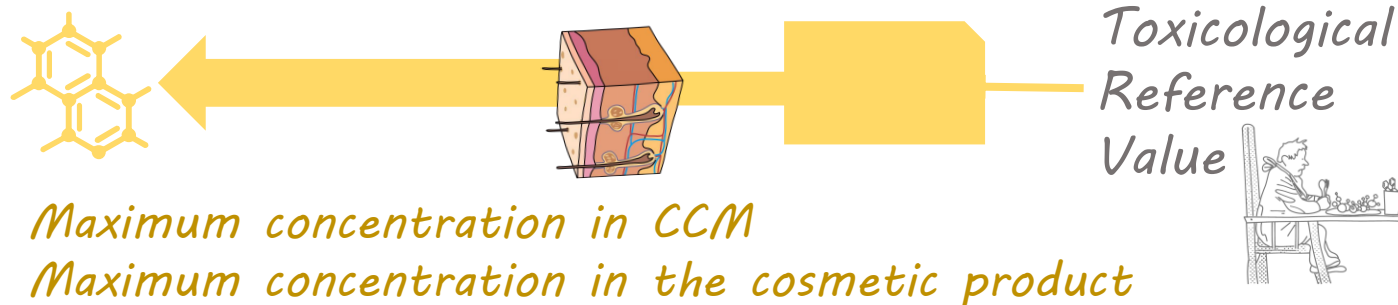
The EU regulation (EC) 1223/2009 of cosmetic products refers to the framework regulation (EC) 1935/2004 of food contact materials (FCM) to manage the risk of contamination of cosmetic contact materials (CCM)



> Is there a unique approach?

How to generalize approaches used for food contact to cosmetic applications?

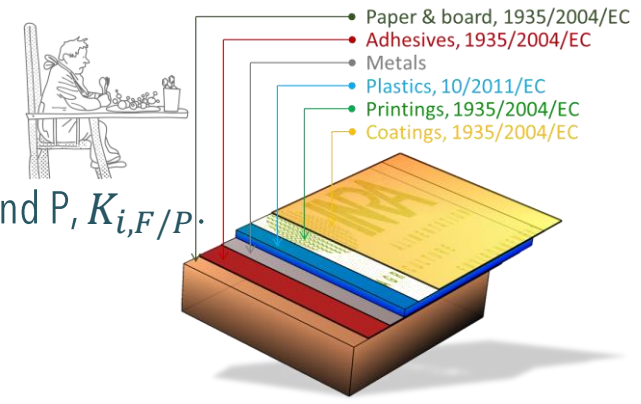
$$\text{real exposure} \leq \text{potential dose} \geq \text{applied dose} \geq \text{internal dose}$$



➤ Analogy with packaged food products

Multiple crises along the year similar causes: uncontrolled mass transfer from the packaging (P) to the food (F)

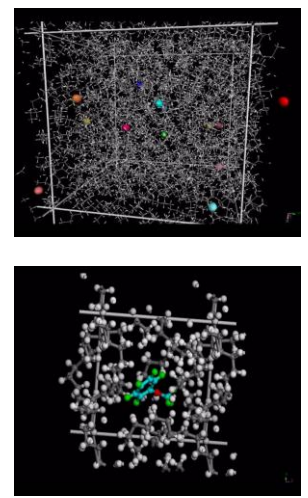
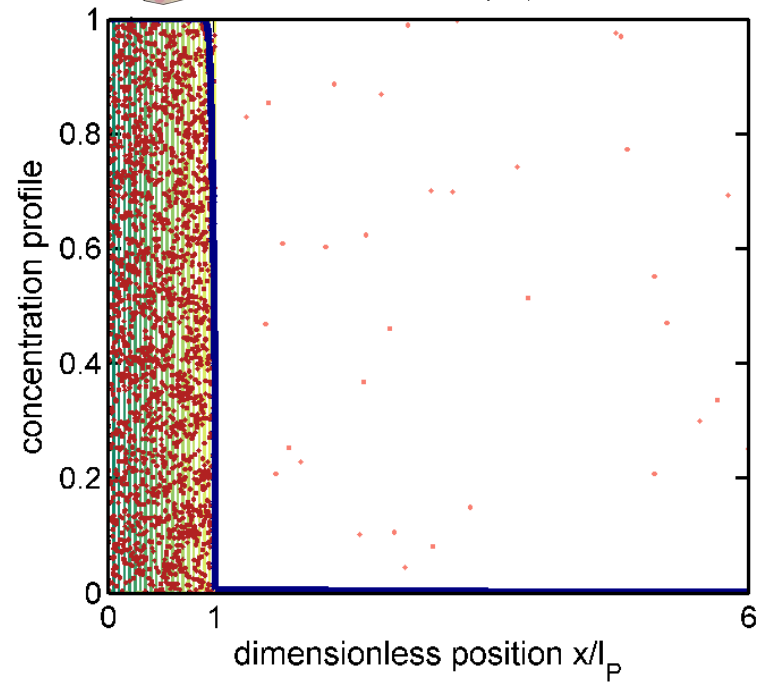
Mass transfer of substance i is governed by its diffusion coefficient $D_{i,P}$ and its partition coefficient between F and P, $K_{i,F/P}$.



$$Fo = \frac{D_{i,P}t}{l_p^2}$$



DESORPTION
Fo = 0.0005 (a.u.)

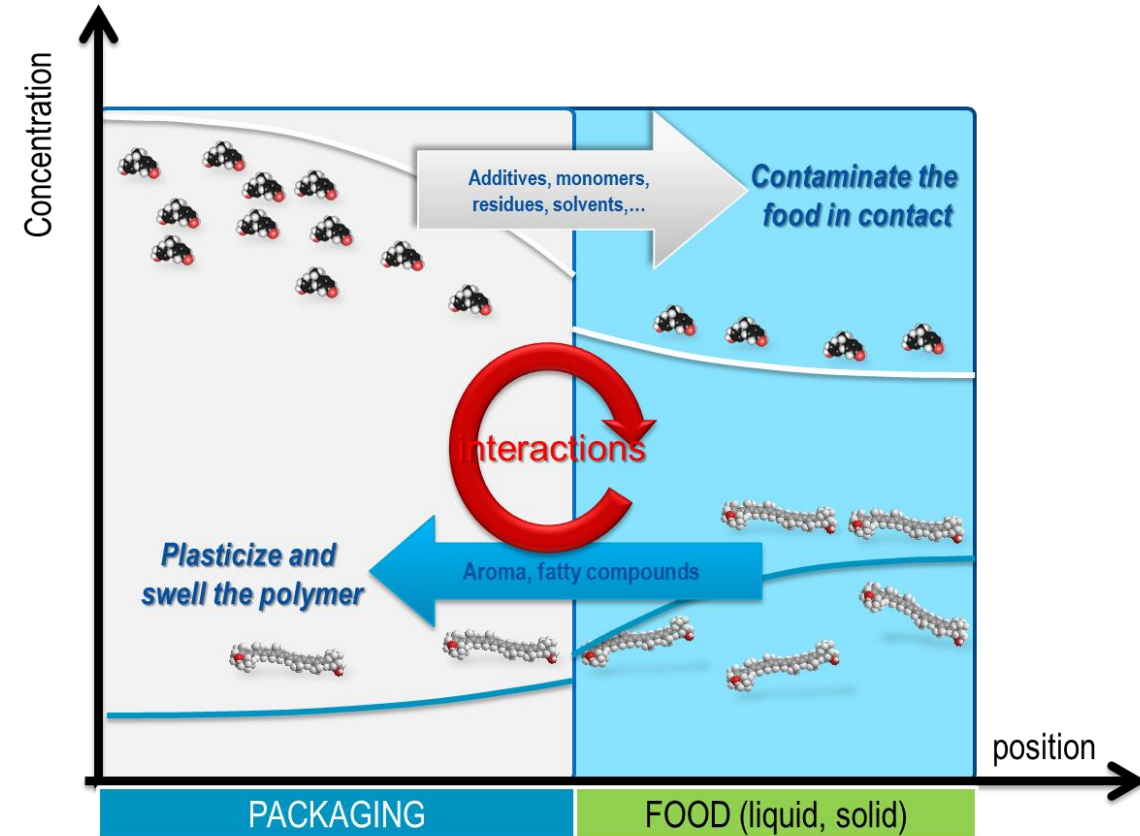
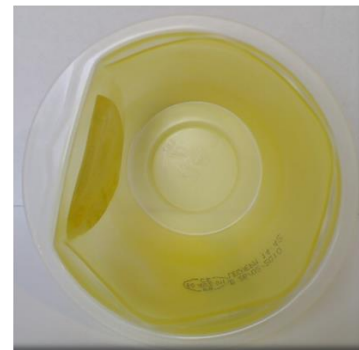


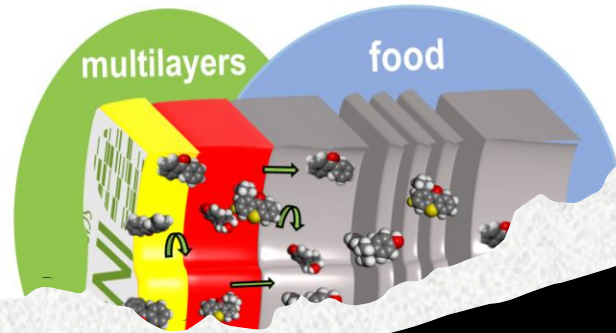
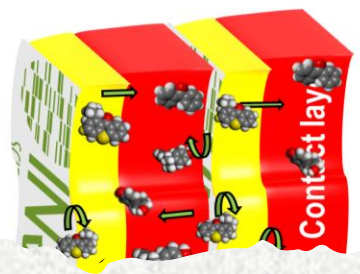
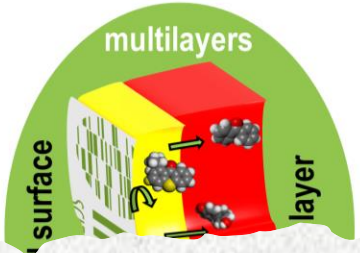
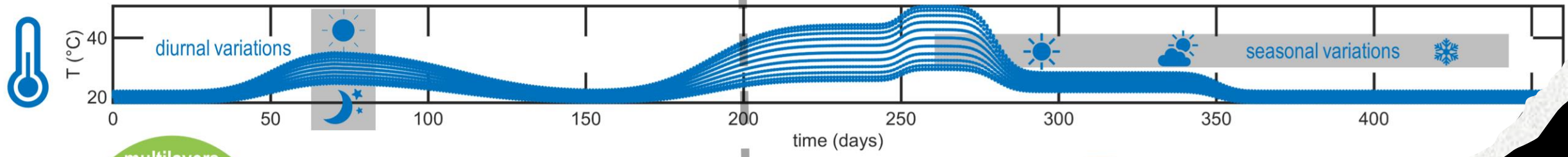
$$K_{i,F/P} = \frac{C_{i,F}^{eq}}{C_{i,P}^{eq}} = \frac{1}{1 - crystallinity} \frac{\gamma_{i,P}^v}{\gamma_{i,F}^v}$$



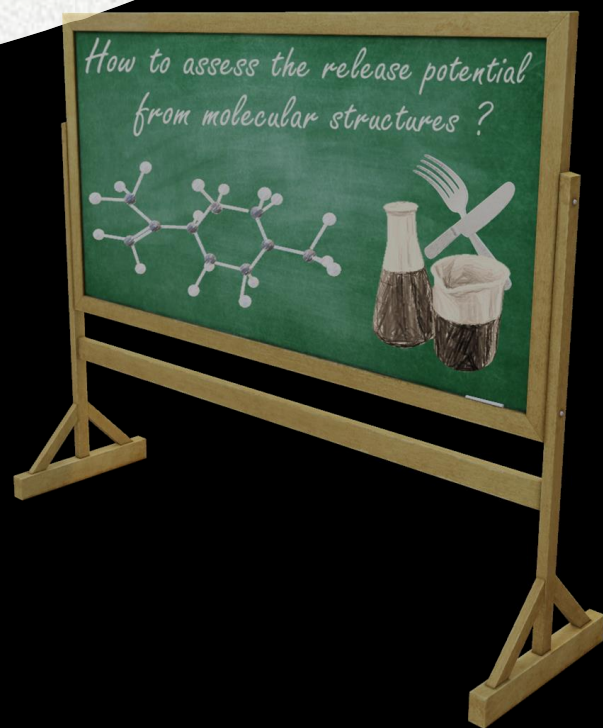
➤ Analogy with packaged food products

Some products may be « aggressive » for the contact material and modify its properties and performances





Risk Assessment



Reviews:

BOOK: Risk Assessment of Migration From Packaging Materials Into Food - <https://doi.org/10.1016/B978-0-08-100596-5.22501-8>

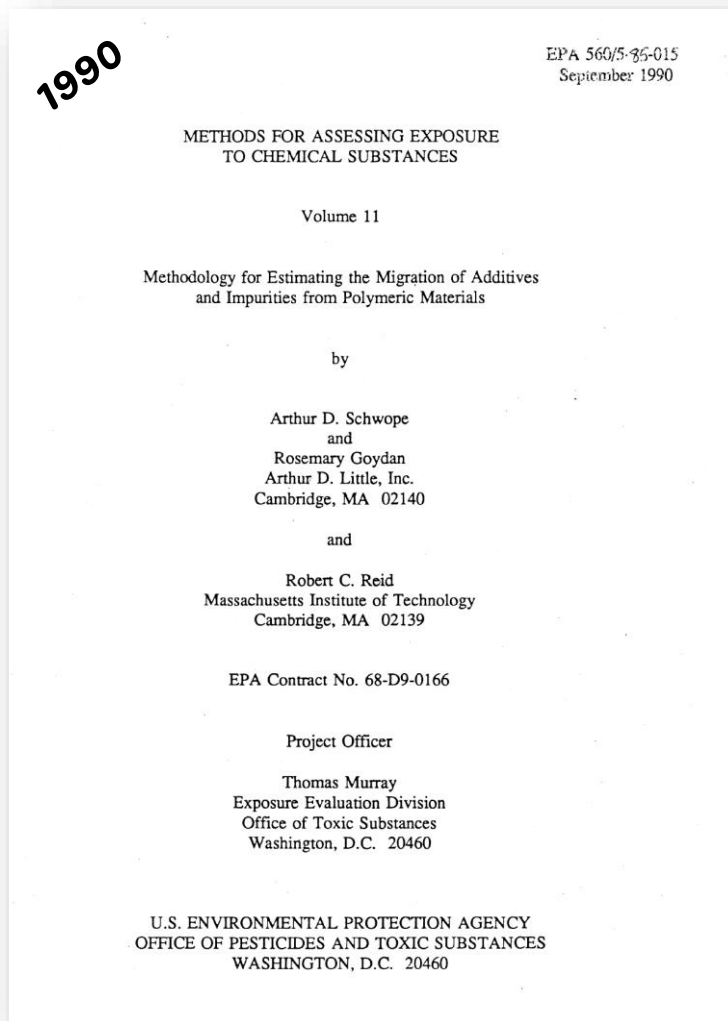
<https://fitness.agroparistech.fr/fitness/references/>

<https://www.foodpackagingforum.org/food-packaging-health/migration-modeling>

➤ Migration modeling is well accepted in the US, Europe and China

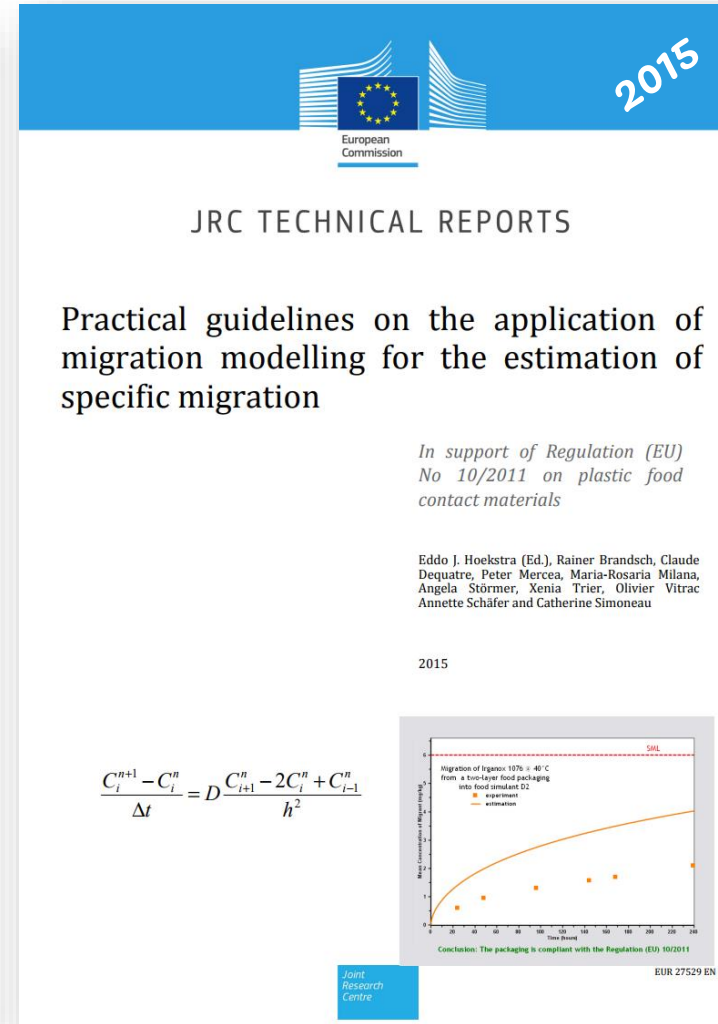
Revisions and to extensions to non-plastic materials are pending

US guidance



Methodology for
Estimating the
Migration of
Additives and
Impurities from
Polymeric Materials

Europe guidance



> The five principles of migration modeling



■ *The first principle ("conservatism")* is that modeling and related calculations should overestimate the real migration or contamination.



■ *The second principle ("reliability")* implies that the foreseen mass transfer pathways and substances obey well-described mechanisms, accepted conditions (e.g., uniform distribution), and proper implementation in software.



■ *The third principle ("consistency")* is that inputs in the model are known or guessed in a way that fulfills the requirements of the first principle.



■ *The fourth principle ("parsimony")* states that sophisticated and refined scenarios should be considered only when simpler ones cannot demonstrate compliance or safety.



■ *The fifth and final principle ("proportionality")* is that non-compliance cannot be demonstrated by calculation.

PLASTICS ARE RIGOROUSLY TESTED TO MAKE SURE THAT MIGRATION - IF ANY - IS SAFE

Testing conditions are specified legally, and need to be used by all actors performing tests in the value chain (from raw materials to packaging producers and to food packers). The test are done at several stages in the value chain to ensure that the plastic sample is suitable in its end-use.

Variables can include:

- Temperature
- Time
- Contact surface
- Food type

Take a sample of the plastic → Test in contact with a food simulant → Monitor migration under standardised conditions → Analyse the results to verify that safety limits are met

Food simulants - as prescribed by law, (e.g. olive oil) - mimic the properties of different food types under typical / worst case conditions.

WHAT DO THE TESTS SHOW?

The tests show how migration occurs in different food types under various conditions. The tests enable us to determine if a plastic packaging can be used for given food and conditions of use.

For example, it may be beneficial for long-term storage, unless they are suitable for high temperature. The tests are designed to exaggerate the real use scenario and therefore to make sure there is a safety margin, e.g. by assuming that all the food is in contact with the packaging, and by exaggerating levels of consumption. These testing conditions ensure that migration — if any — is far below the safety level.

Migration into food

Safe limit

Material 2: Unsuitable

Material 1: Suitable

Time

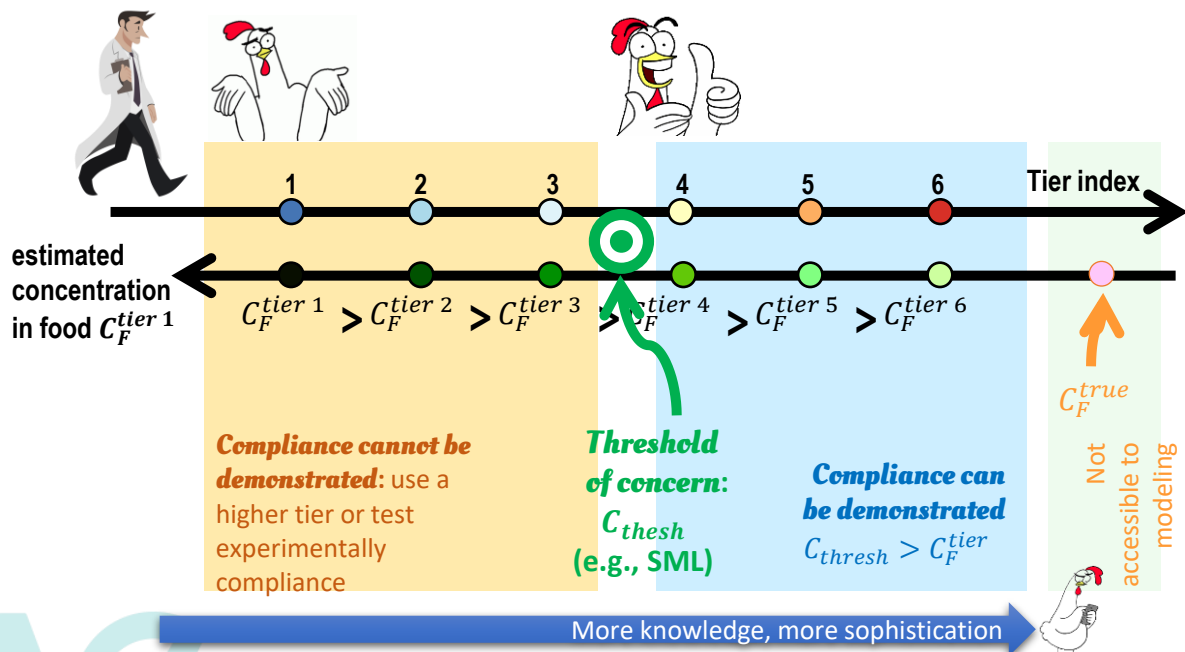
> Parsimony vs. sophistication

During the last decade migration modeling became high throughput, multiscale and connected to chemometric approaches

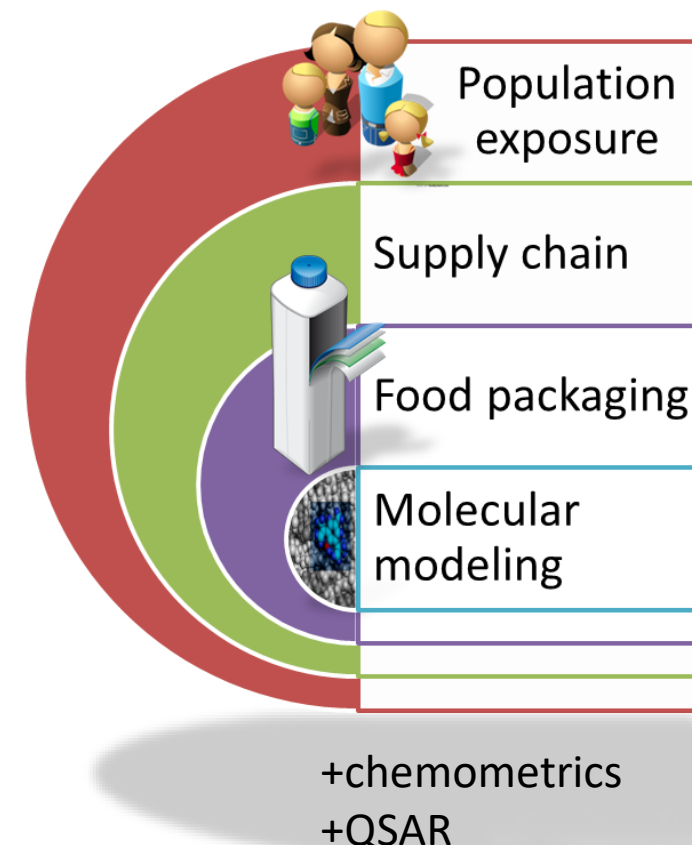
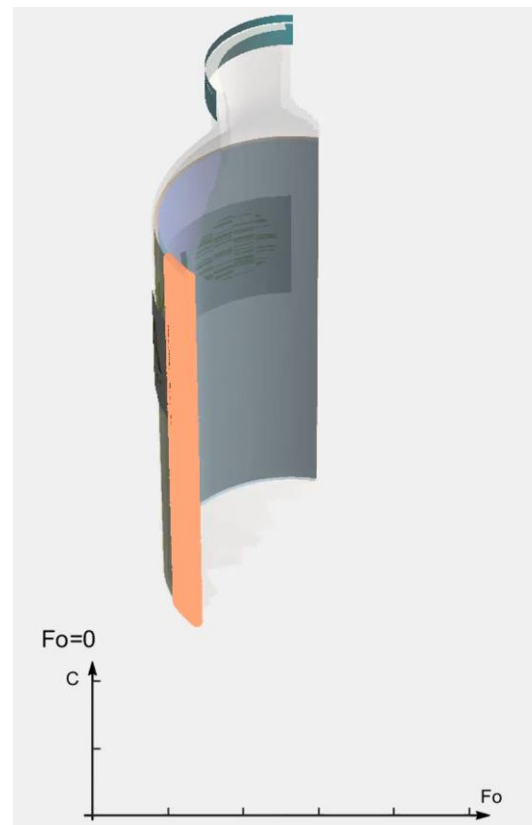


What is the goal?

The art of migration modeling consists in building a sequence of scenarios so that the last scenario provides a value lower than the threshold of concern while being large than the real concentration (unknown).



Multiscale modeling





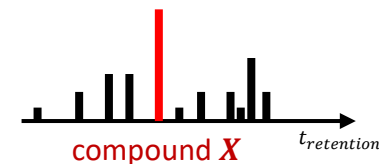
The challenge of uncertainty

Propagating uncertainty with the risk that no decision can be reached

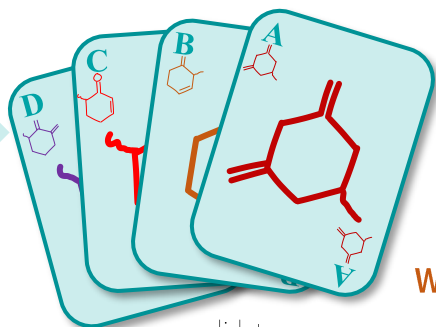


$$Severity(X) = 100 \times$$

$$\max \left(\frac{\widehat{C}_F^A}{\widehat{T}_A}, \frac{\widehat{C}_F^B}{\widehat{T}_B}, \frac{\widehat{C}_F^C}{\widehat{T}_C}, \frac{\widehat{C}_F^D}{\widehat{T}_D} \right)$$

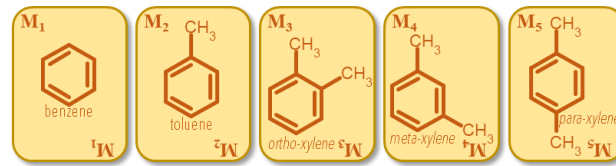
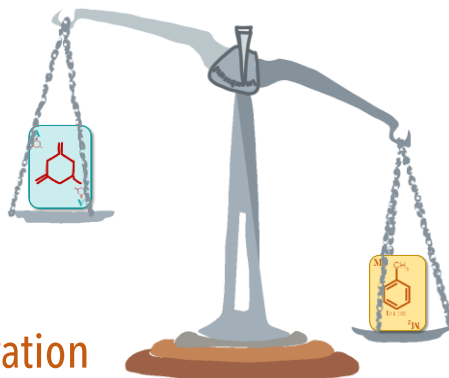


all compounds



candidates

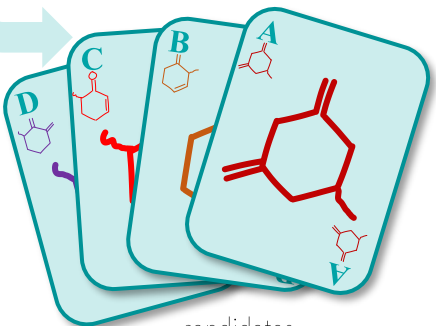
worst-case migration



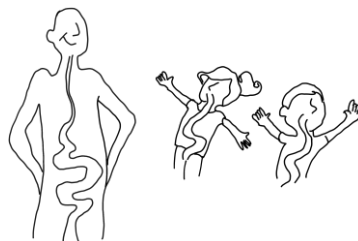
C-hat_F

T-hat

| | | | | | | | |
|---------------------|----------------|------------------------------|--------------------------------|----------------------|----------------------|----------------------|-------------------------|
| T ₁ | T ₂ | T ₃ | T ₄ | T ₅ | T ₆ | T ₆ | T ₇ |
| genotox 0.15 ppb | TOR 1 ppb | detection limit 10 ppb | organo- phosphate 18 ppb | Cramer III 90 ppb | Cramer II 540 ppb | Cramer I 1800 ppb | positive list SML |
| t _I | z _I | ε _I | t _I | s _I | ρ _I | ρ _I | t _I |



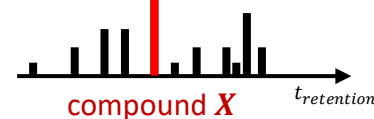
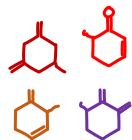
candidates



acceptable threshold



exposure
assessment



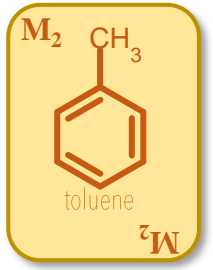
hazard
analysis



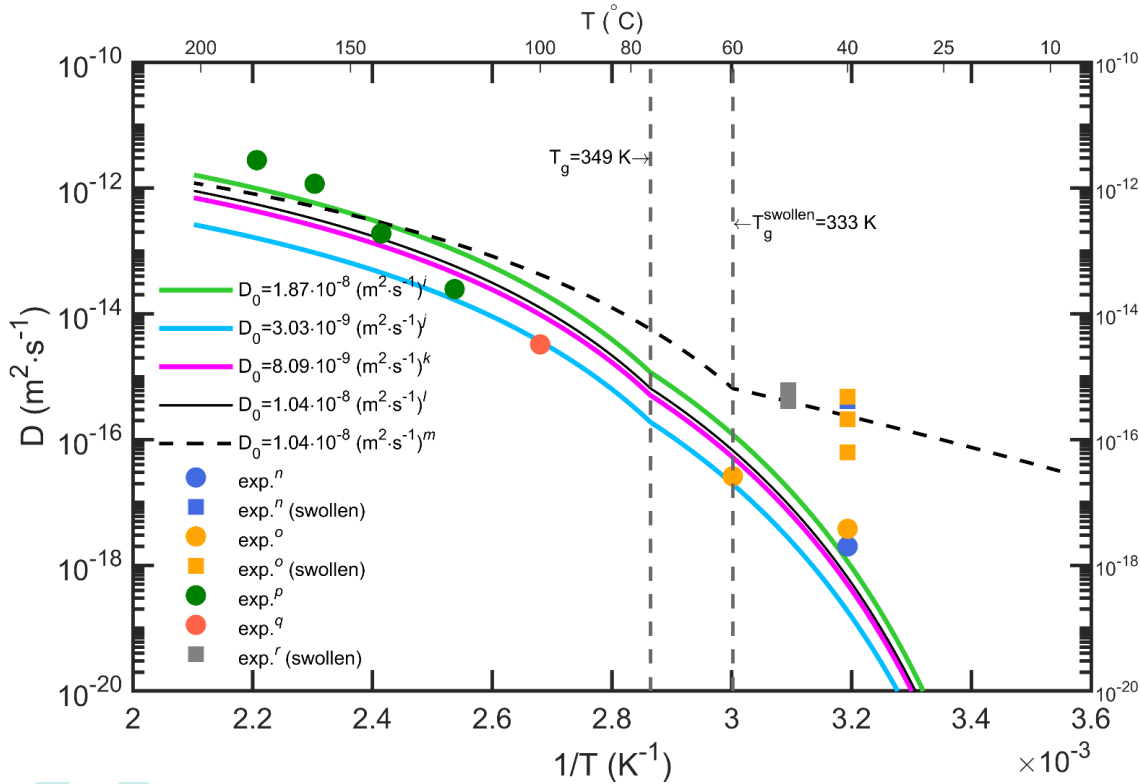
EXAMPLE: Toluene as a generic surrogate

Diffusion coefficients of toluene can be predicted by free-volume theory in almost in any polymer (plasticized or not), at any temperature - other surrogates are also available

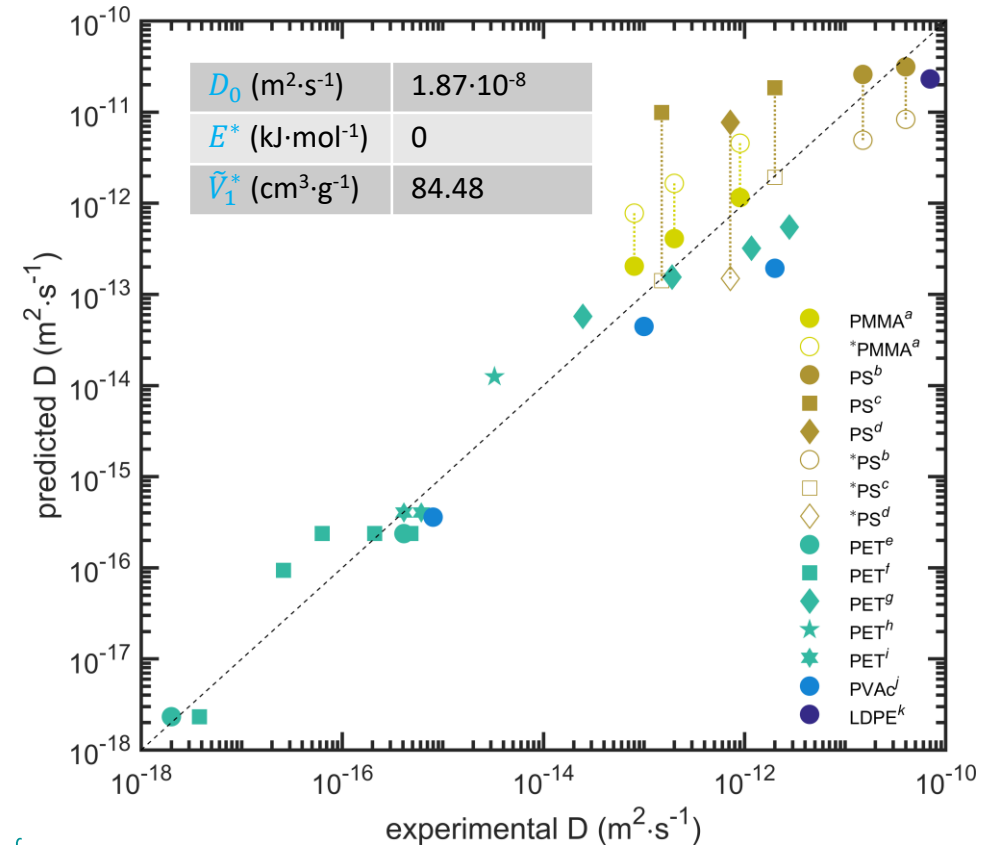
$$D(\xi, T, T_g) = D_0 \exp\left(-\frac{E^*}{RT}\right) \exp\left(-\tilde{V}_1^* \frac{\alpha_{lin}(T, T_g) + 1}{0.24}\right)$$



Diffusivity of toluene in PET Effects of T, plasticizing, subcooling



Diffusivities of toluene in 6 polymers Predicted vs calculated



Zhu, Y., Welle, F., et Vitrac, O. (2019). A blob model to parameterize polymer hole free volumes and solute diffusion. *Soft Matter*, 2019, 15, 8912-8932

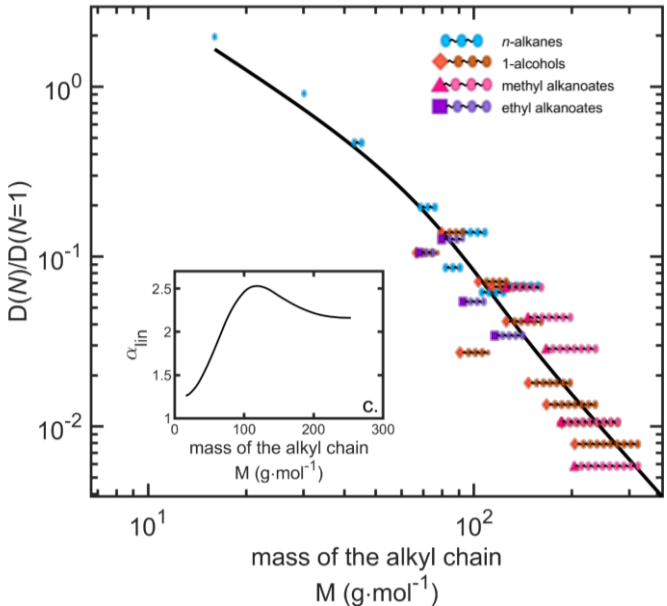
Accurate diffusion model at rubber and molten state to support the processing of recycled materials (scaling of oligomers)



HDPE



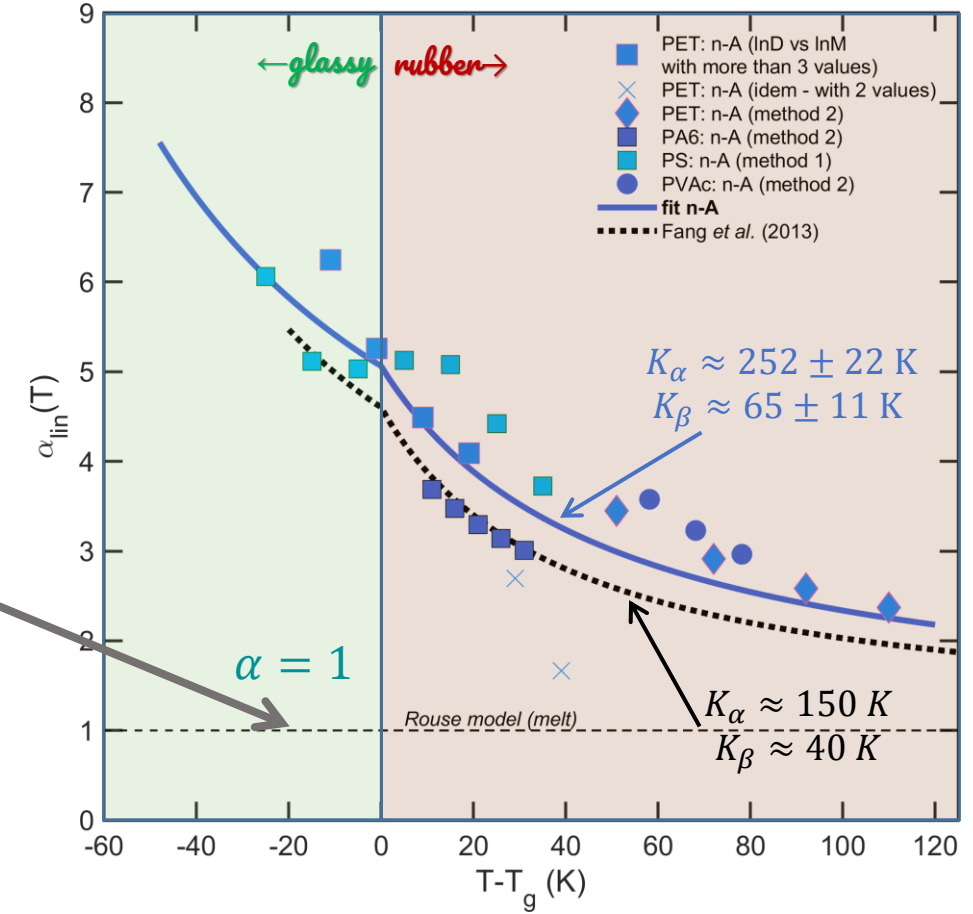
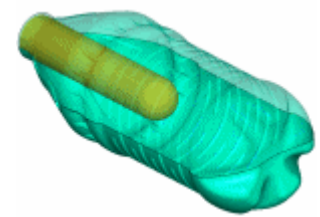
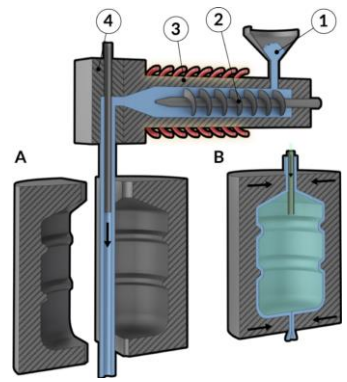
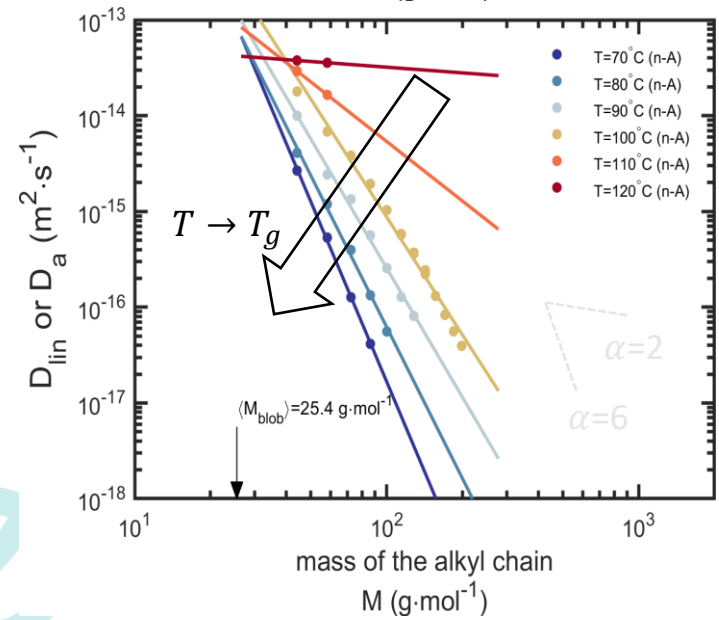
PET



$$\frac{D_{lin}(M,T)}{D_{lin}(M_{blob},T)} \propto \left(\frac{M}{M_{blob}}\right)^{-\alpha_{lin}(T,T_g)}$$

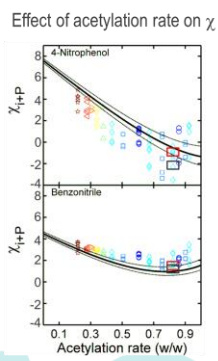
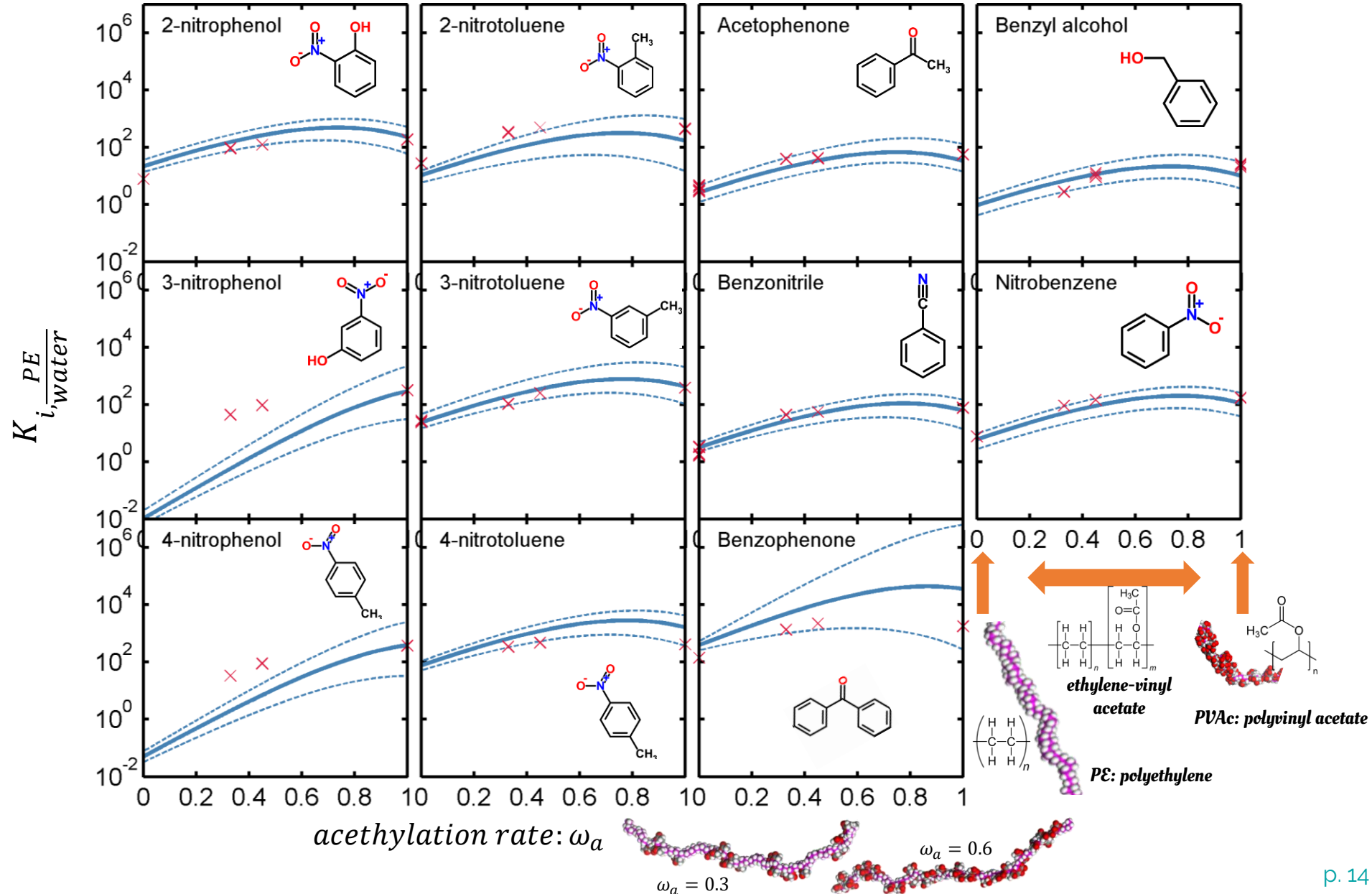
$$\alpha_{lin}(T,T_g) = 1 + \frac{K_\alpha}{r(T - T_g) + K_\beta}$$

with $r = \begin{cases} 1 & \text{when } T \geq T_g \\ \frac{\alpha_g}{\alpha_c} & T < T_g \end{cases}$

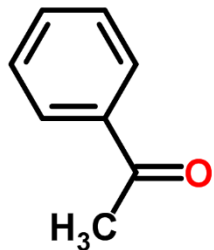


Zhu et al. *Soft Matter*, 2019, 15, 8912-8932
 Fang, et al. *Macromolecules*, 2013, 46(3), 874-888.

➤ Partition coefficients water-EVA for polar surrogates



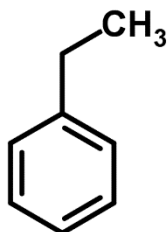
> PARTITION COEFFICIENTS WITH AIR



>> FMECAKairP acetophenone

```
LOAD_CHEMSPIDER    extraction of ChemSpiderID=7132 ('acetophenone') completed in 10.26 s
LOAD_CHEMISPIDER: updated cache
                    7132.mat      21-sept.-2015 21:37:19      77.6 kBytes   C:\Data\Olivier\INRA\Codes\MS\cache.ChemSpider
CHEMSPIDER reuses cached data for 'acetophenone' (date=21-sept.-2015 21:37:19)
```

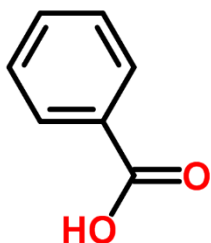
```
ans =
      9.1995e-06
```



>> FMECAKairP ethylbenzene

```
LOAD_CHEMSPIDER    extraction of ChemSpiderID=7219 ('ethylbenzene') completed in 11.9 s
LOAD_CHEMISPIDER: updated cache
                    7219.mat      21-sept.-2015 21:42:34     107.1 kBytes  C:\Data\Olivier\INRA\Codes\MS\cache.ChemSpider
CHEMSPIDER reuses cached data for 'ethylbenzene' (date=21-sept.-2015 21:42:34)
```

```
ans =
      2.2485e-04
```

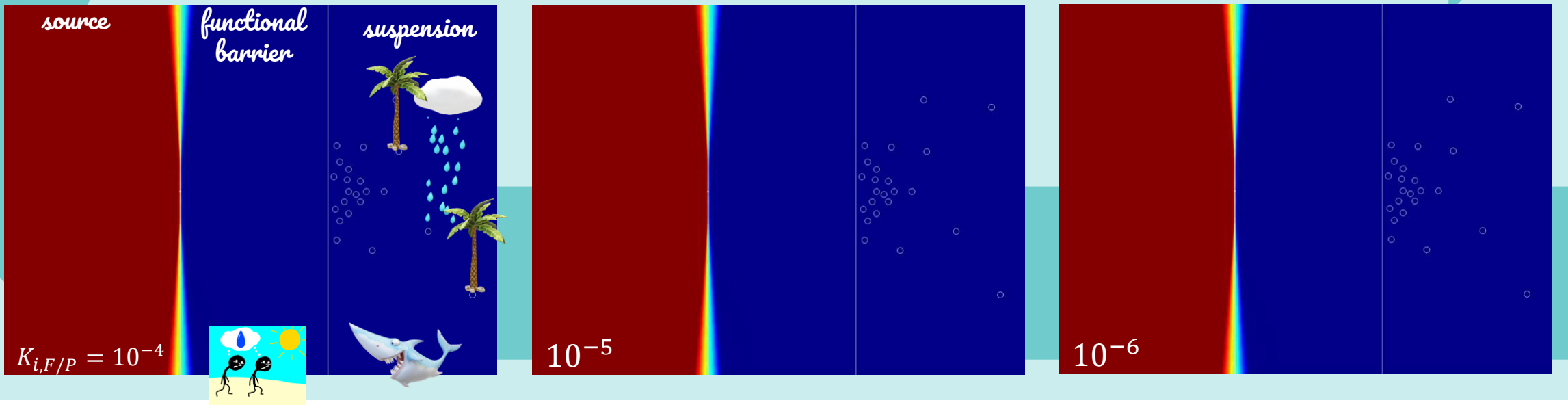
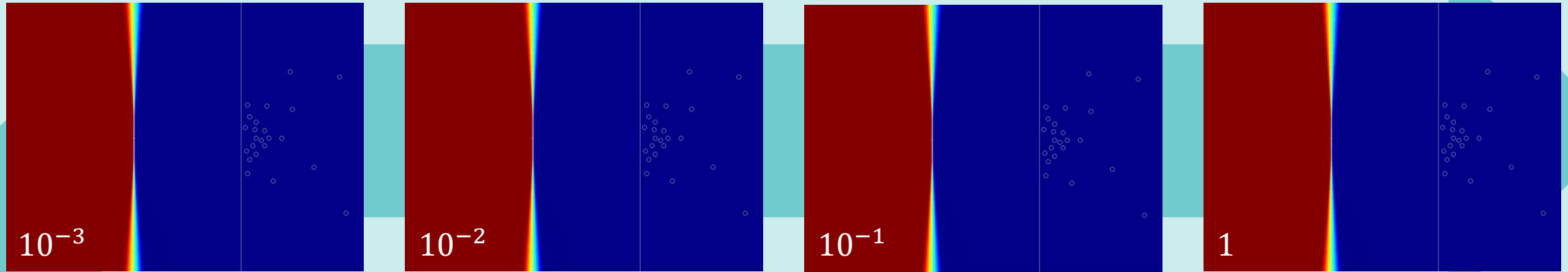
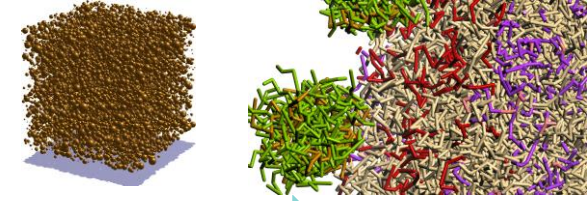


>> FMECAKairP 'benzoic acid'

```
LOAD_CHEMSPIDER    extraction of ChemSpiderID=238 ('benzoic acid') completed in 5.746 s
LOAD_CHEMISPIDER: updated cache
                    238.mat      21-sept.-2015 21:45:01      41.2 kBytes   C:\Data\Olivier\INRA\Codes\MS\cache.ChemSpider
CHEMSPIDER reuses cached data for 'benzoic acid' (date=21-sept.-2015 21:45:01)
```

```
ans =
      1.3674e-08
```


➤ Transfer with more than two phases



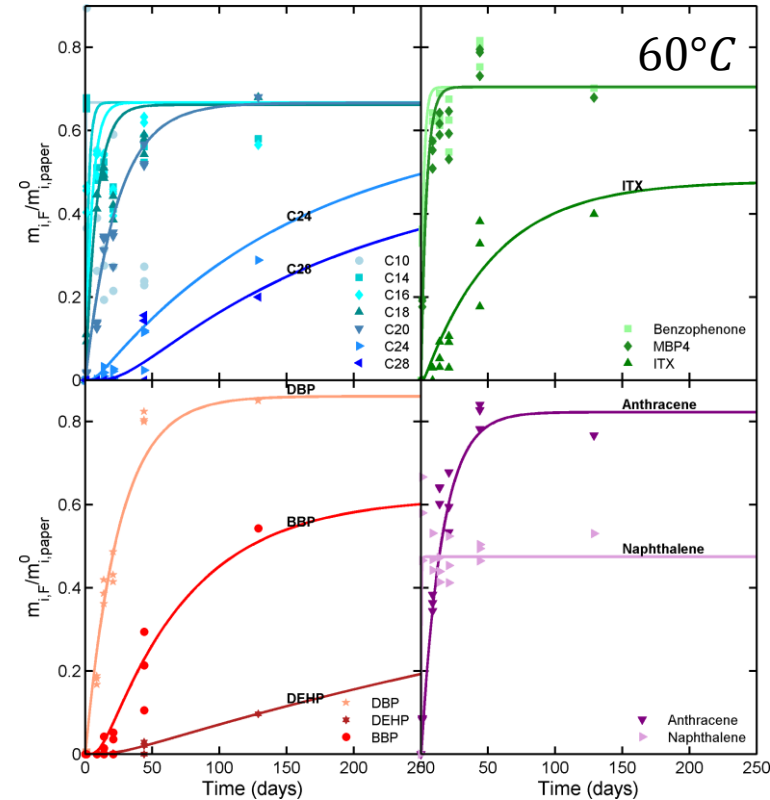
chemical affinity for the continuous phase

➤ CONTAMINATION THROUGH THE GAS PHASE

TENAX packed within a 50 μm thick BOPP bag and exposed to a cardboard material formulated with 15 surrogates



| SURROGATES (i) |
|------------------------------------|
| Decane (C10) |
| Tetradecane (C14) |
| Hexadecane (C16) |
| Octadecane (C18) |
| Eicosane (C20) |
| Tetracosane (C24) |
| Octacosane (C28) |
| Dibutyl phthalate (DBP) |
| Bis(2-ethylhexyl) phthalate (DEHP) |
| Benzylbutyl phthalate (BBP) |
| Benzophenone |
| 4-methyl benzophenone (MBP4) |
| Isopropyl-9H-thioxanthen-9-one |
| Anthracene |
| Naphthalene |



$$\frac{m_{i,F}(t)}{m_{i,P}^0} = \frac{V_F}{m_{i,P}^0} \int_0^t C_{i,F}(\tau) d\tau$$



Experimental results at 60°C, i=1...15

Detailed modeling with FMECAengine

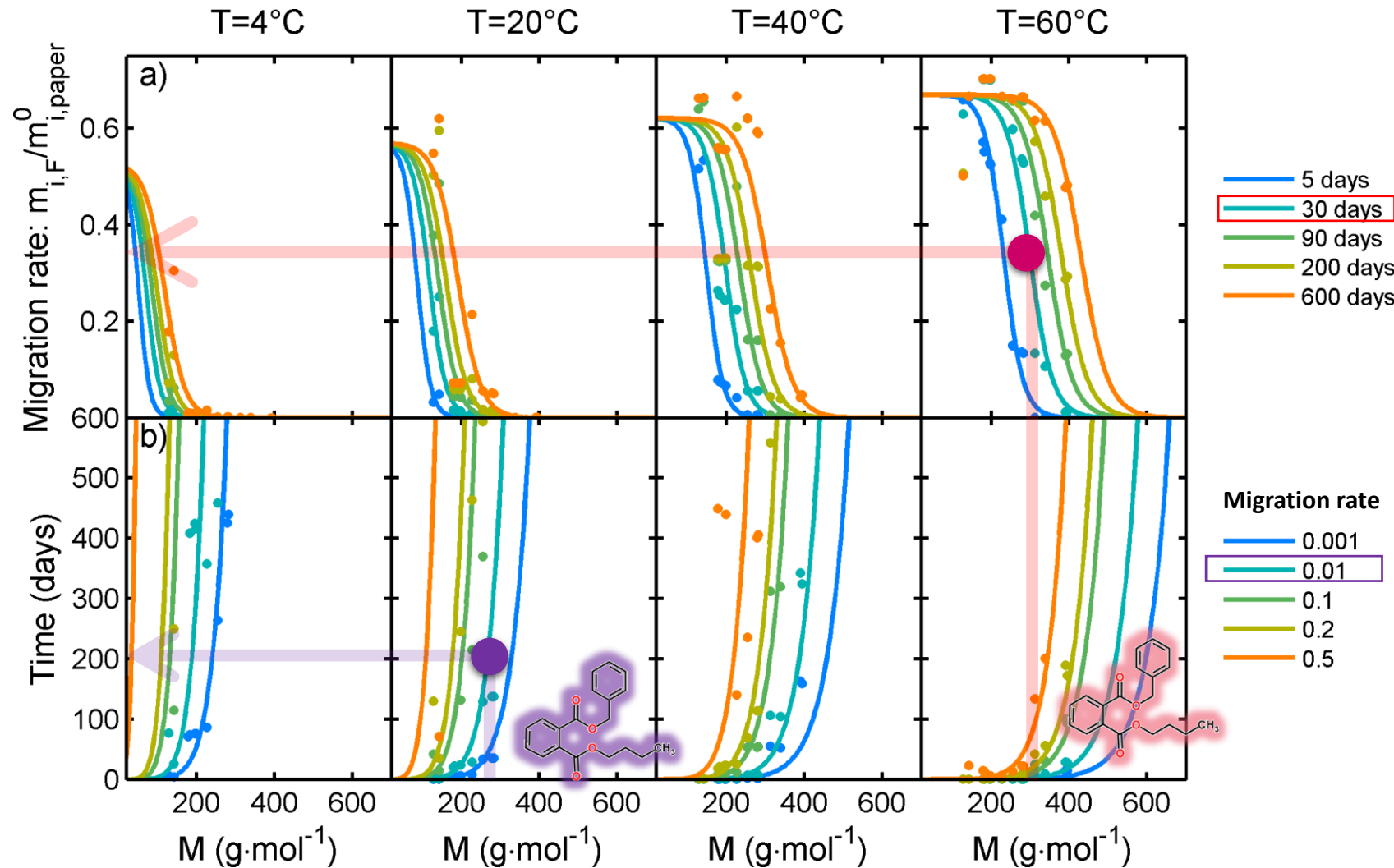
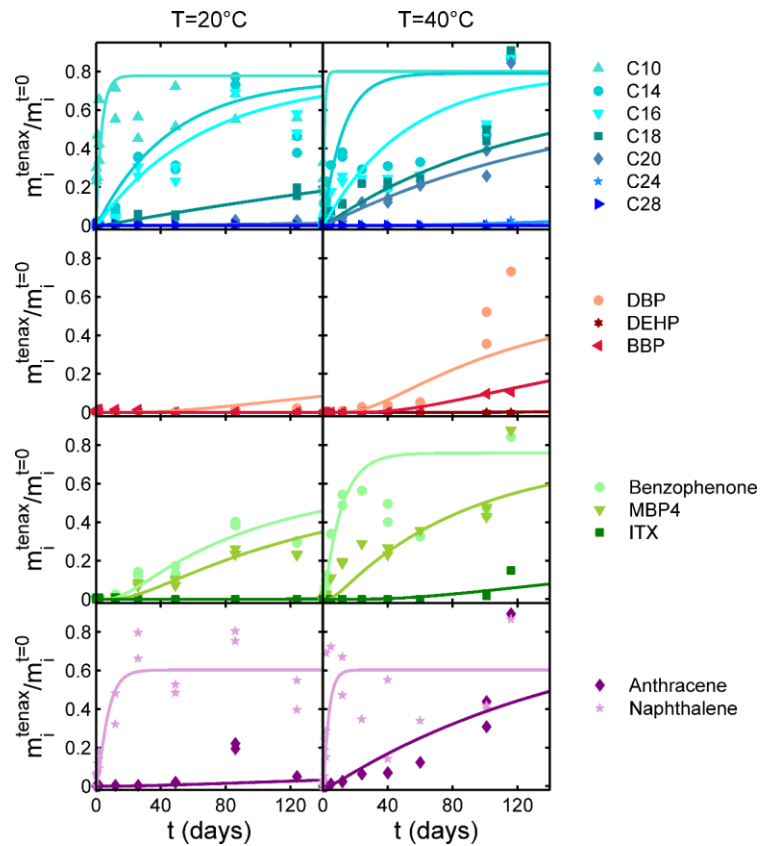
$\widehat{C}_F(T, t, i)$
i = 1..15 solutes at any temperature

Simplified modeling Solute independent

$\widetilde{C}_F(T, t, M)$
simplified at any temperature

➤ CONTAMINATION THROUGH THE GAS PHASE

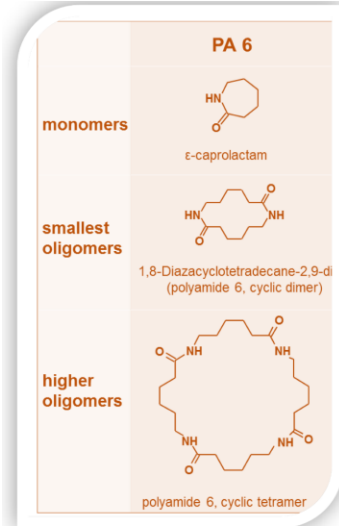
TENAX packed within a 50 μm thick BOPP bag and exposed to a cardboard material formulated with 15 surrogates



UBIQUITOUS CROSS-CONTAMINATION IN SINGLE-USE APPLICATIONS

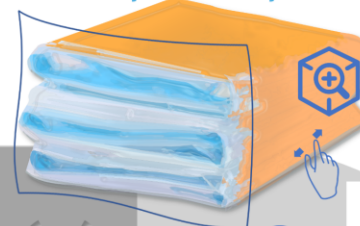
Five key steps

- 1) Overpouch containing monomers (e.g. from PA6)
- 2) Storage for several months before shipping
- 3) Mass-transfer across the bags (folded or not)
- 4) Migration in the culture medium
- 5) Ubiquitous contamination of lots



Example of chemical present in the over-pouch

Single-use bags folded and packed in a sealable plastic over-pouch



Over-pouch = tri layer material

Migration across the overpack

Sterilization by gamma-irradiation of bags and systems sealed within an over-pouch.

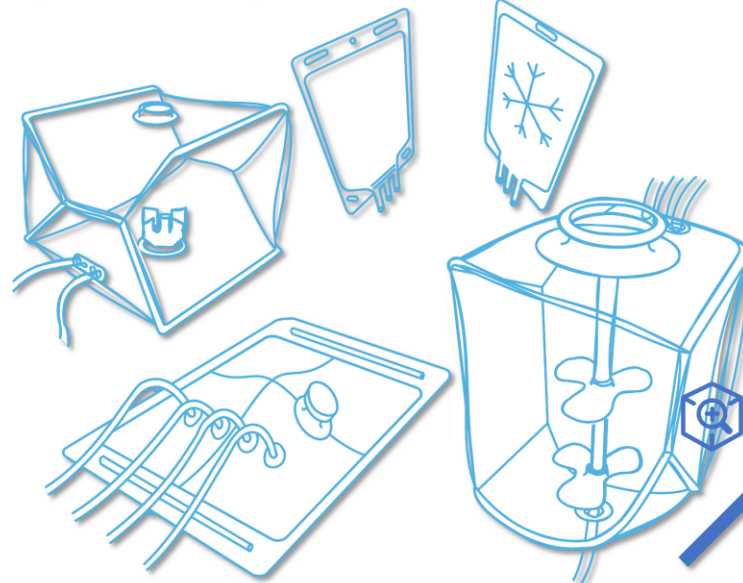
Storage of several months + Shipping



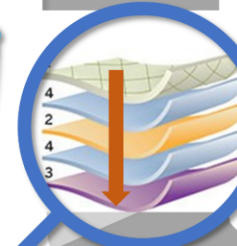
Production (from hours to weeks)



Contamination of drugs, vaccines etc.



Single-use bags and systems

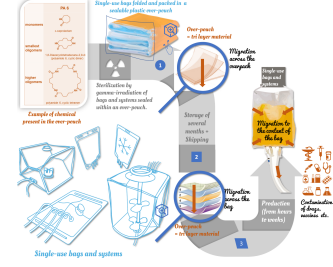


Over-pouch = tri layer material

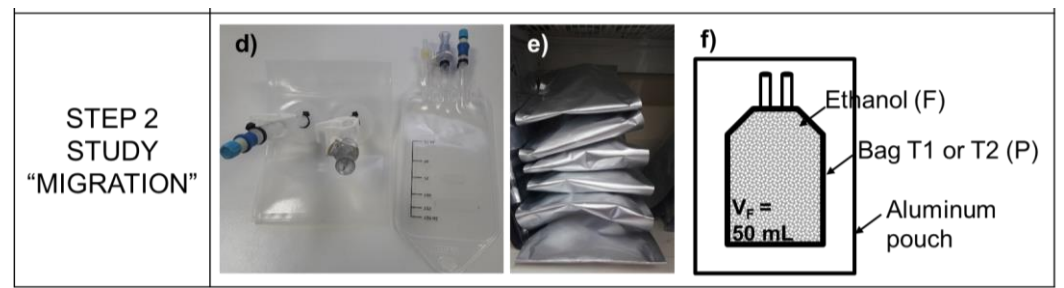
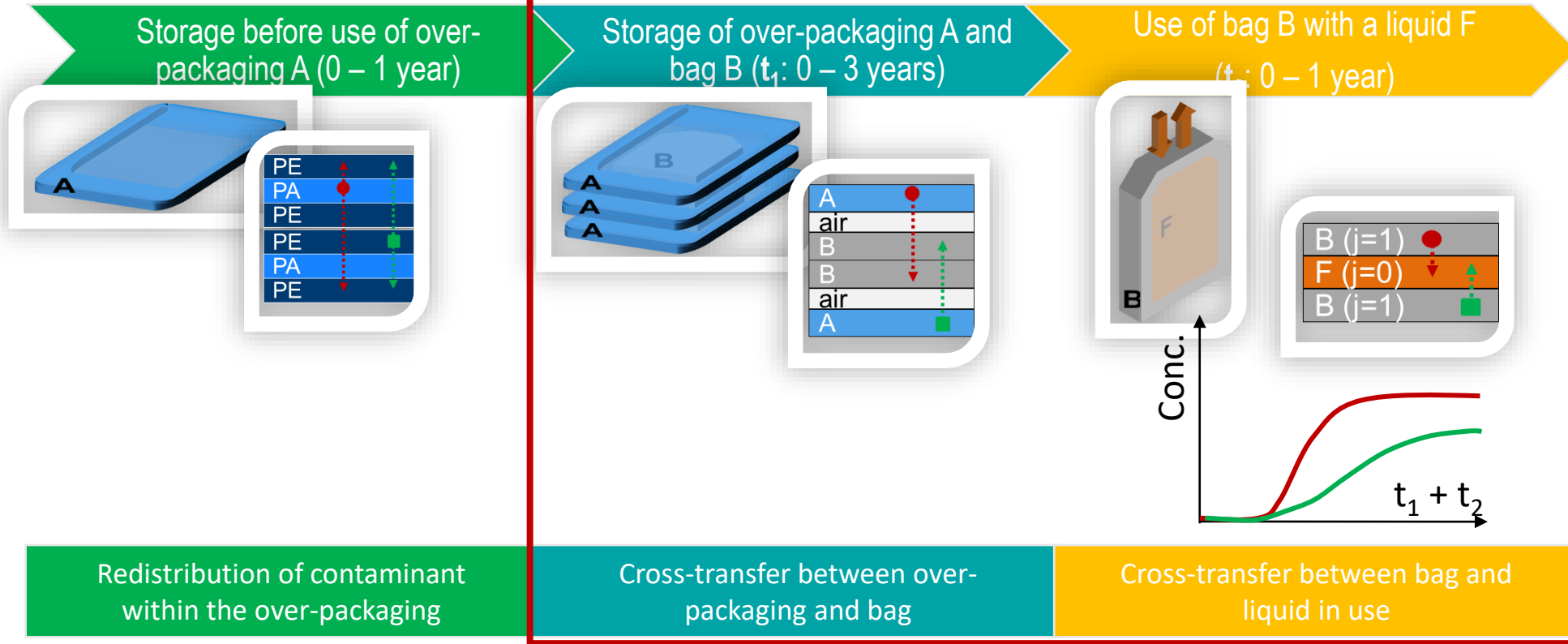
Migration across the bag



UBIQUITOUS CROSS-CONTAMINATION IN SINGLE-USE APPLICATIONS



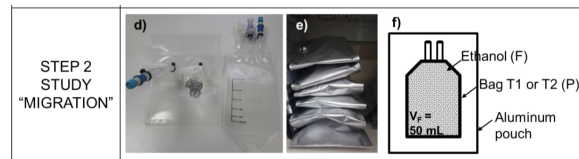
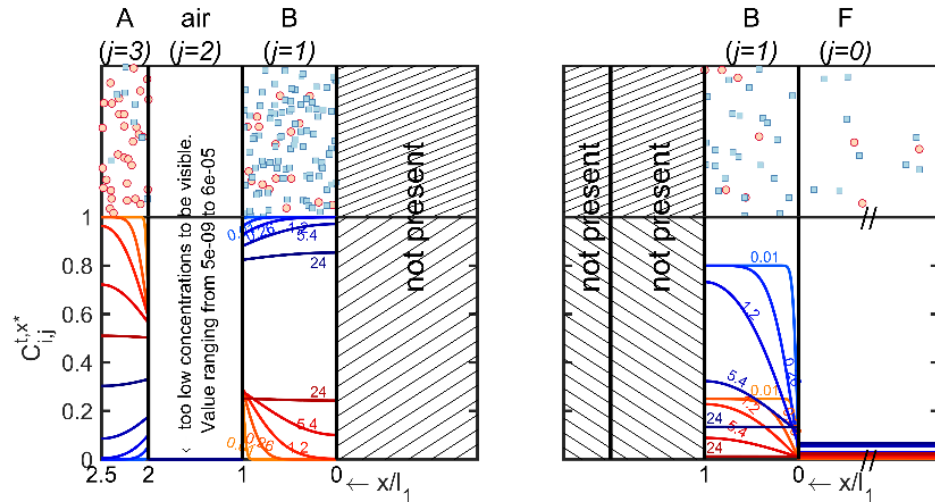
Experiments



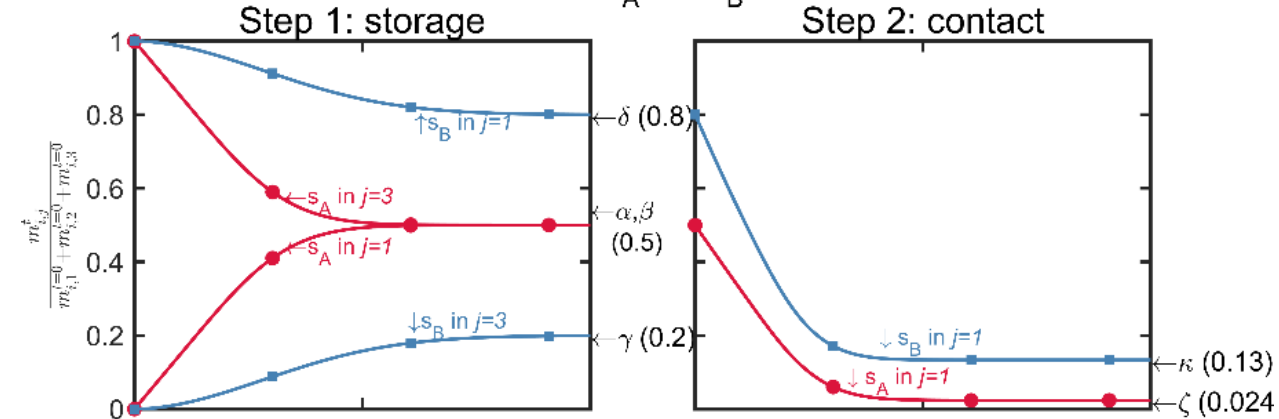
UBIQUITOUS CROSS-CONTAMINATION IN SINGLE-USE APPLICATIONS

Modeling

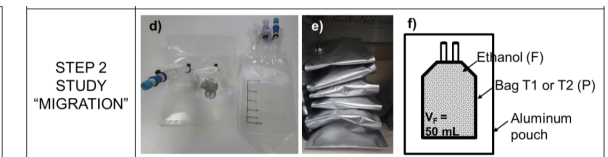
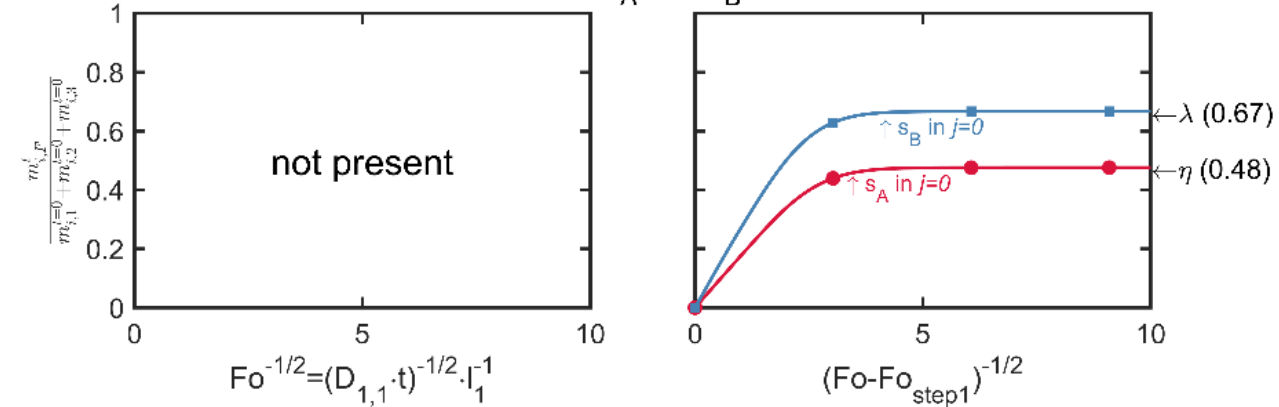
a) Migrant distributions and concentration profiles



b) Concentration kinetics of migrants s_A and s_B in A and B



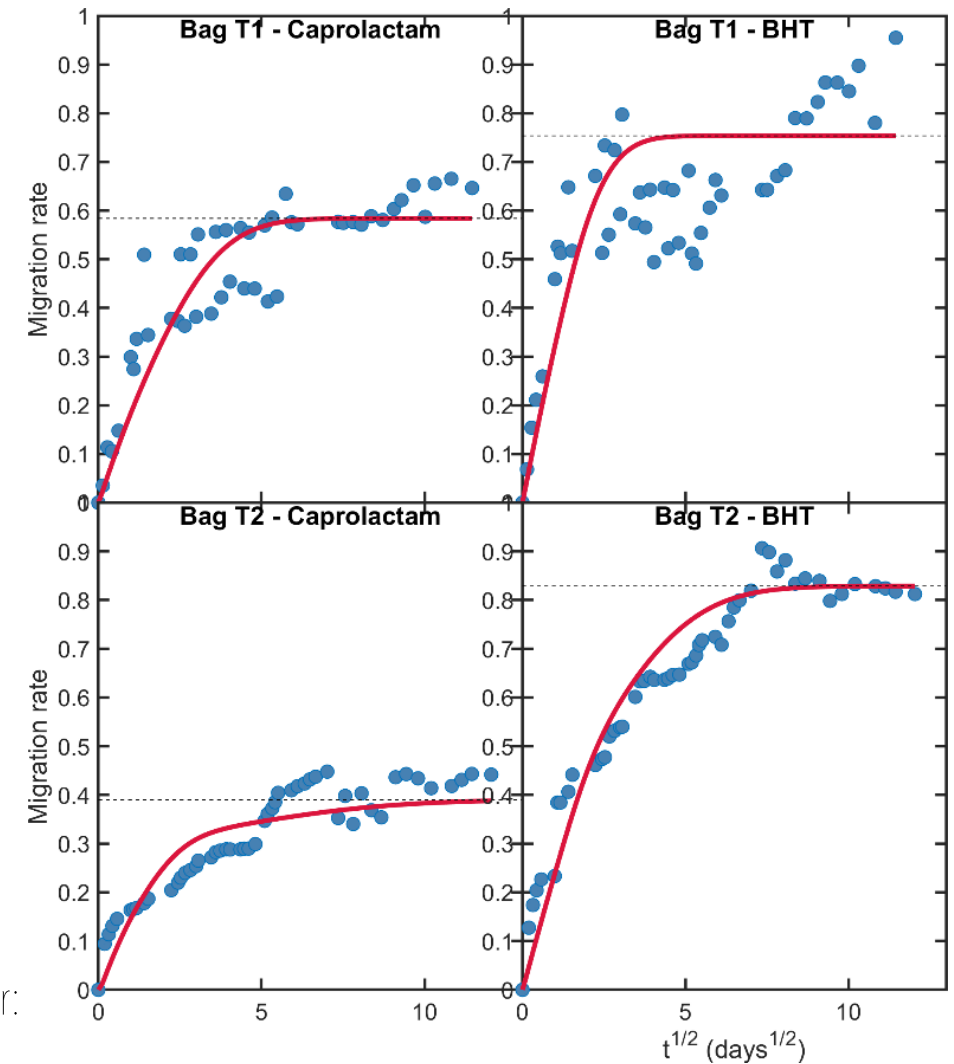
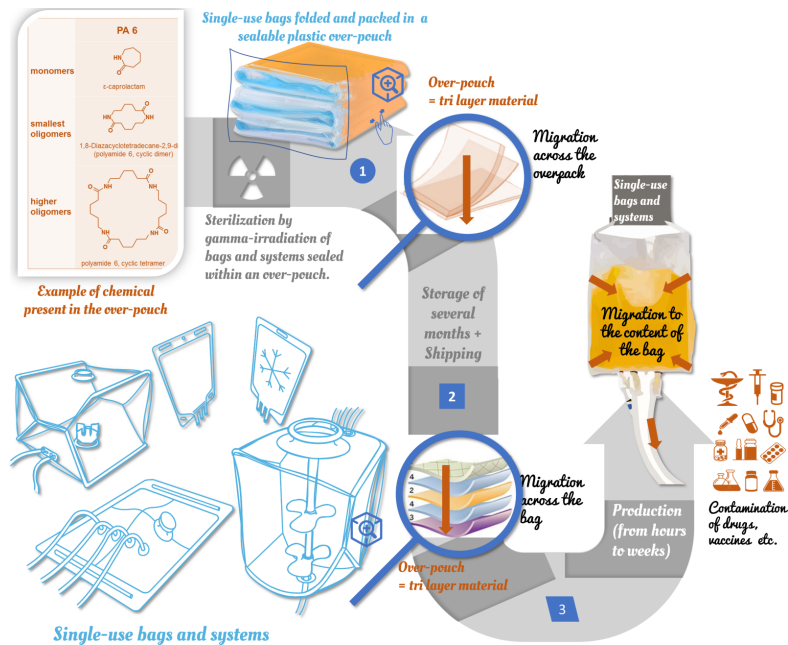
c) Concentration kinetics of migrants s_A and s_B in F



➤ COMPARISON BETWEEN PREDICTION AND EXPERIMENTS

Migration in simlants (ethanol 95% and ethanol 50% have been tested)

Results between bags (3 measurements per bag) but the trends are well predicted by the model.



Nguyen P-M, Dorey S, Vitrac O. The Ubiquitous Issue of Cross-Mass Transfer: Applications to Single-Use Systems. *Molecules*. 2019;24:3467.

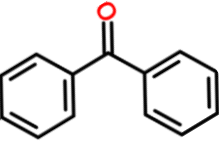


Preventive Approaches

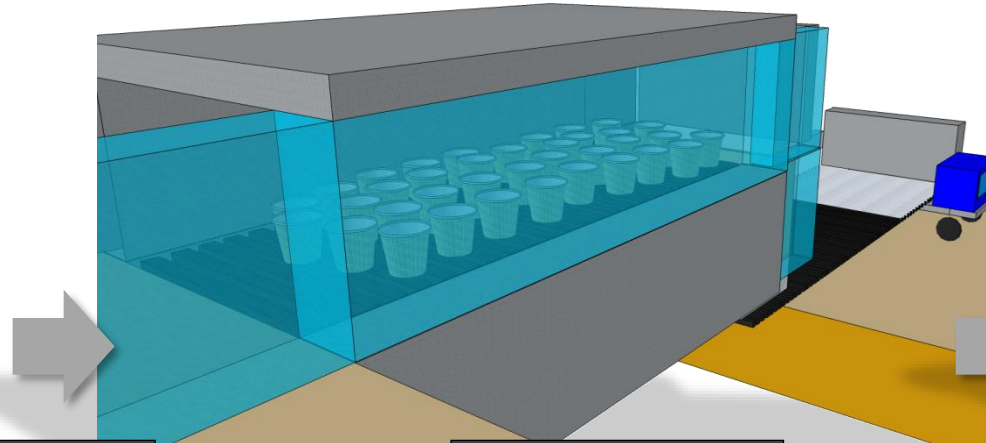
(Failure Mode Effects and Critical Analysis, Safe-by-design, Integrated engineering)

➤ CHAINED STEPS: where is the critical step?

Risk of contamination by a photoinitiator from UV-curing printing ink



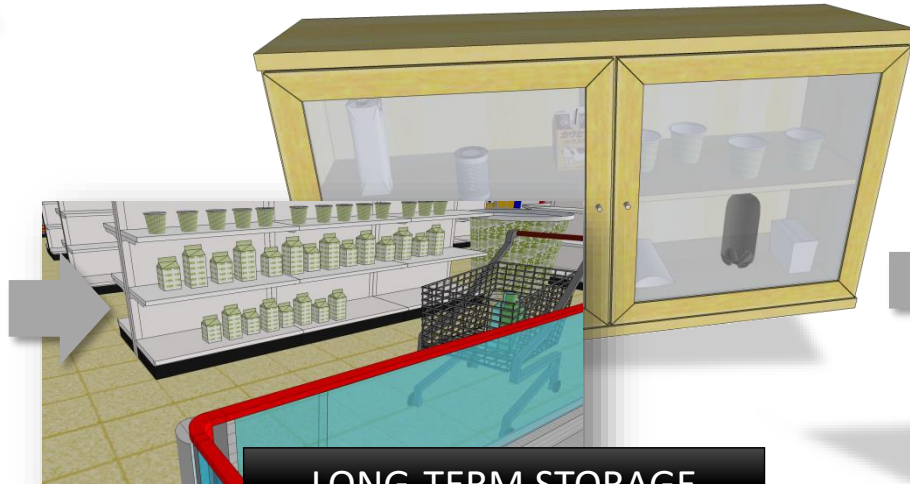
STORAGE "BEFORE USE"



HOT FILLING



FATTY CONTACT

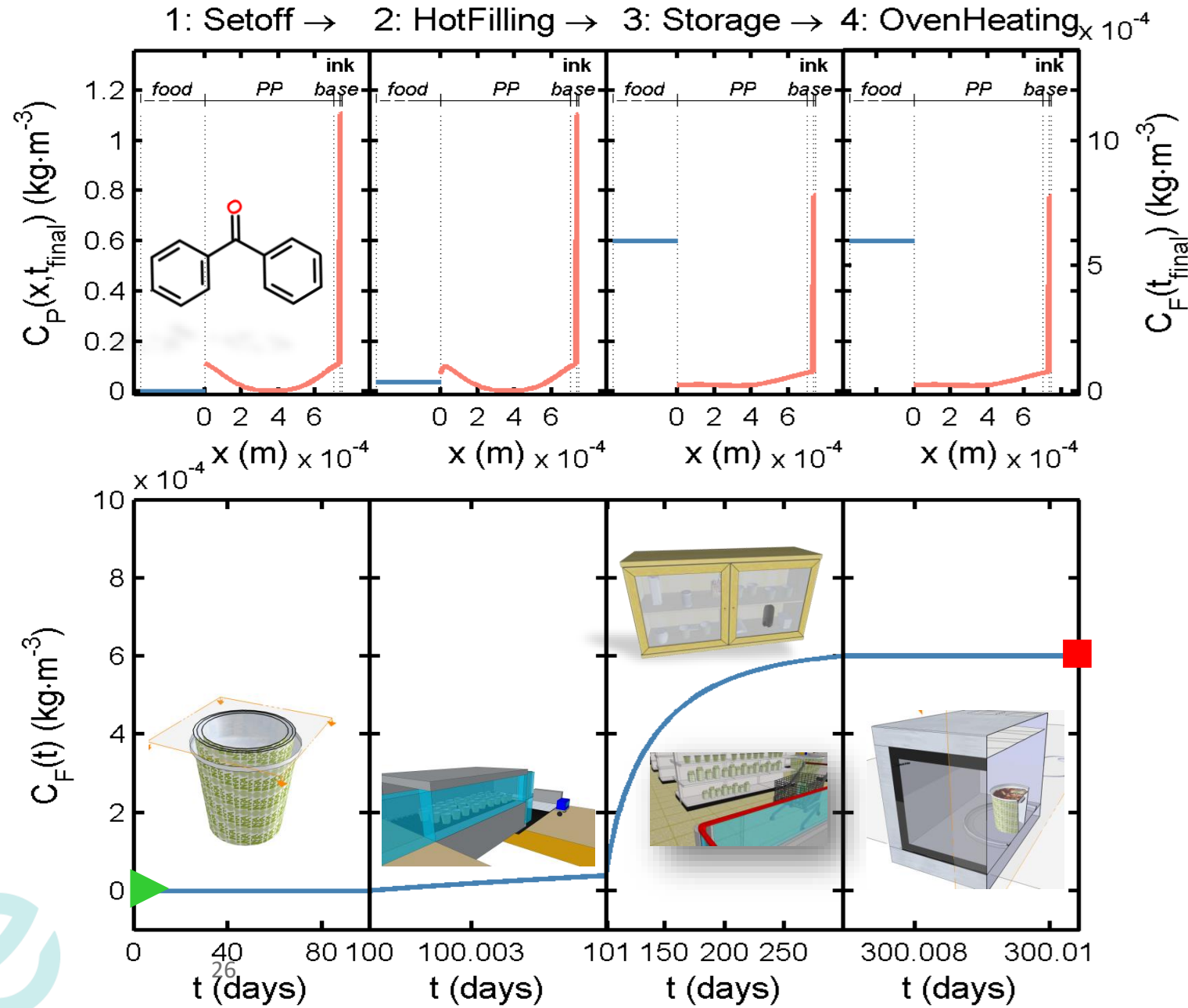


LONG-TERM STORAGE



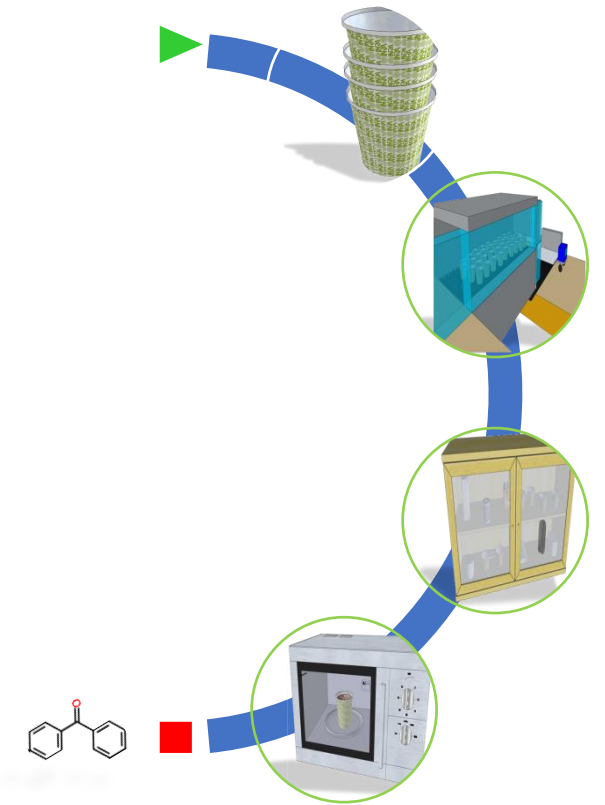
MICROWAVE OVEN HEATING





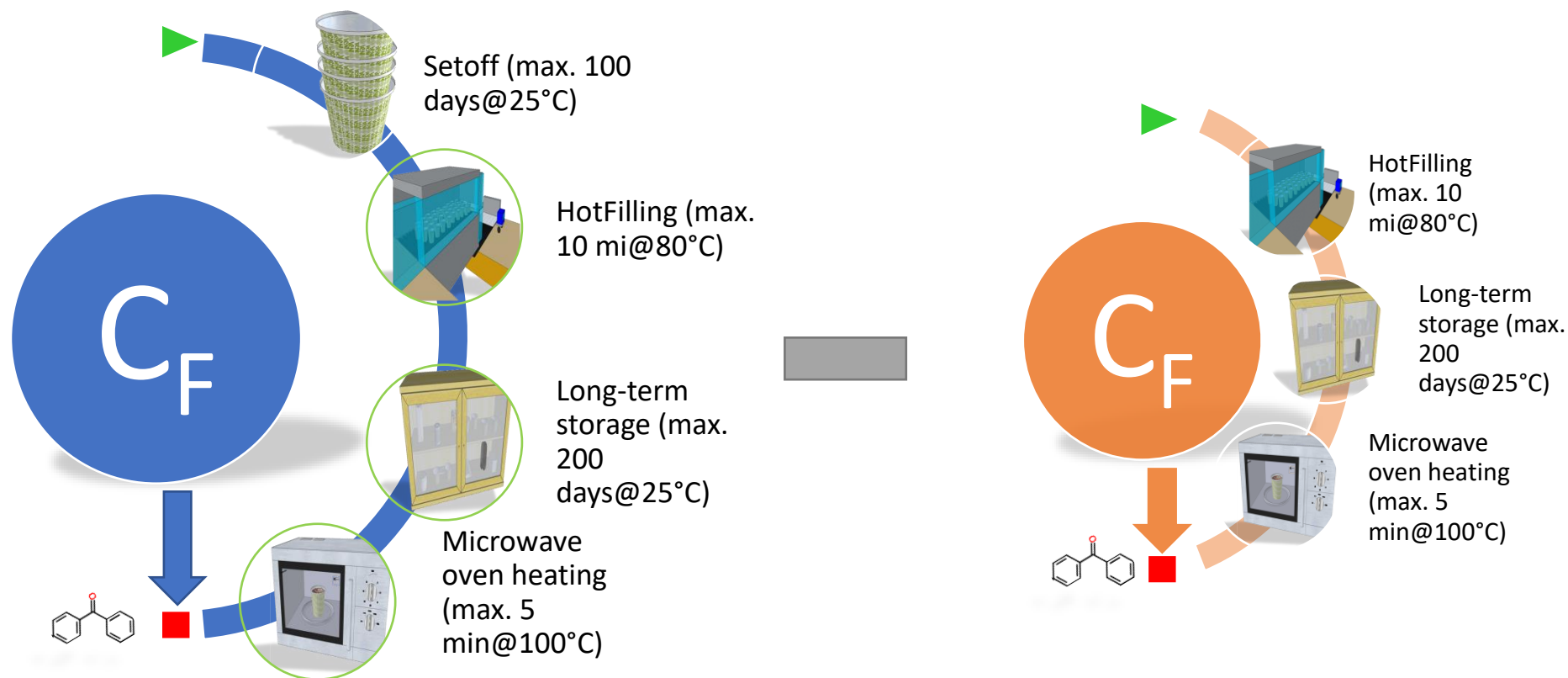
➤ CHAINED STEPS

UV-curing printing ink



➤ ASSESSING THE SEVERITY OF A SINGLE STEP

CASE OF "SETOFF" STEP



comparison with step i alone

$$\text{Severity}(\hat{C}_F(\text{step } i)) = f\left(\max(C_{F_M}|_{1 \rightarrow 2 \rightarrow \dots \rightarrow M} - C_{F_M}|_{1 \rightarrow 2 \rightarrow \dots \rightarrow M/i}, C_{F_i}|_i)\right)$$

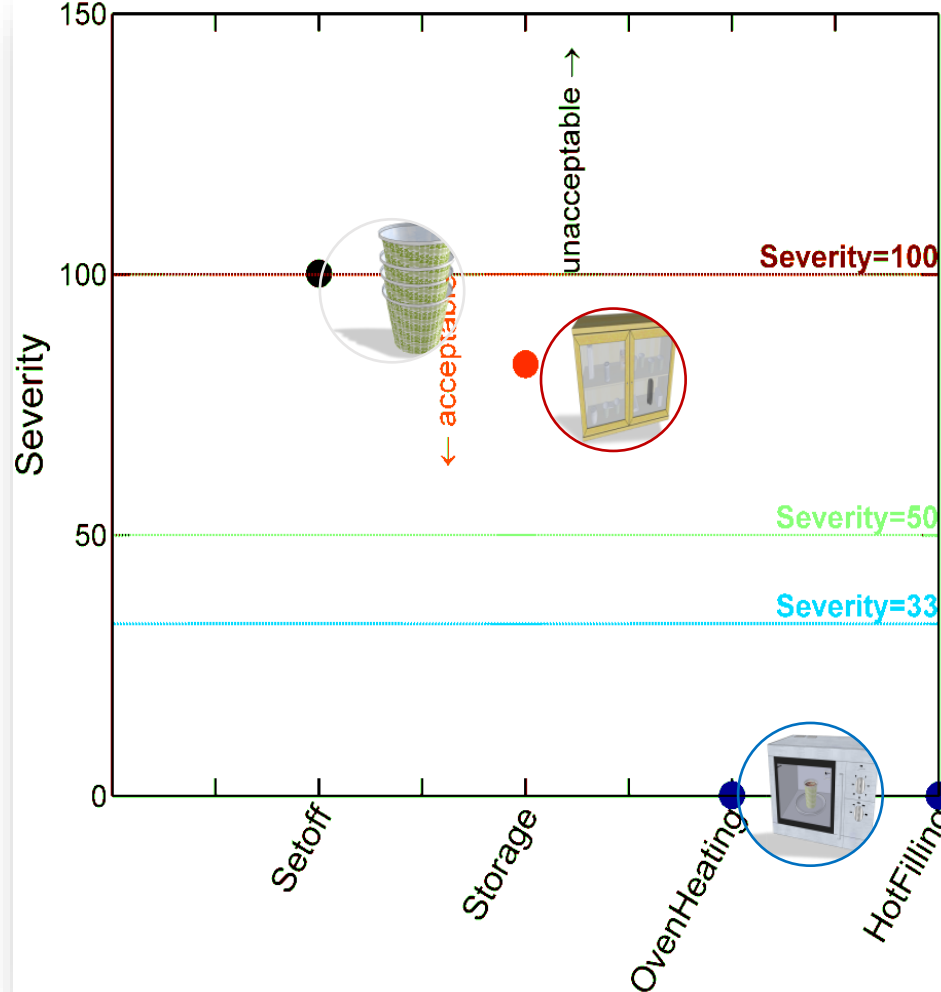
comparison with step i removed



➤ CONCURRENT ENGINEERING: COMPARING THE SEVERITY OF SEVERAL STEPS, PACKAGING DESIGNS, SUBSTANCES...

AIChE Journal, 59(4), 1183-1212

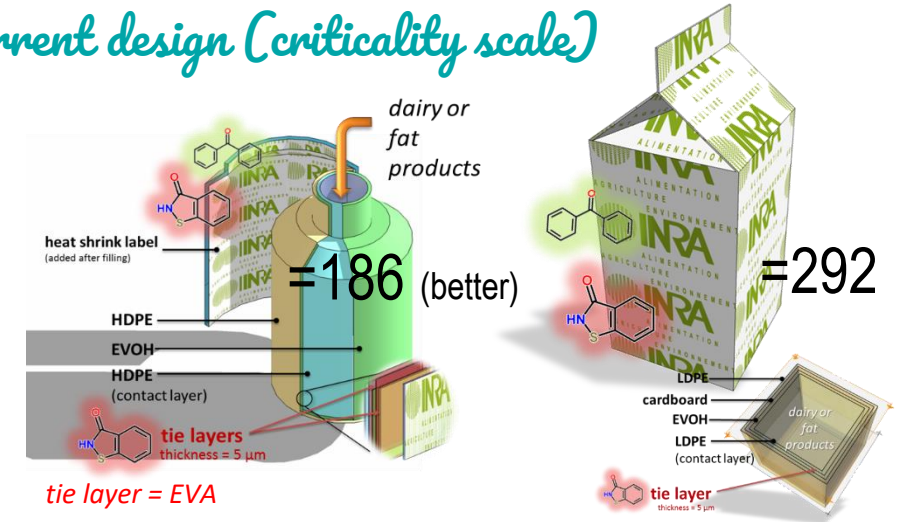
Critical step (severity scale)



$$severity = 100 \times \frac{C_F}{SML}$$

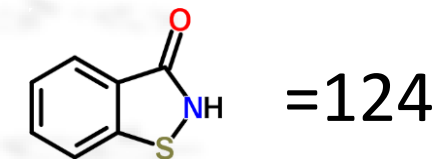
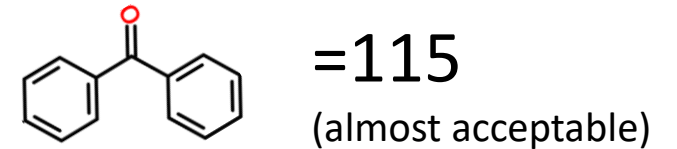
Unacceptable when *severity* > 100

Concurrent design (criticality scale)



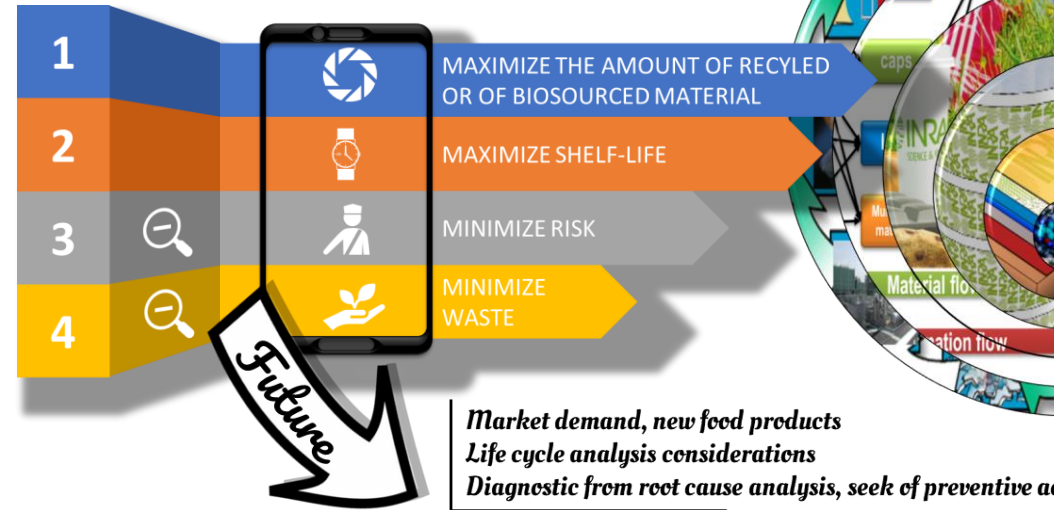
$$criticality = \sum_{all\ components} \sum_{all\ substances} \sum_{all\ modalities} pr(modality) \times severity$$

Critical substance



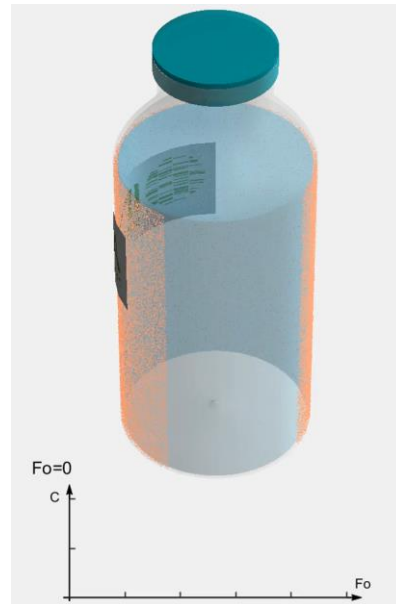
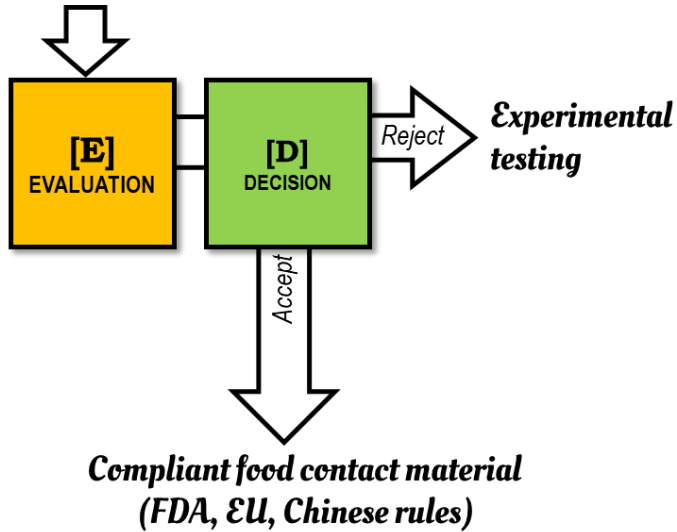
➤ Beyond concurrent design, integrated engineering

Multicriteria optimization

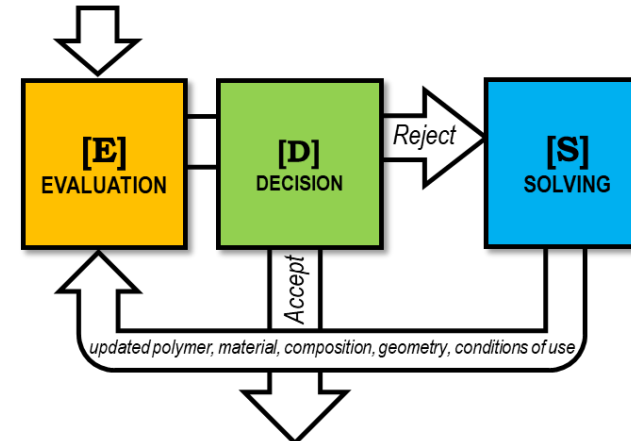


| | |
|----------------------------------|---|
| Closed-loop supply chain | <ul style="list-style-type: none"> • Consumer practices (including misuse) • Recycling process |
| Open-loop supply chain | <ul style="list-style-type: none"> • Industrial practices (process, intermediate storage, etc.) • Retailing practices |
| Real food and packaging | <ul style="list-style-type: none"> • Geometry • Shelf-life |
| Components | <ul style="list-style-type: none"> • Relationships • Cross-contamination |
| Materials | <ul style="list-style-type: none"> • Composition • Formulation • Conditions of use |
| Molecular properties | <ul style="list-style-type: none"> • Diffusion • Sorption |
| Nested Migration Modeling | |

*New substance
New material
New recycling process
New food packaging*

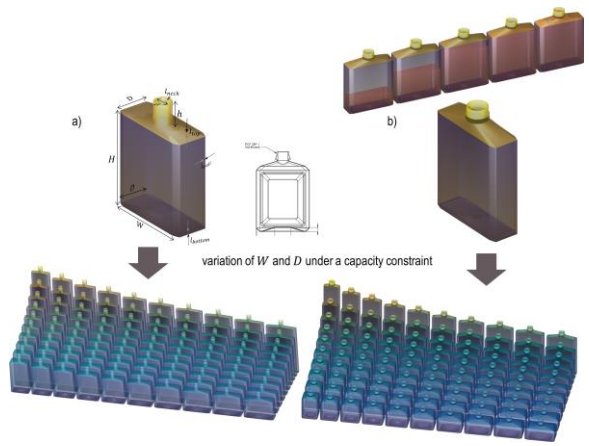


*Market demand, new food products
Life cycle analysis considerations
Diagnostic from root cause analysis, seek of preventive actions
Computer-aided drafting*



Rapid prototyping and compliance
Good manufacturing and design practices
Safer food products
Improved shelf-life
Eco-designed packaging

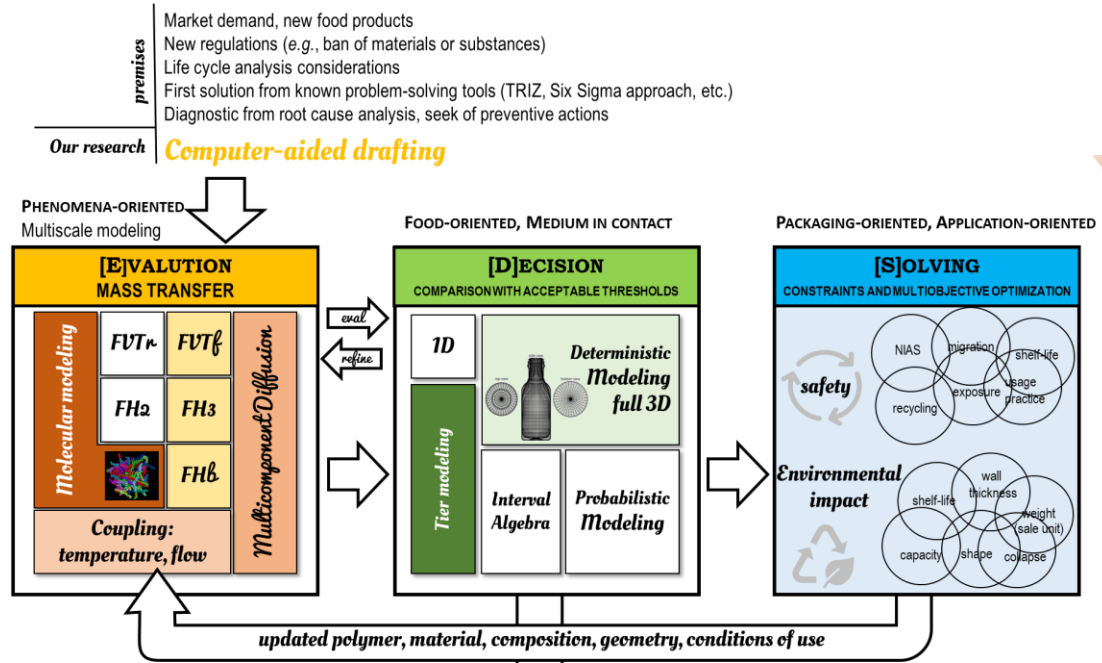




Example: redesign of PET bottle for alcoholic beverages (optimized shape, recycled content, reduced weight, improved shelf-life)

3D prototype printed the same day

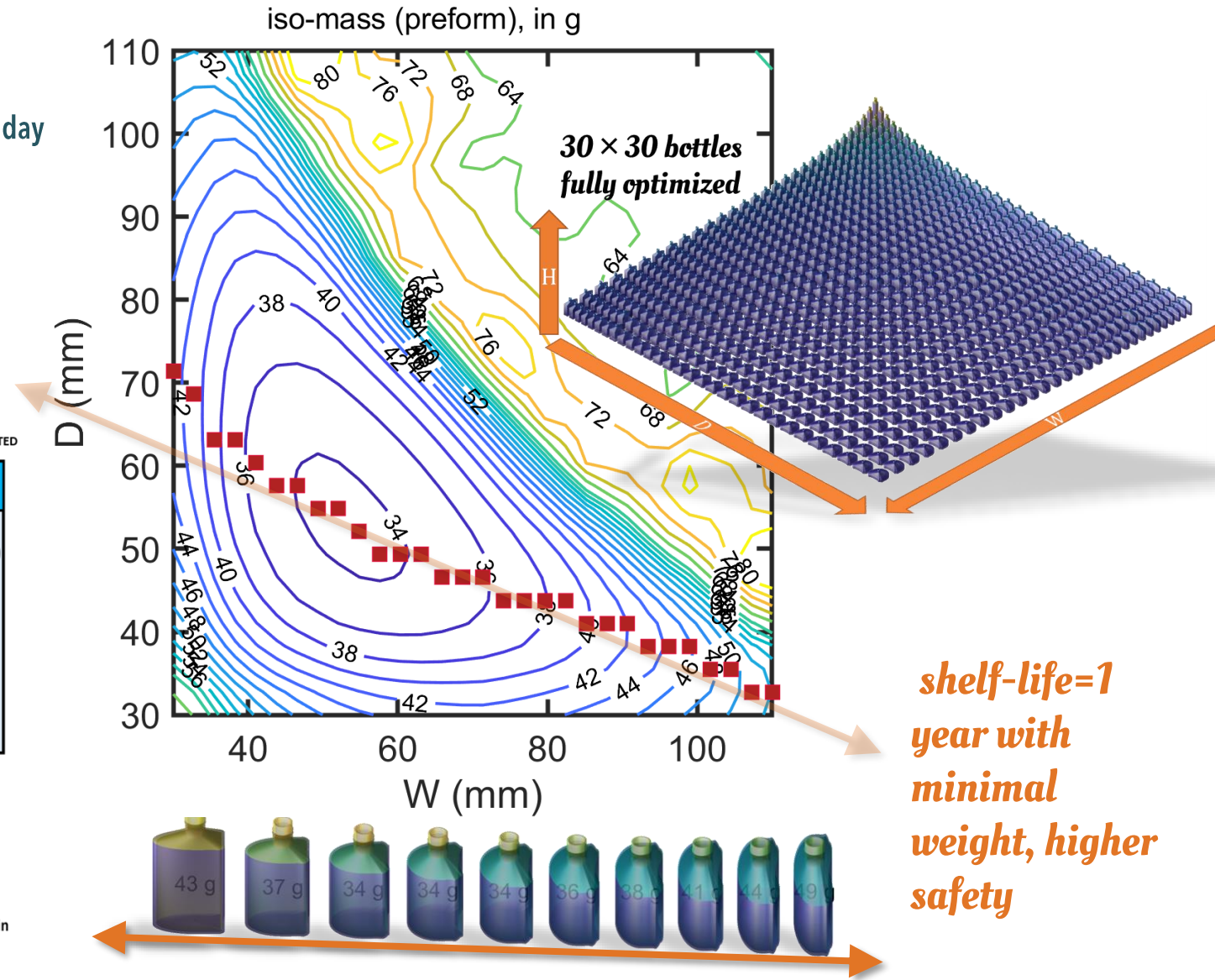
Integrated engineering



Feasible solutions (Optimal or Pareto-optimal)

Our research *Rapid prototyping*

applications
 Minimized waste, migration risk, optimized shelf-life, optimized process and supply chain
 Computer-aided engineering (mechanical resistance) and manufacturing (extrusion-blowing)
 Additional validation (e.g., consumer acceptance)
 Global environmental footprint
 Safe-by-design and eco-design approaches
 3D printing, augmented-reality



Zhu, Y., Guillemat, B., et Vitrac, O. (2019). Rational Design of Packaging: Toward Safer and Ecodesigned Food Packaging Systems. *Frontiers in Chemistry*, 7(349).

➤ Train yourself to become green

Three months online curriculum on packaging design

<https://fitness.agroparistech.fr/>



roatia, France, Germany, Portugal, Spain

Main menu About Us job offers

Welcome to FITNESS

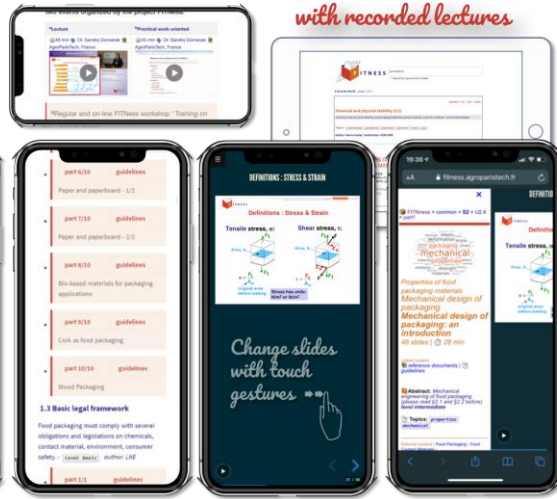
Fitness stands for **Food packaging open courseware for higher education and staff of companies**

All lectures, interactive contents and Quiz are provided "AS IS". The content (85 lectures from Common to Specialized Modules) is under development and may contain inconsistencies and inaccuracies. It will be updated regularly.

trainee/ student view



with recorded lectures



ecodesign

Search by keywords in slides

7 lectures found | page 1 of 1

| # num. lectures | book | recorded | guidelines | extra | case-studies | how-to | solution |
|-----------------|------|----------|------------|-------|--------------|--------|----------|
| 5 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |

specialized > S5 > U5.3 > part1

Computer-aided FMECA applied to mass transfer

Computer-aided approaches facilitate the deployment of FMECA approaches. The lecture illustrates various situations calculated with the open-source software FMECAEngine identification of critical steps, components, substances - level advanced

Topics: **design** **prevention** **safe-by-design** **migration** **risk** **safety** **modeling**

Author: Olivier Vitrac | Institution: INRAE

Read Lecture

2 slides found

THIS PROJECT HAS RECEIVED FUNDING FROM THE EUROPEAN UNION'S ERASMUS PROGRAMME UNDER CONTRACT N° 2017-1-FR01-KA202-037441

COORDINATOR ACTIA-LNE

COMPUTER-EVOLUTIONARY ECO-DESIGN & SAFE-BY-DESIGN

Case of plastic bottles for alcoholic beverages

Beverage Consumption rate Storage Supply chain

Life cycle

ACCELERATING THE INNOVATION PROCESS FULL DIGITAL PROTOTYPING

max min min



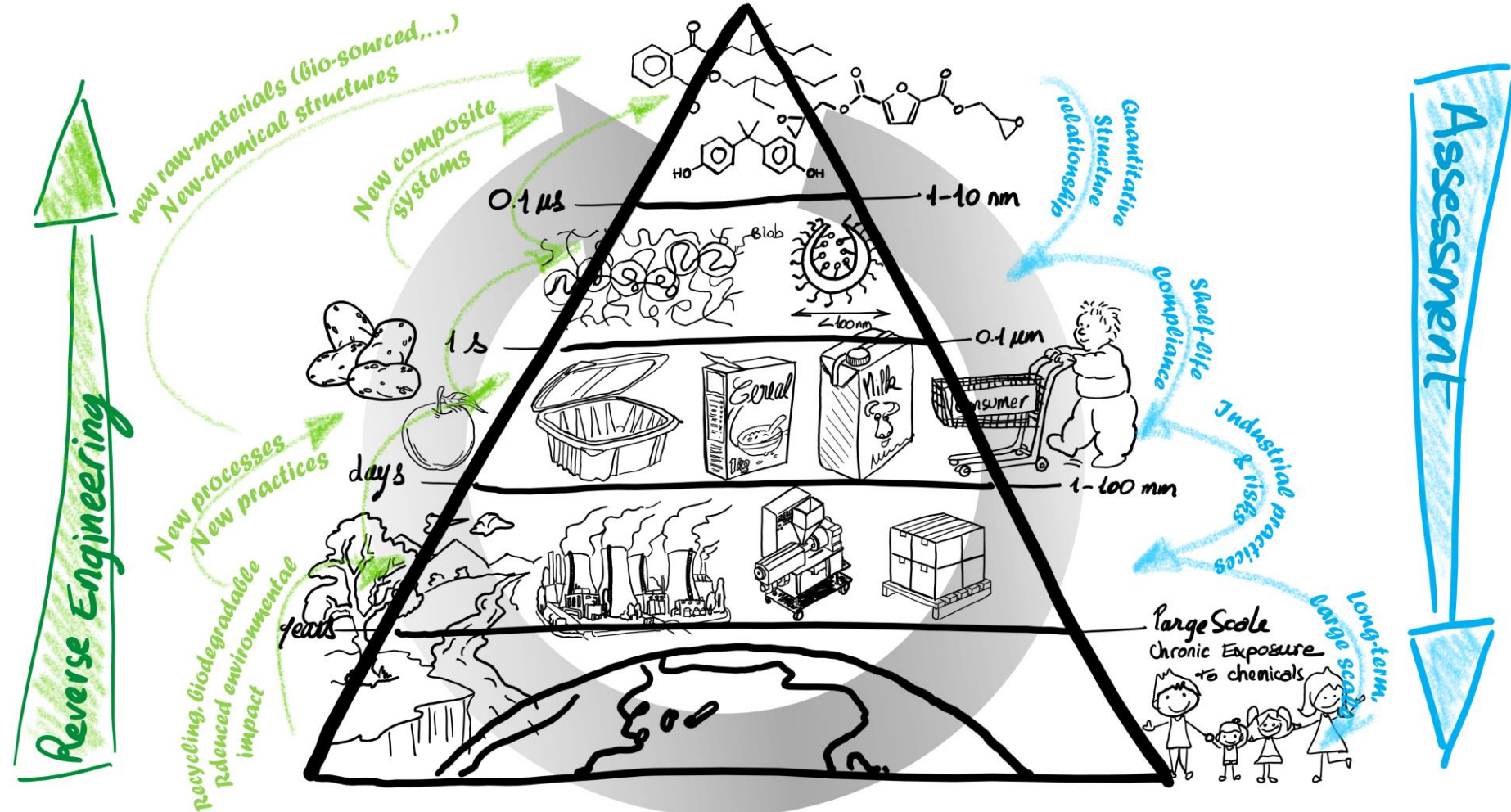
Conclusions & Perspectives

Is it so simple to shift from food contact applications to cosmetic ones.



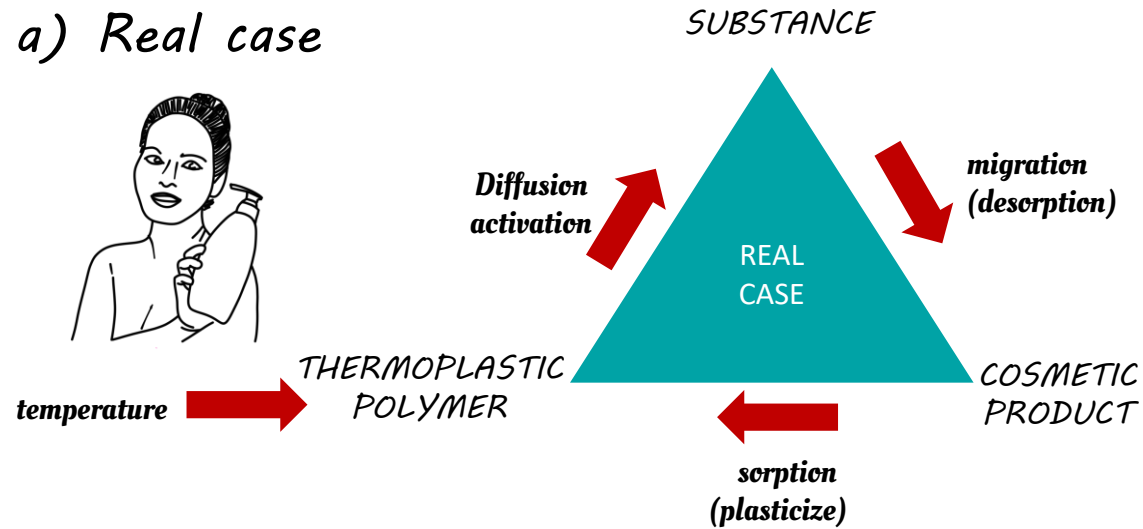
➤ Future of packaging design = safe-by-design + ecodesign

Think
BIG
with engineering








> PROJET COSMETOPACK

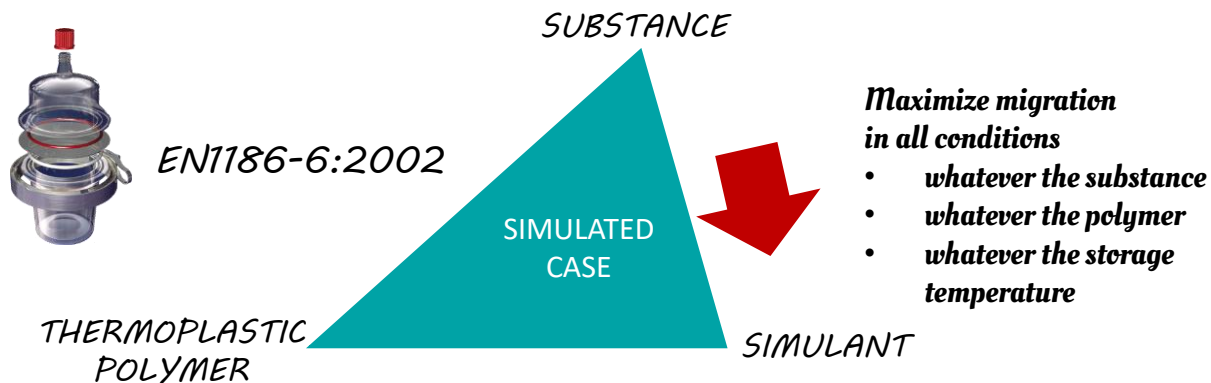
a) Real case






Migration is affected by:

-  Amounts in the material(s)
-  Rates of diffusion of the substance (migration) and cosmetic product's constituents (sorption) in the polymer
-  Chemical affinity of the substance for the cosmetic product (migration) and affinities of cosmetic product's constituents for the polymer (sorption)
-  Diffusion activation by T and plasticizing (i.e., lowering of T_g)
-  polymer relaxation (swelling)

b) Considered case for evaluation (test, calculation)



Migration is overestimated by:

-  Maximizing temperature \times time
-  New simulants maximizing interactions
-  Maximizing chemical affinities

