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

Risk assessment and management of material in contact with cosmetic products

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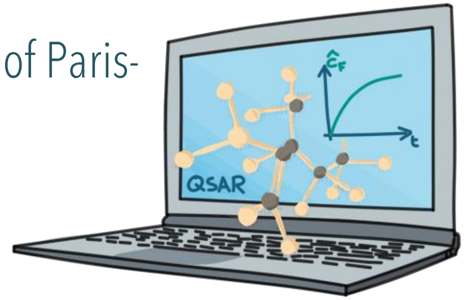
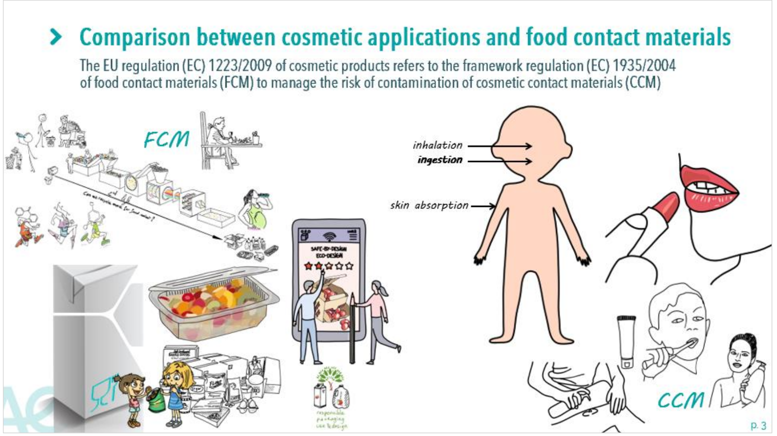
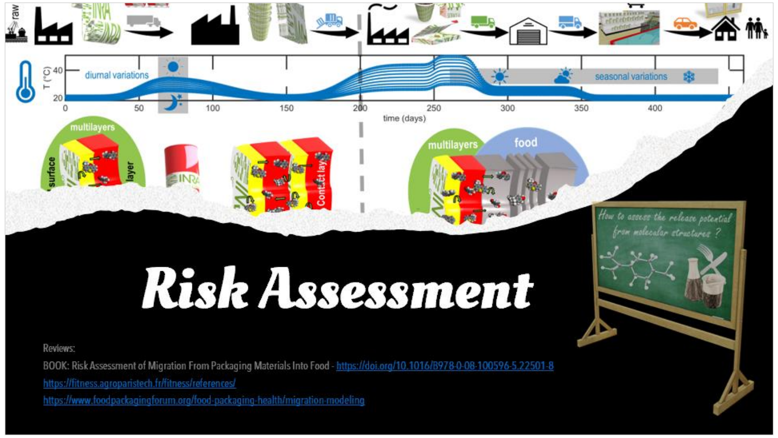
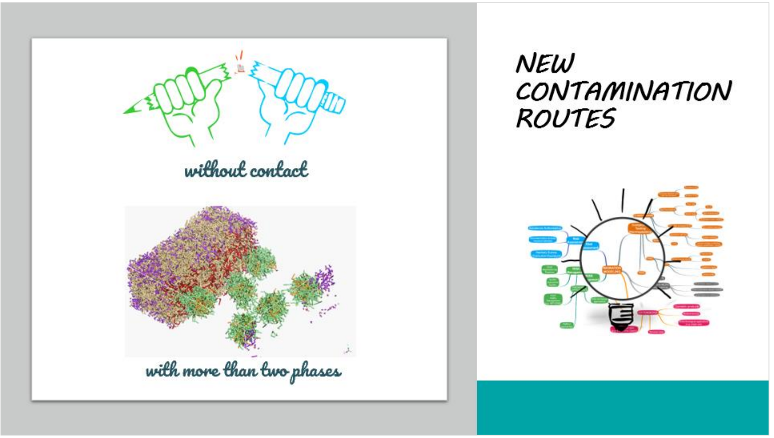
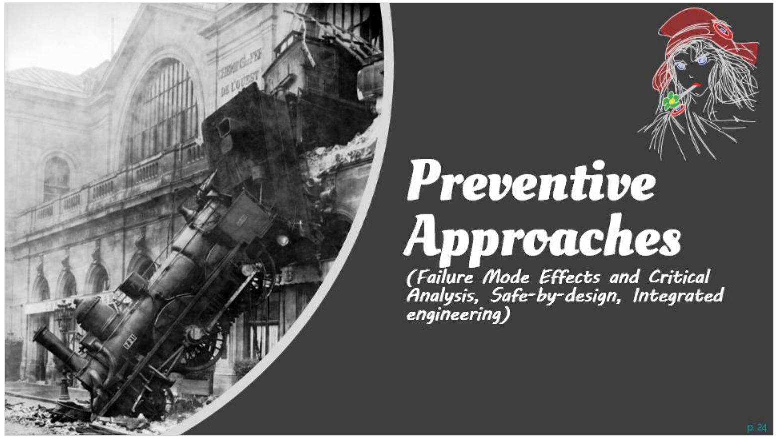


Content overview



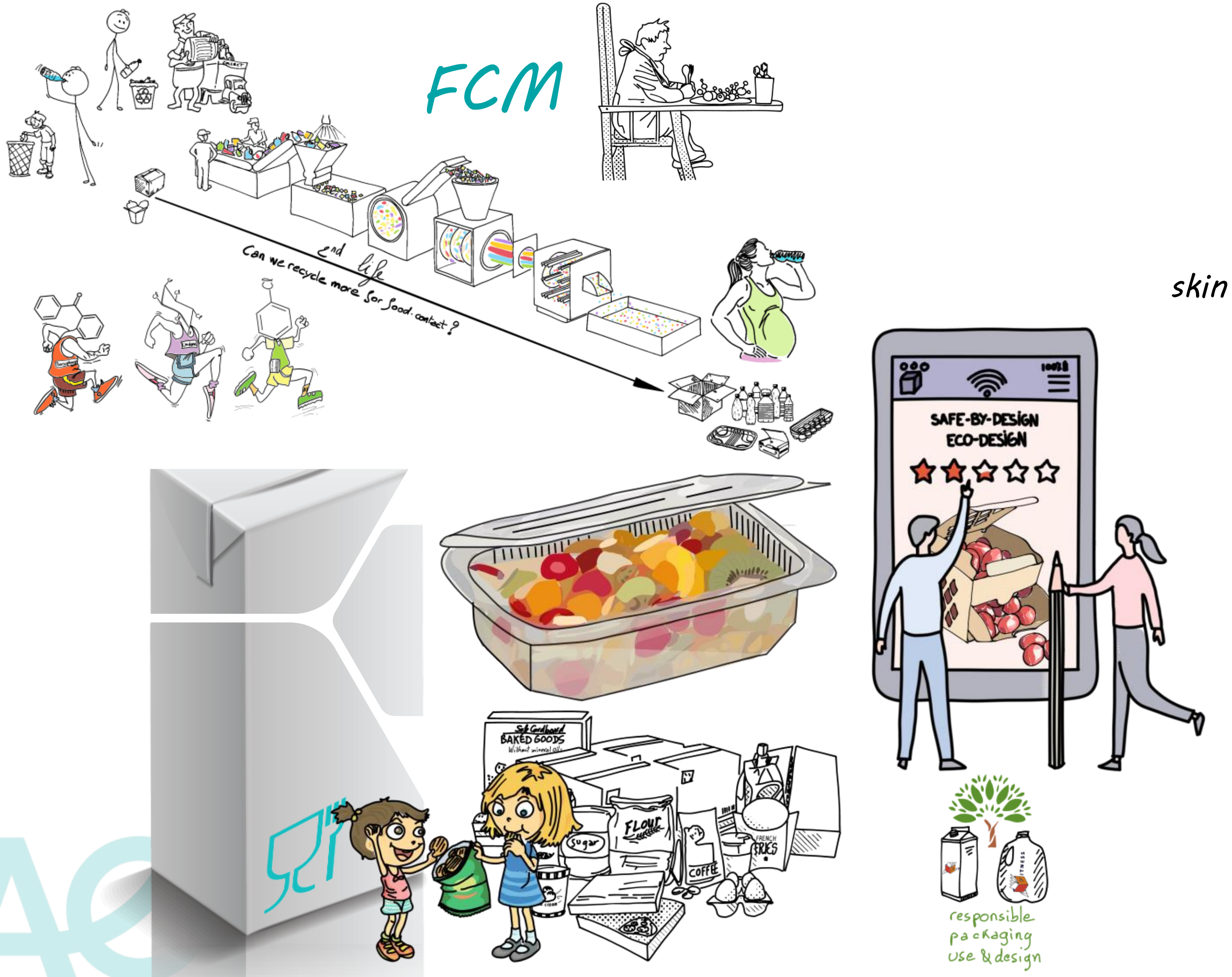


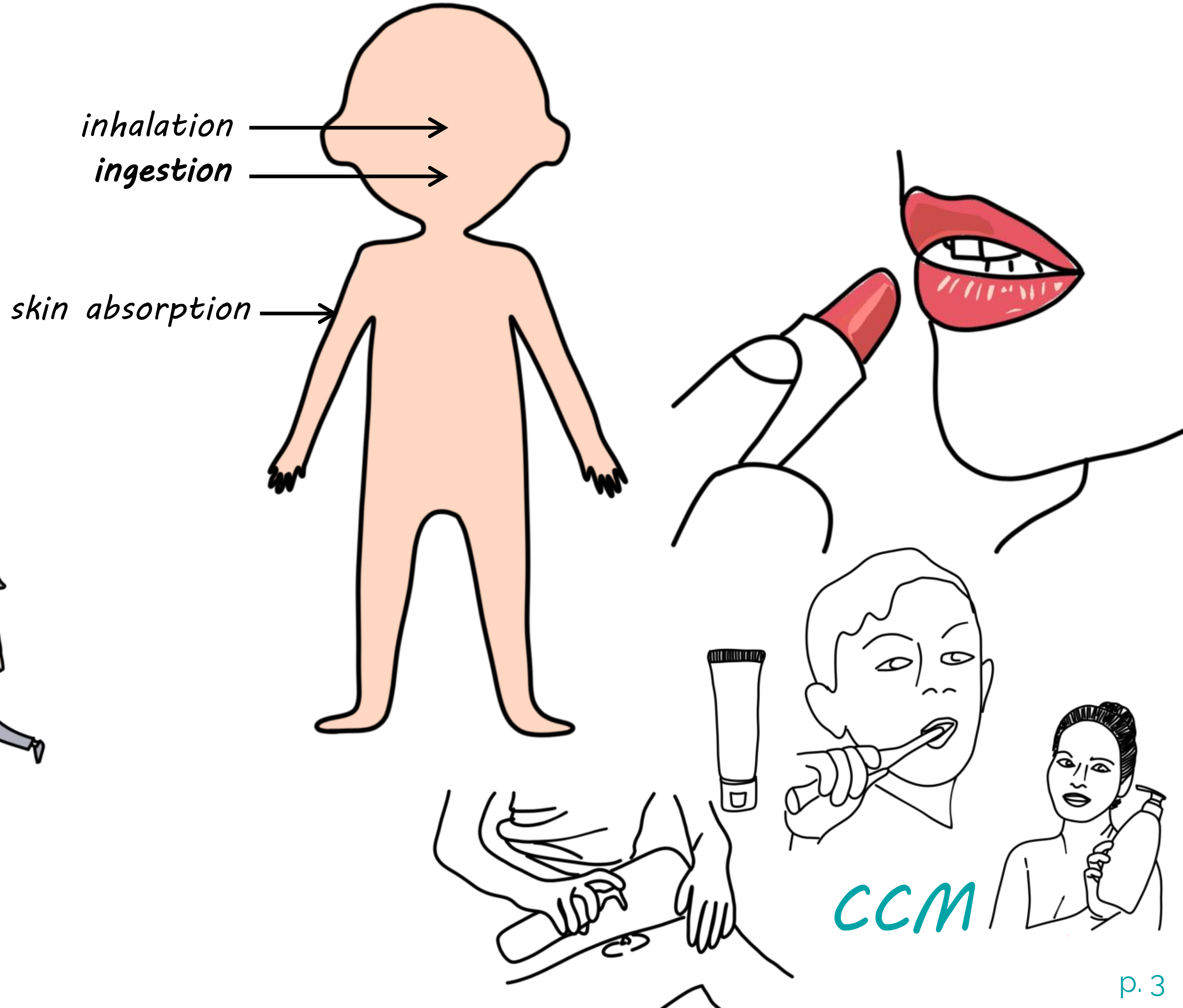




Comparison between cosmetic applications and food contact materials

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)

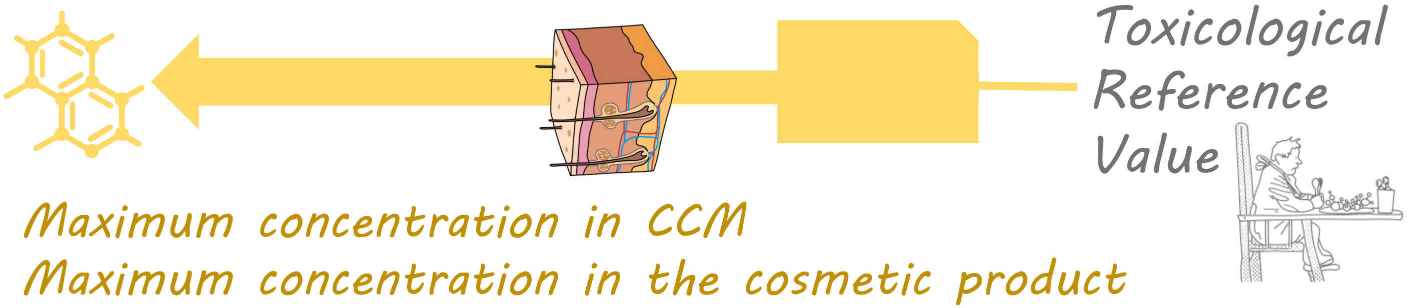


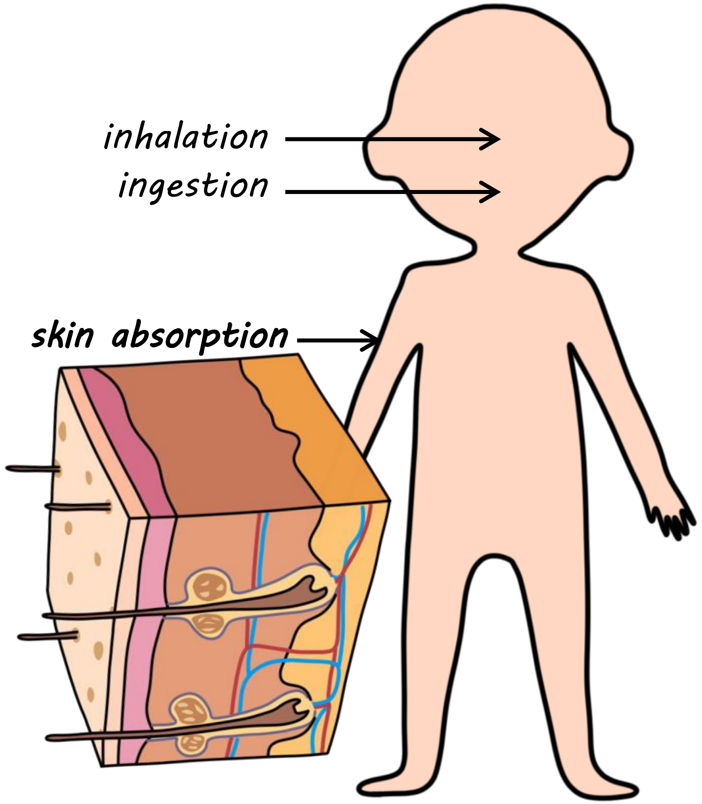


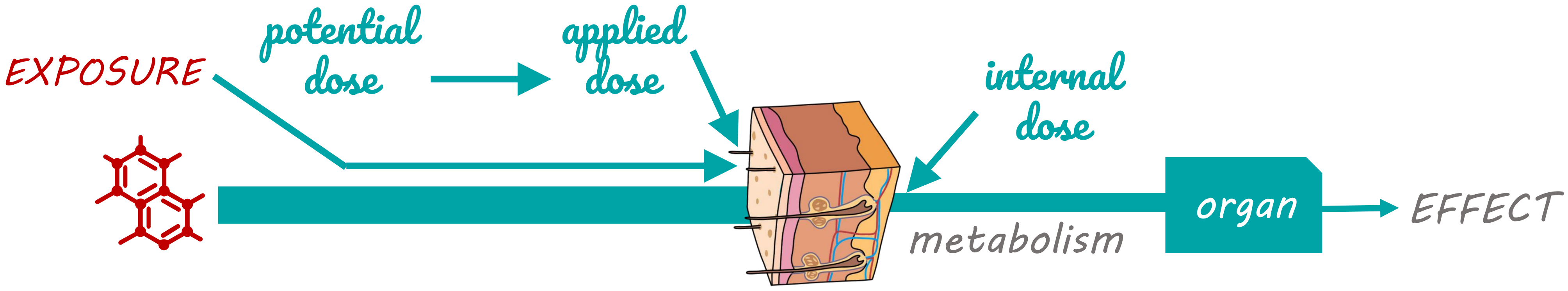
Is there a unique approach?

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

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





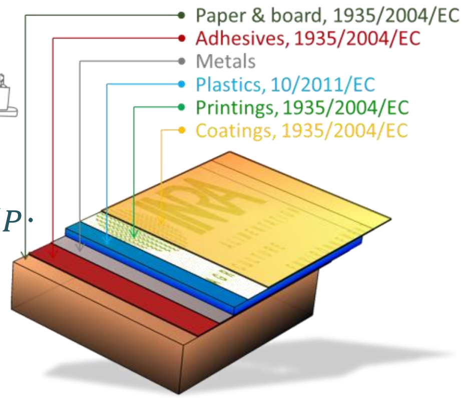


adapted from exposure and dose (US EPA, 1992)

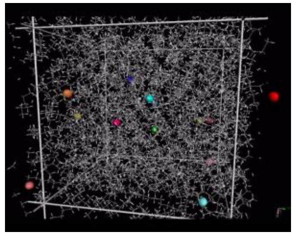
Analogy with packaged food products

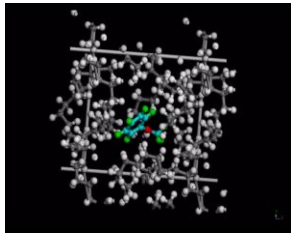
Multiple crises along the year similar causes: uncontrolled mass transfer from the packaging (P) to the food (F)

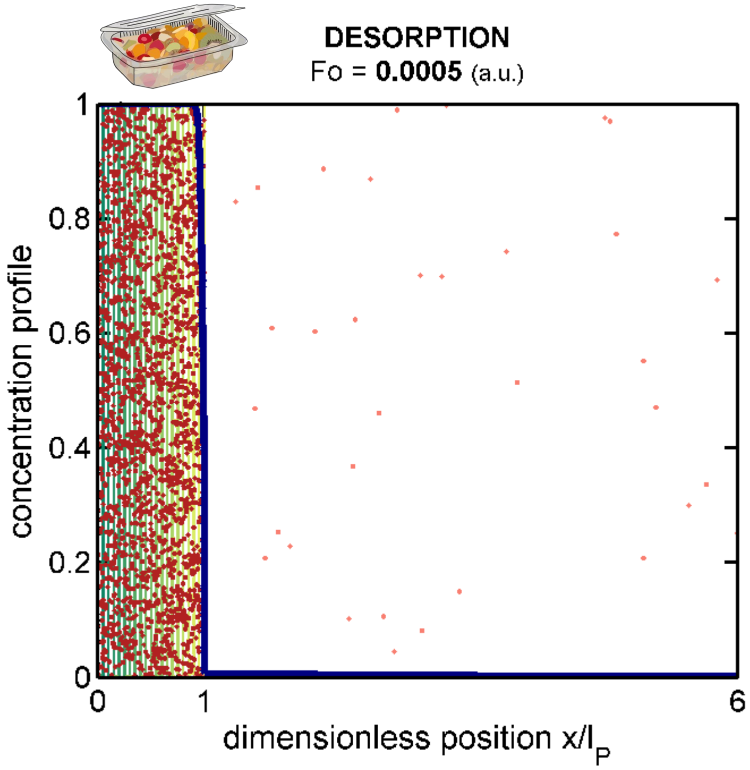
Mass transfer of substance i is governed by its diffusion coefficient $D_{i,P}$ and its partition coefficient between F and P, $K_{i,F/P}$.



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



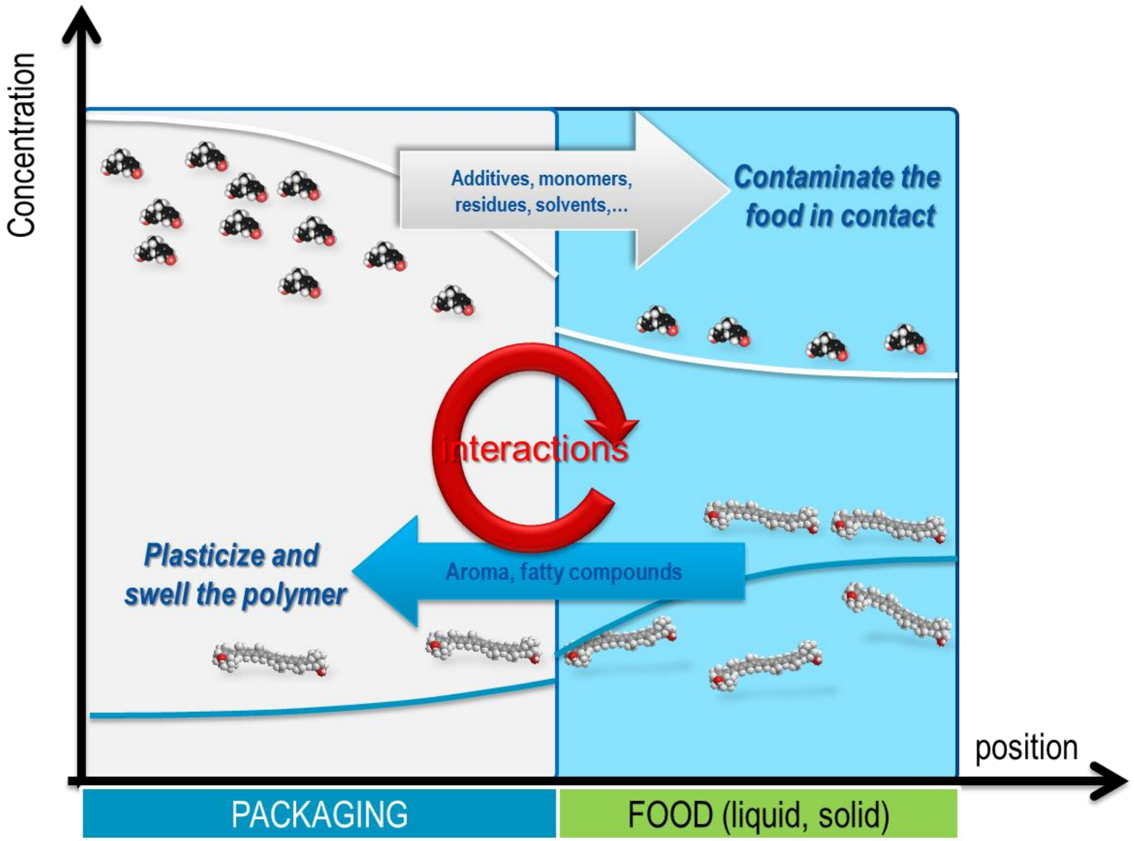


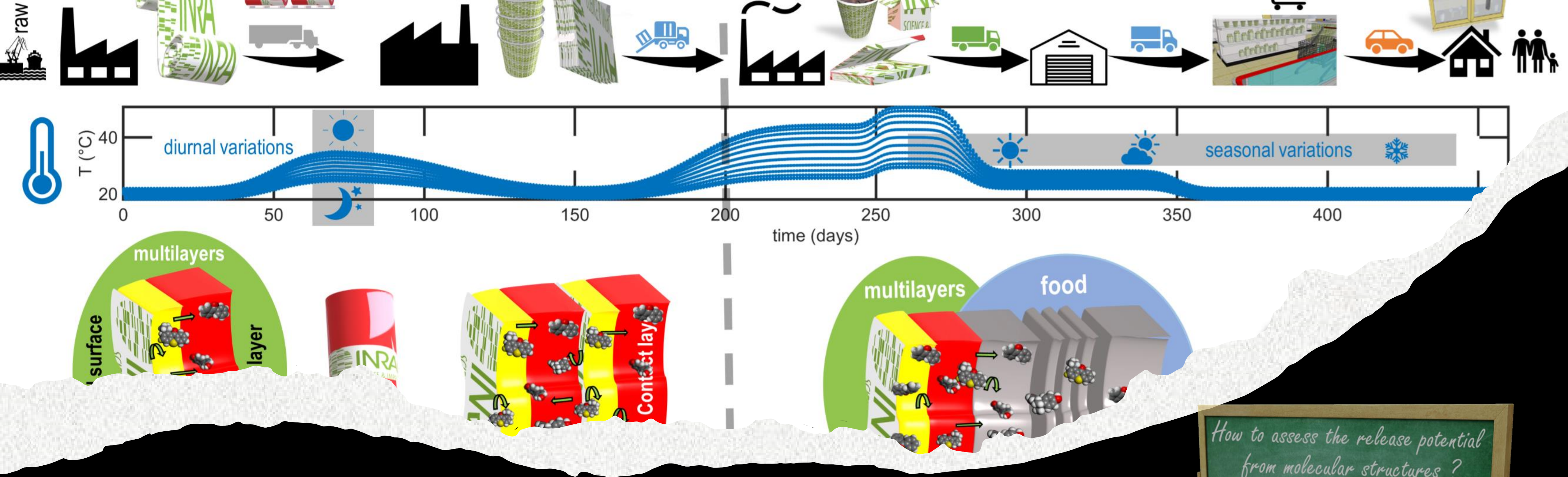


$$K_{i,F/P} = \frac{C_{i,F}^{eq}}{C_{i,P}^{eq}} = \frac{1}{1 - crystallinity} \frac{\gamma^{v}_{i,P_{amorphous}}}{\gamma^{v}_{i,F}}$$

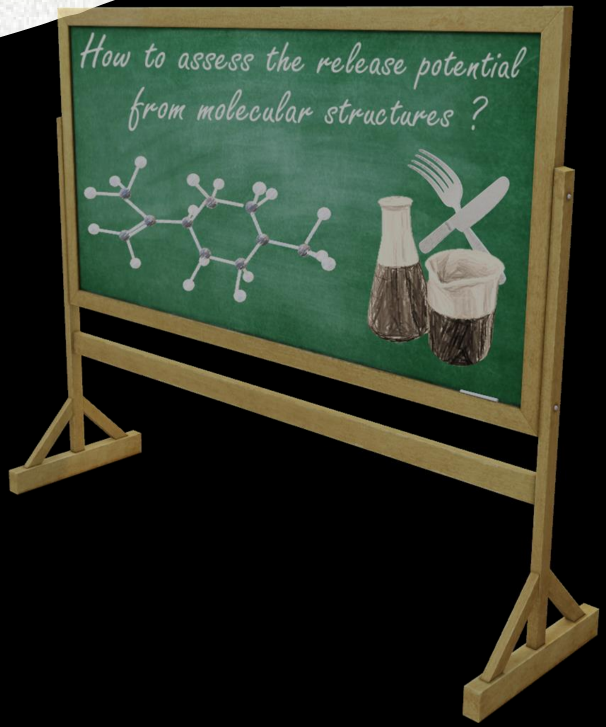
Analogy with packaged food products

Some products may be « agressive » 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

1990

EPA 560/5-85-015
September 1990

METHODS FOR ASSESSING EXPOSURE
TO CHEMICAL SUBSTANCES

Volume 11

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

by

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EPA Contract No. 68-D9-0166

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U.S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDES AND TOXIC SUBSTANCES
WASHINGTON, D.C. 20460

https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P100BCMB.TXT

Europe guidance

2015

European Commission

JRC TECHNICAL REPORTS

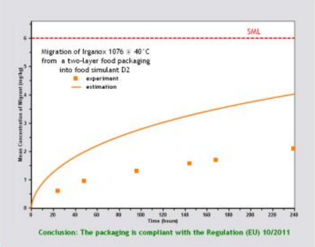
Practical guidelines on the application of migration modelling for the estimation of specific migration

In support of Regulation (EU) No 10/2011 on plastic food contact materials

Eddo J. Hoekstra (Ed.), Rainer Brandsch, Claude Dequatre, Peter Mercea, Maria-Rosaria Milana, Angela Störmer, Xenia Trier, Olivier Vitrac, Annette Schäfer and Catherine Simoneau

2015

$$\frac{C_i^{n+1}-C_i^n}{\Delta t}=D\frac{C_{i+1}^n-2C_i^n+C_{i-1}^n}{h^2}$$



Joint Research Centre

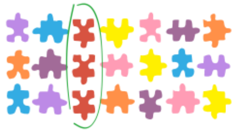
EUR 27529 EN

http://publications.jrc.ec.europa.eu/repository/handle/JRC98028

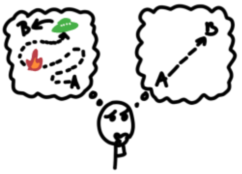
The five principles of migration modeling

- *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.

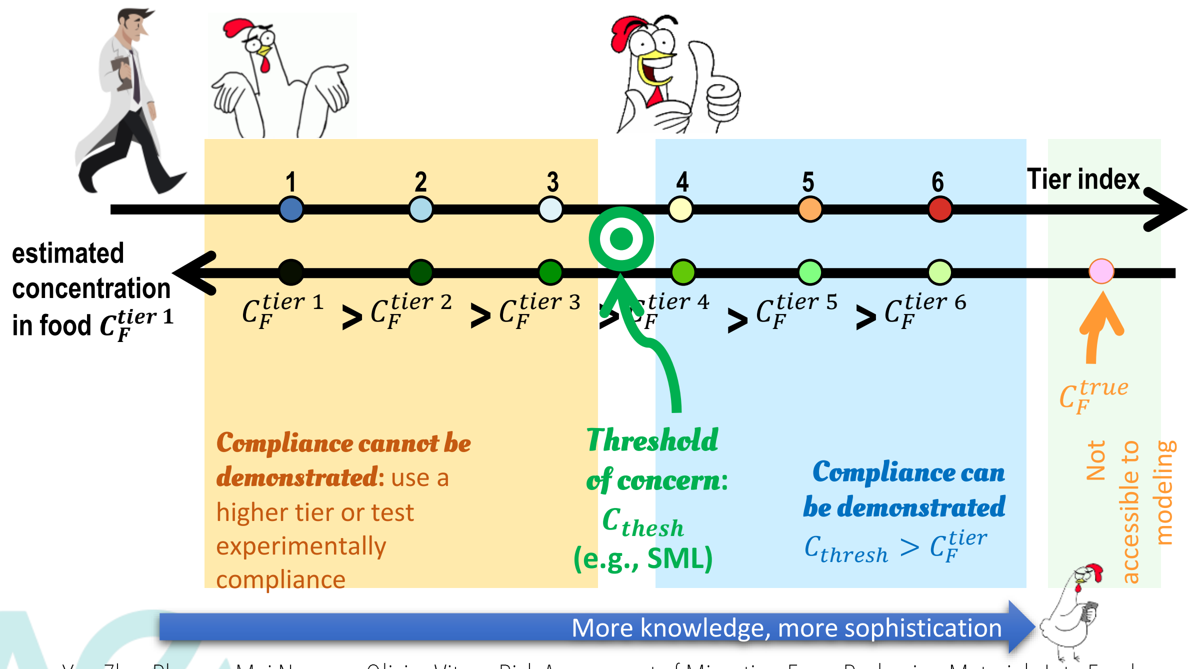
- *The fifth and final principle* ("**proportionality**") is that non-compliance cannot be demonstrated by calculation.

Parsimony vs. sophistication

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

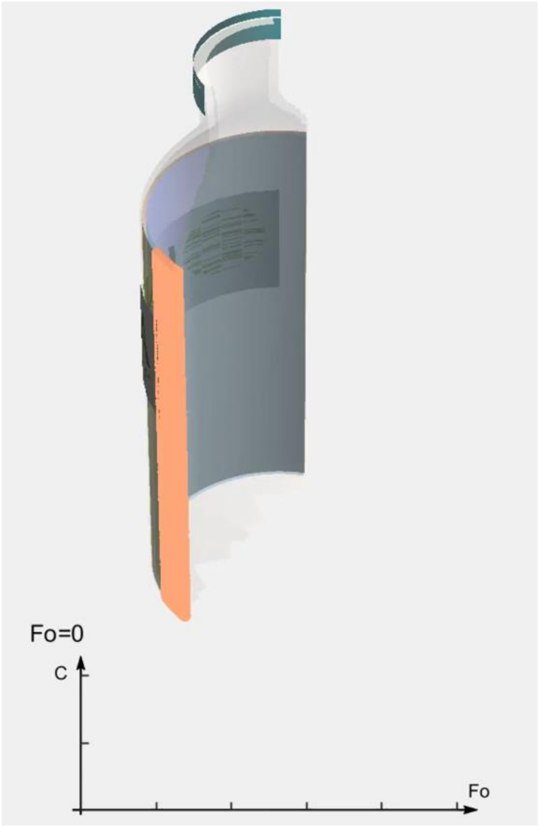
What is the goal?

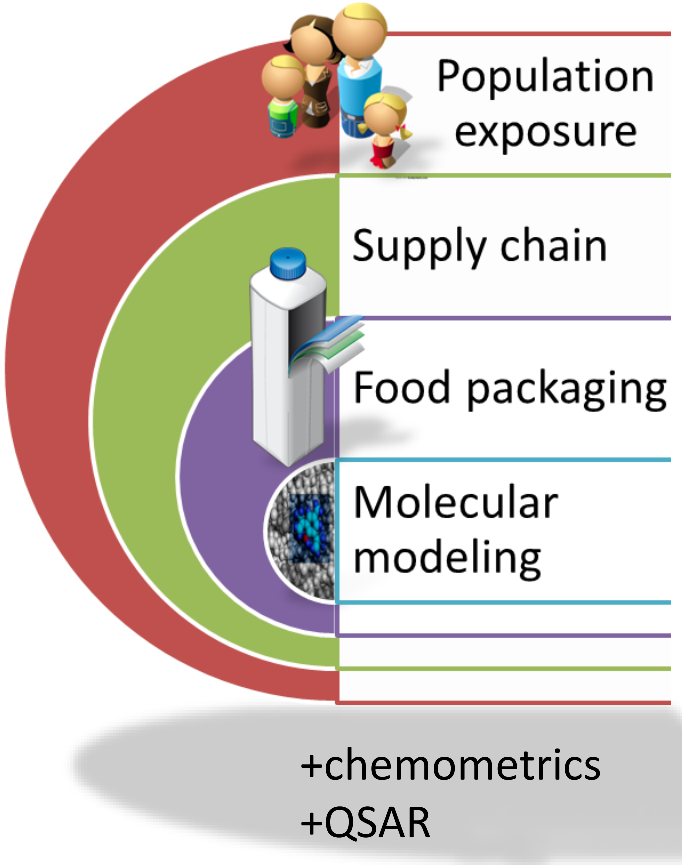
The art of migration modeling consists in building a sequence of scenarios so that the last scenario provides a value lower than the threshold of concern while being large than the real concentration (unknown).



Yan Zhu, Phuong-Mai Nguyen, Olivier Vitrac, Risk Assessment of Migration From Packaging Materials Into Food, Reference Module in Food Science, Elsevier, 2019, https://doi.org/10.1016/B978-0-08-100596-5.22501-8.

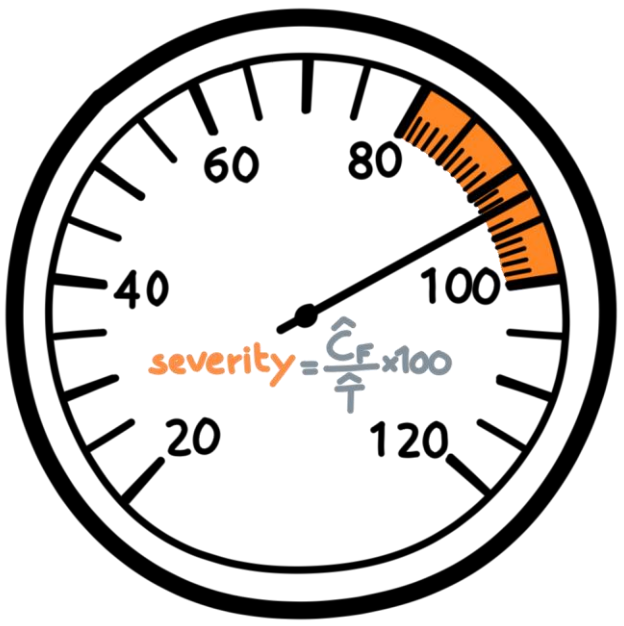
Multiscale modeling

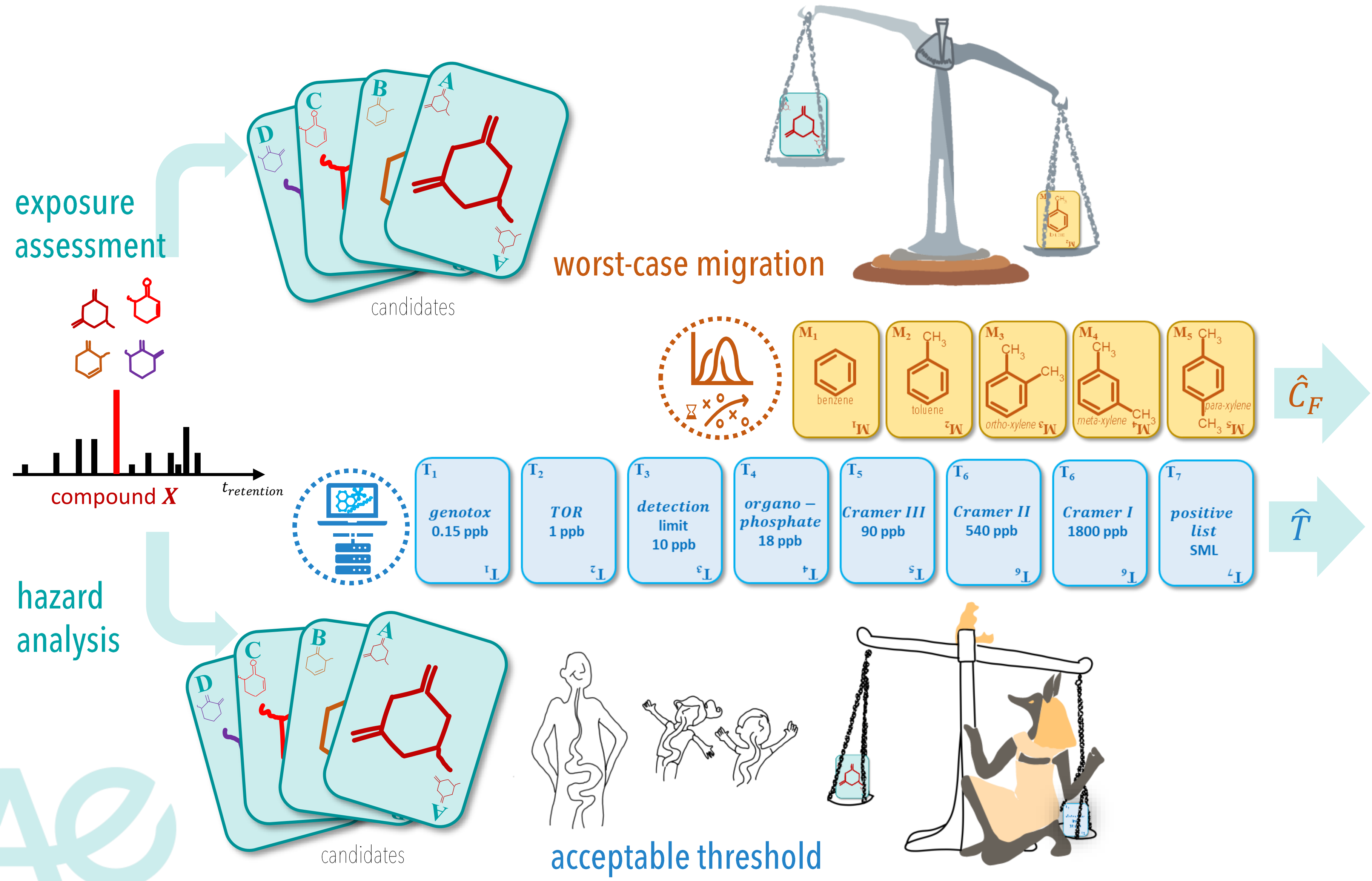




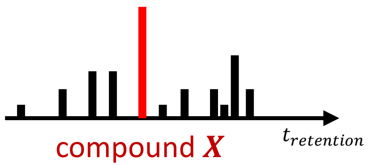
The challenge of uncertainty

Propagating uncertainty with the risk that no decision can be reached





$$Severity(X) = 100 \times \max\left(\frac{\widehat{C_F^A}}{\widehat{T_A}}, \frac{\widehat{C_F^B}}{\widehat{T_B}}, \frac{\widehat{C_F^C}}{\widehat{T_C}}, \frac{\widehat{C_F^D}}{\widehat{T_D}}\right)$$

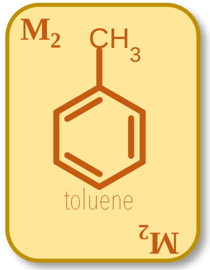


all compounds

EXAMPLE: Toluene as a generic surrogate

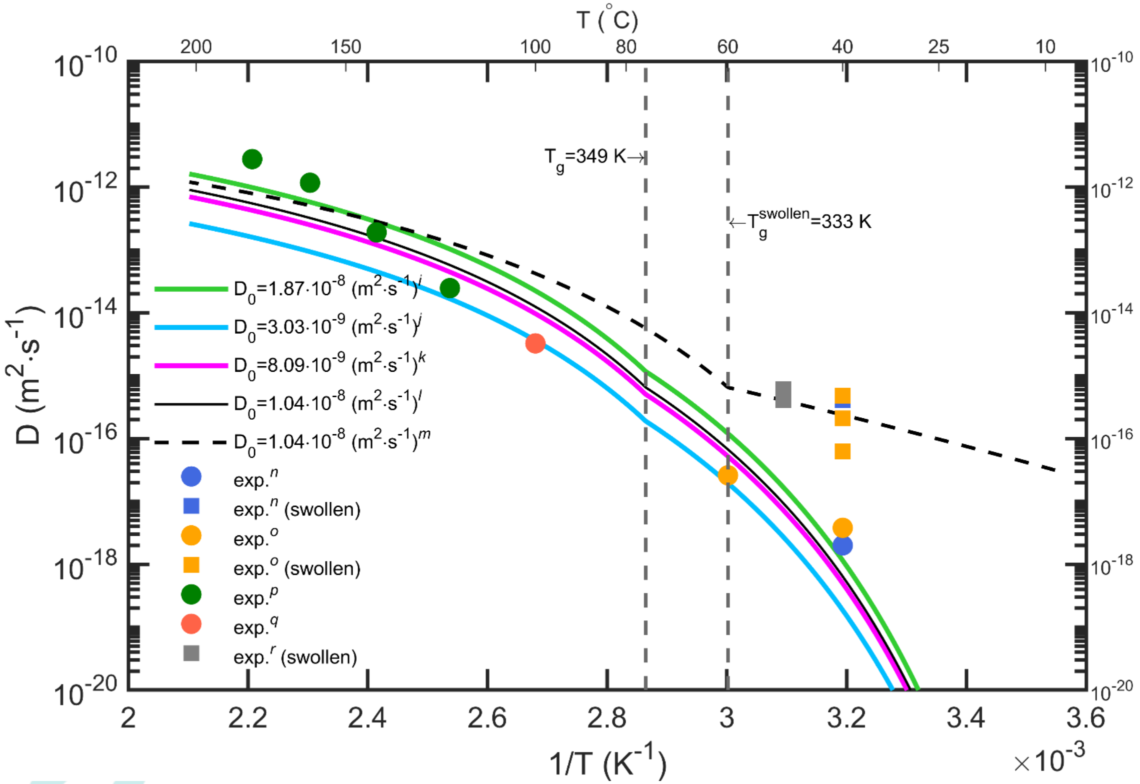
Diffusion coefficients of toluene can be predicted by free-volume theory in almost in any polymer (plasticized or not), at any temperature – *other surrogates are also available*

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



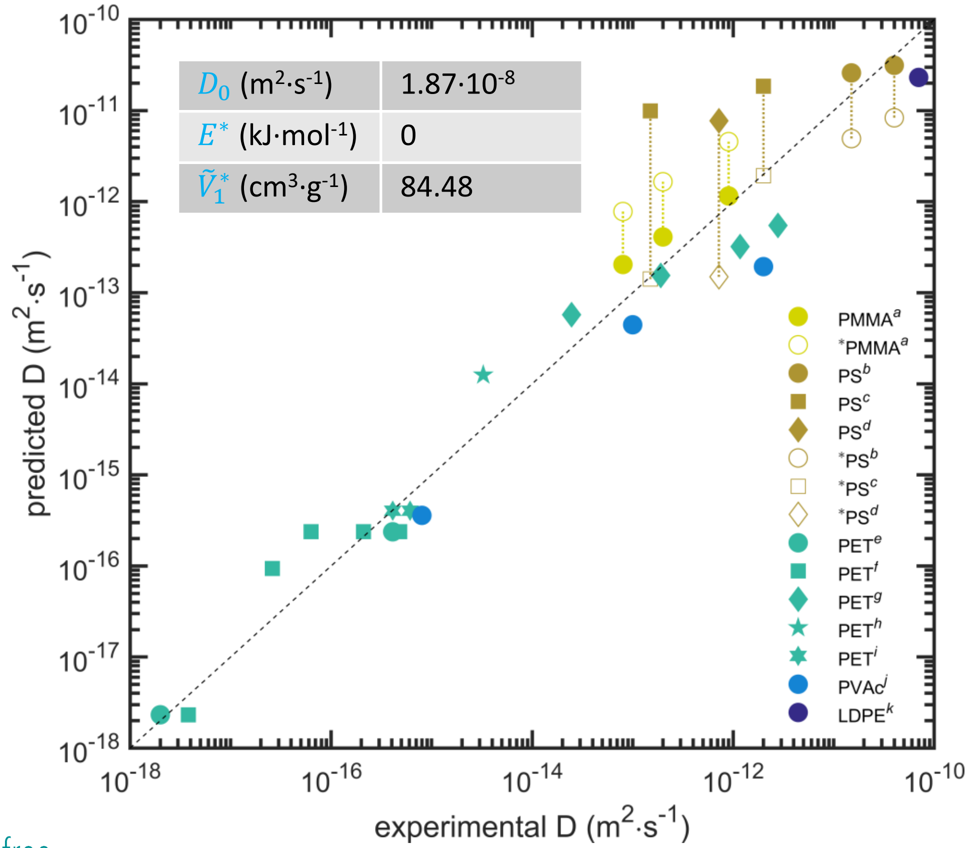
Diffusivitity of tolune in PET

Effects of T, plasticizing, subcooling



Diffusivities of toluene in 6 polymers

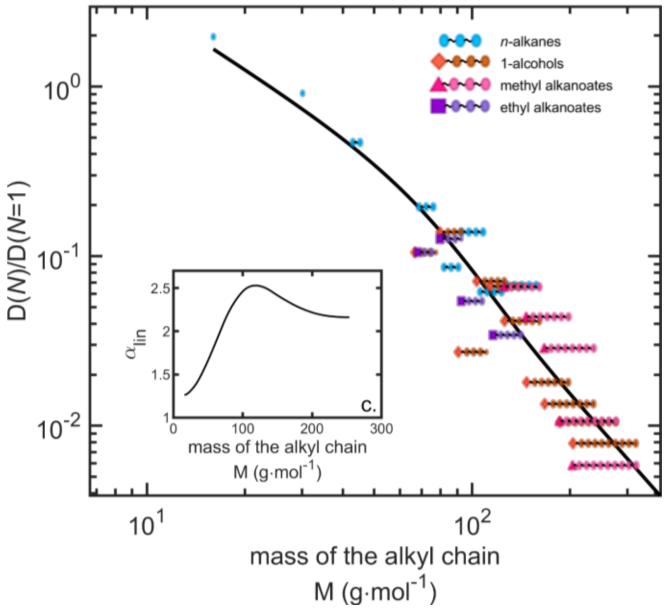
Predicted vs calculated



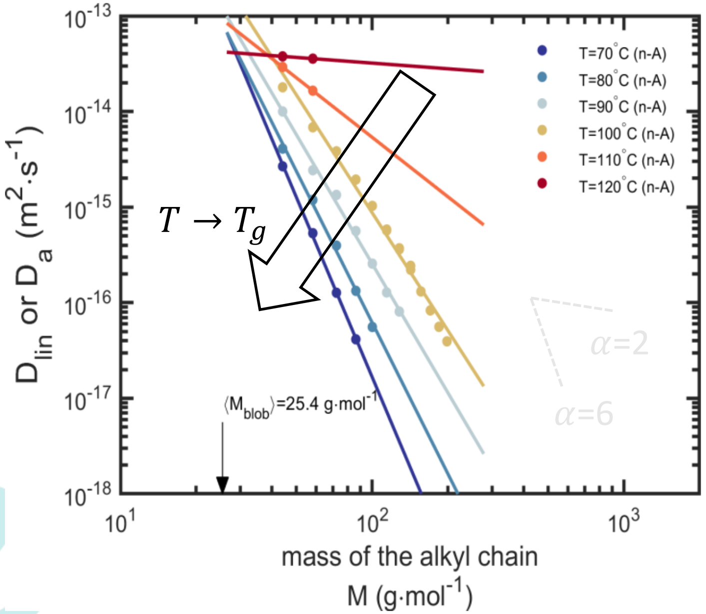
Zhu, Y., Welle, F., et Vitrac, O. (2019). A blob model to parameterize polymer hole free volumes and solute diffusion. *Soft Matter, 2019, 15, 8912-8932*

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

HDPE



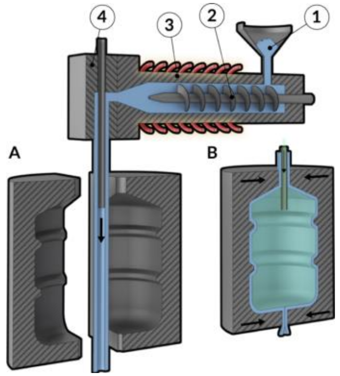
PET

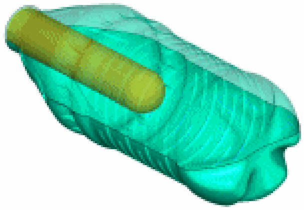


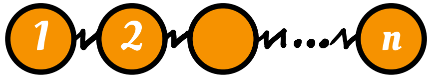
$$\frac{D_{lin}(M,T)}{D_{lin}(M_{blob},T)} \propto \left(\frac{M}{M_{blob}}\right)^{-\alpha_{lin}(T,T_g)}$$

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

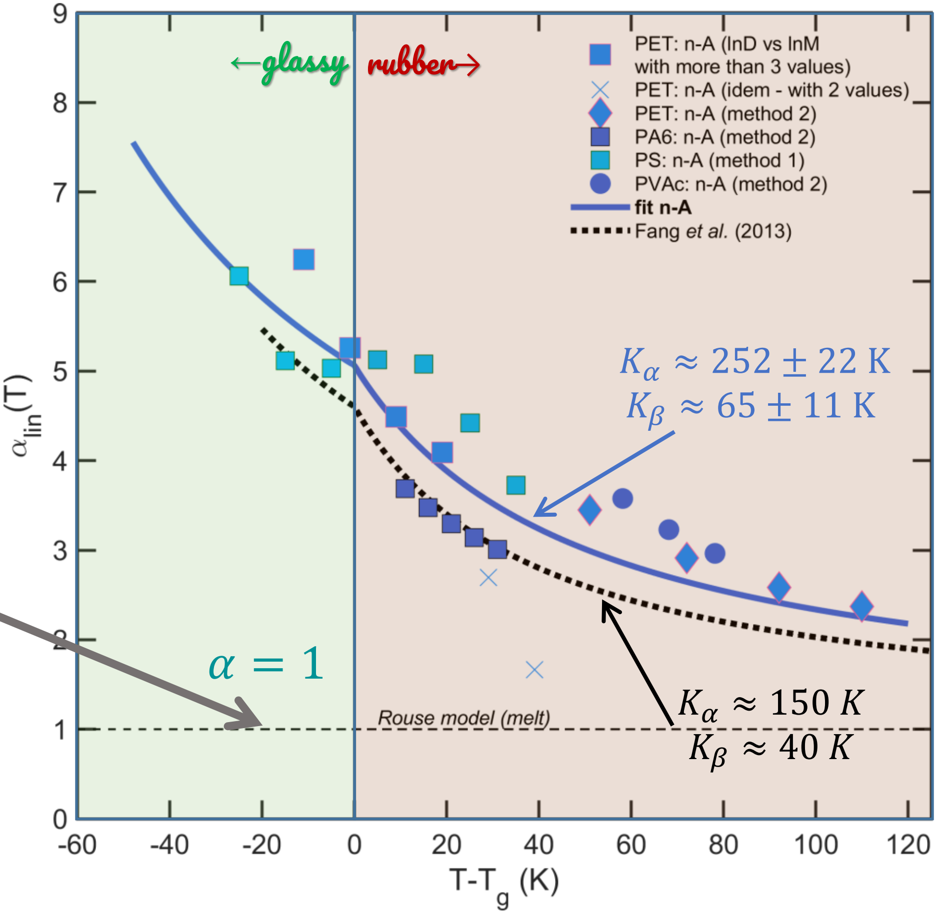
$$with\ r = \begin{cases} 1 & when\ T \geq T_g \\ \frac{\alpha_g}{\alpha_c} & T < T_g \end{cases}$$





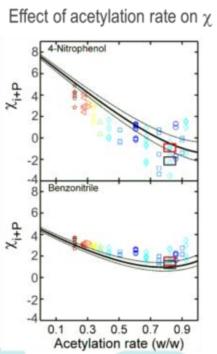


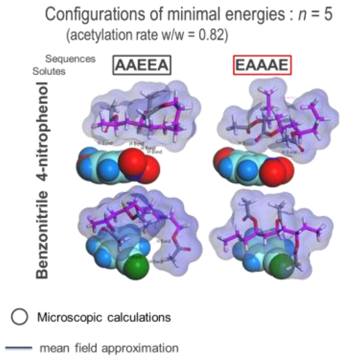
$M = n \cdot M_{blob}$

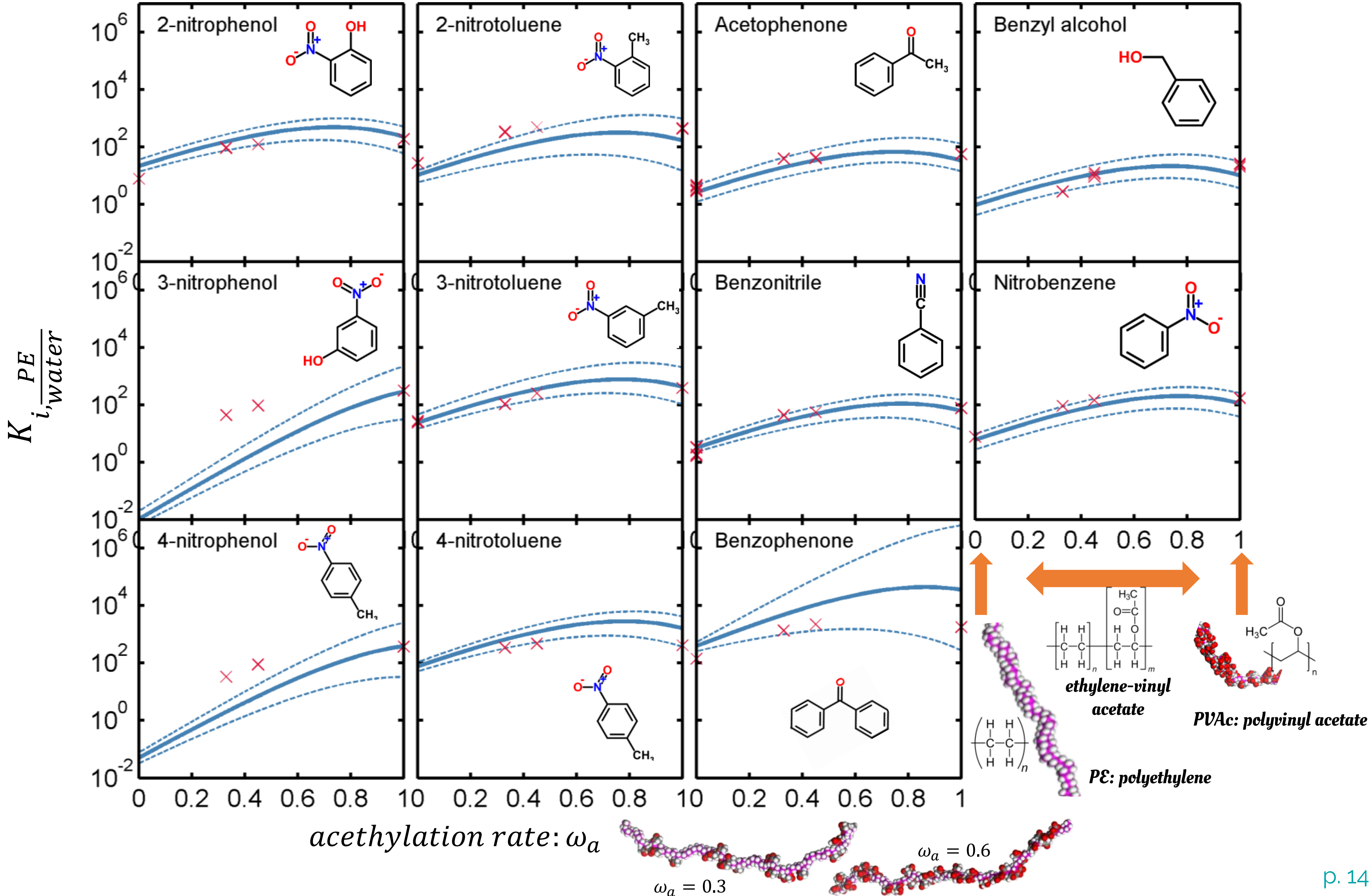


Zhu et al. Soft Matter, 2019, 15, 8912-8932
Fang, et al. . Macromolecules, 2013, 46(3), 874-888.

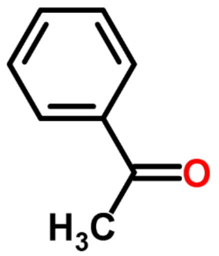
Partition coefficients water-EVA for polar surrogates







PARTITION COEFFICIENTS WITH AIR

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>> FMECAKairP acetophenone
LOAD_CHEMSPIDER    extraction of ChemSpiderID=7132 ('acetophenone') completed in 10.26 s
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       7132.mat      21-sept.-2015 21:37:19       77.6 kBytes    C:\Data\Olivier\INRA\Codes\MS\cache.ChemSpider
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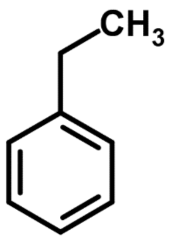


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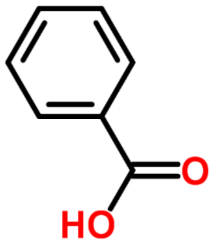


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CHEMSPIDER reuses cached data for 'benzoic acid' (date=21-sept.-2015 21:45:01)
ans =
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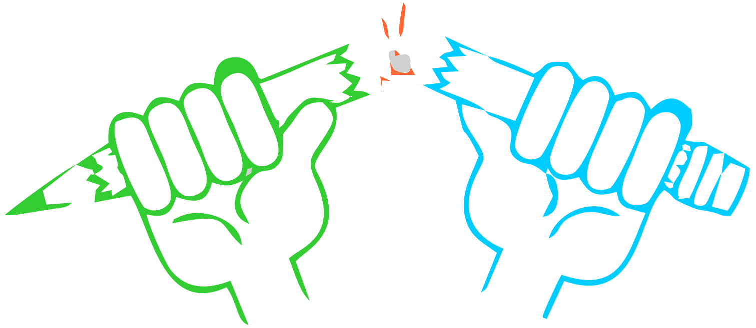
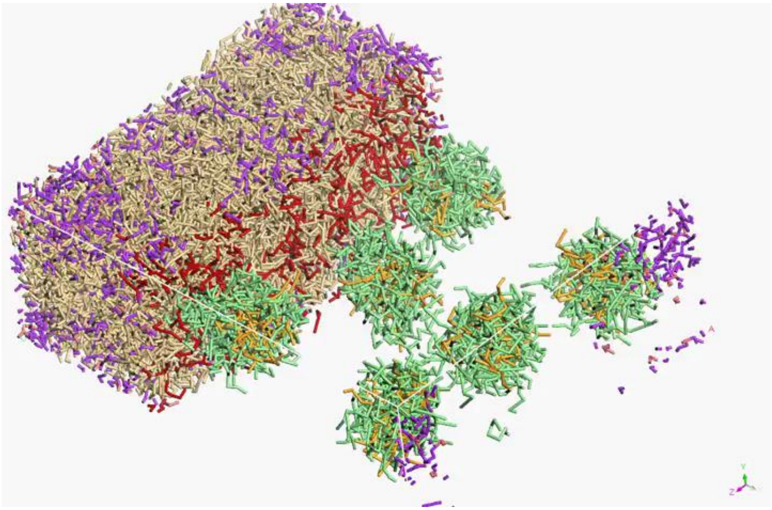
Food Additives and Contaminants 2017, 34 (10), 1703-1720
https://github.com/ovitrac/FMECAengine

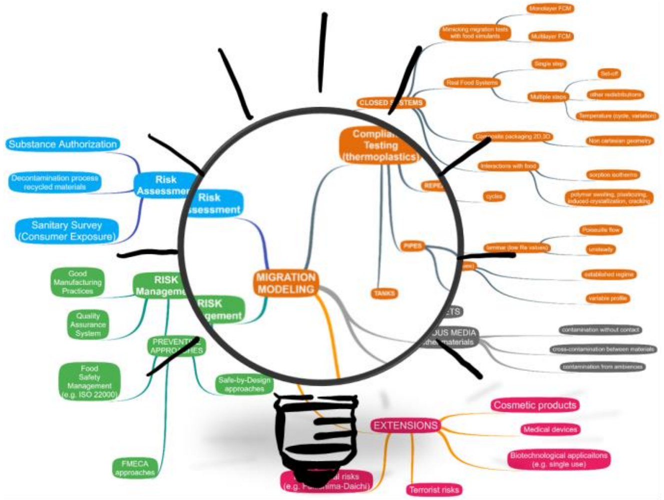
NEW CONTAMINATION ROUTES



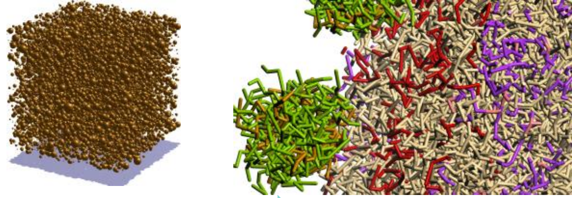
without contact

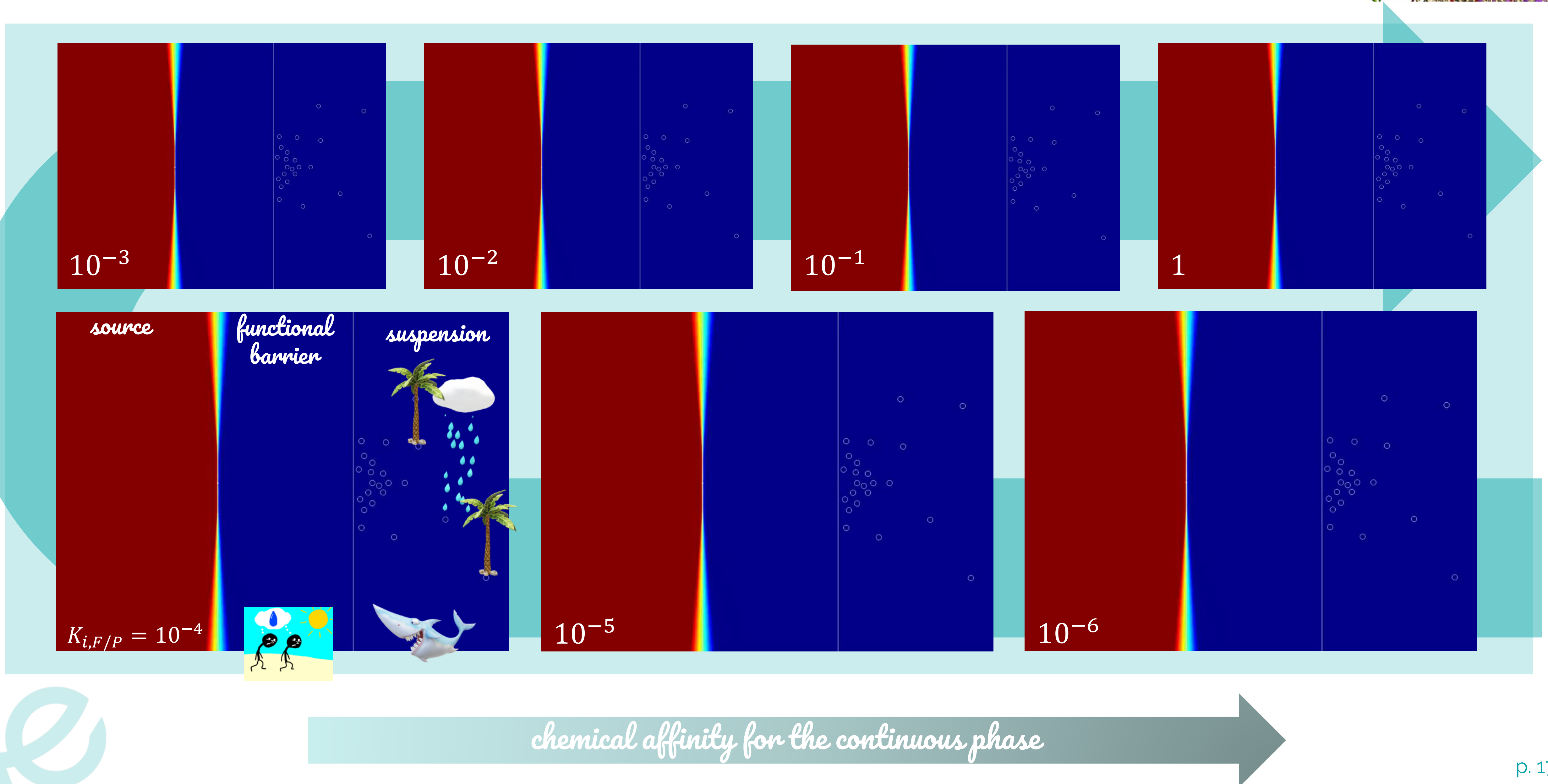


with more than two phases



Transfer with more than two phases

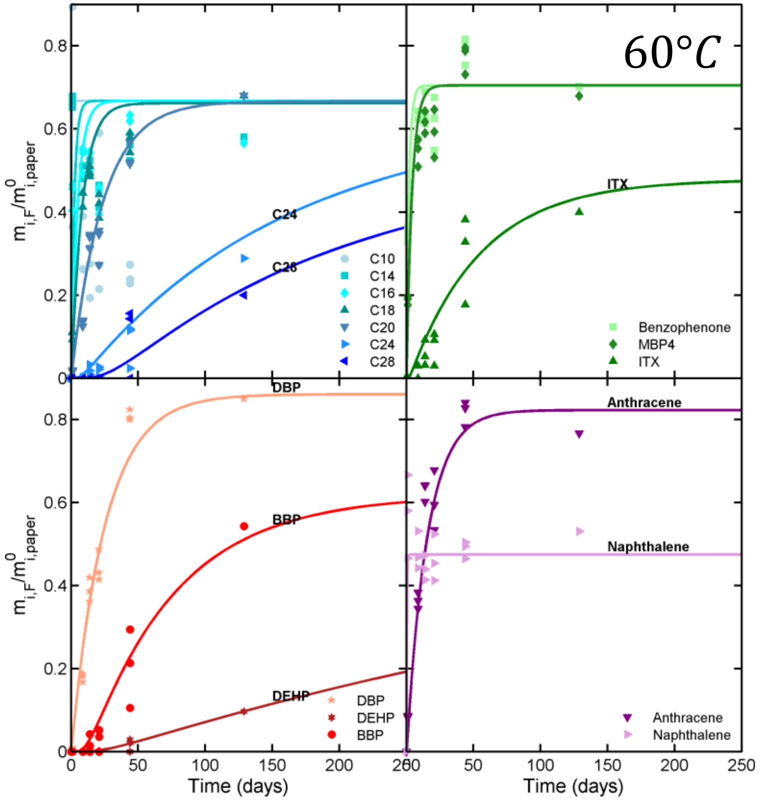




CONTAMINATION THROUGH THE GAS PHASE

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



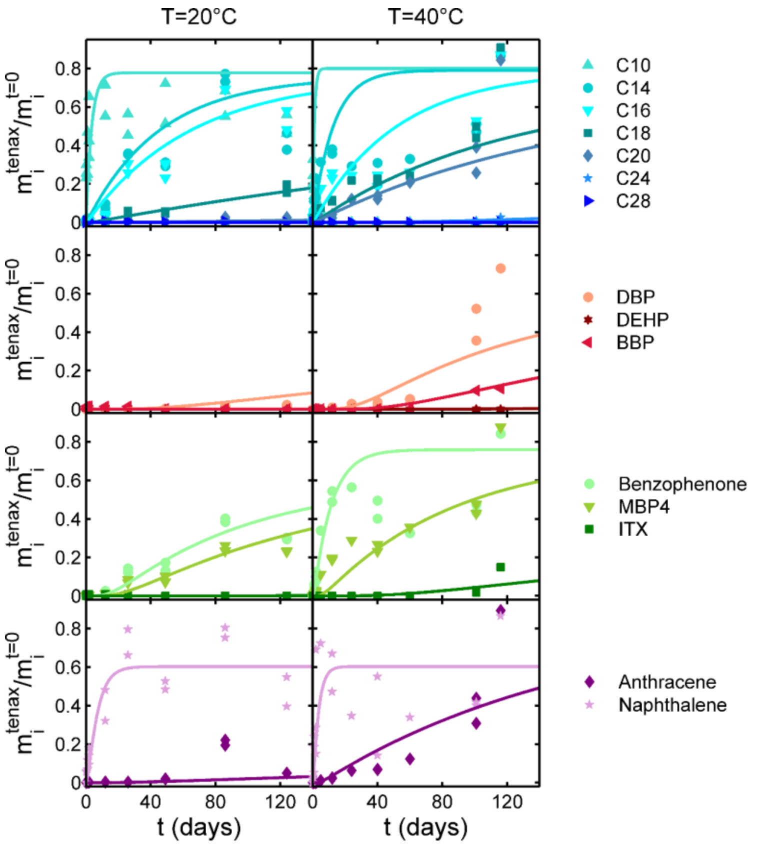
$$\frac{m_{i,F}^{(t)}}{m_{i,P}^{0}} = \frac{V_F}{m_{i,P}^{0}} \int_0^t C_{i,F}^{(t)}\, d\tau$$

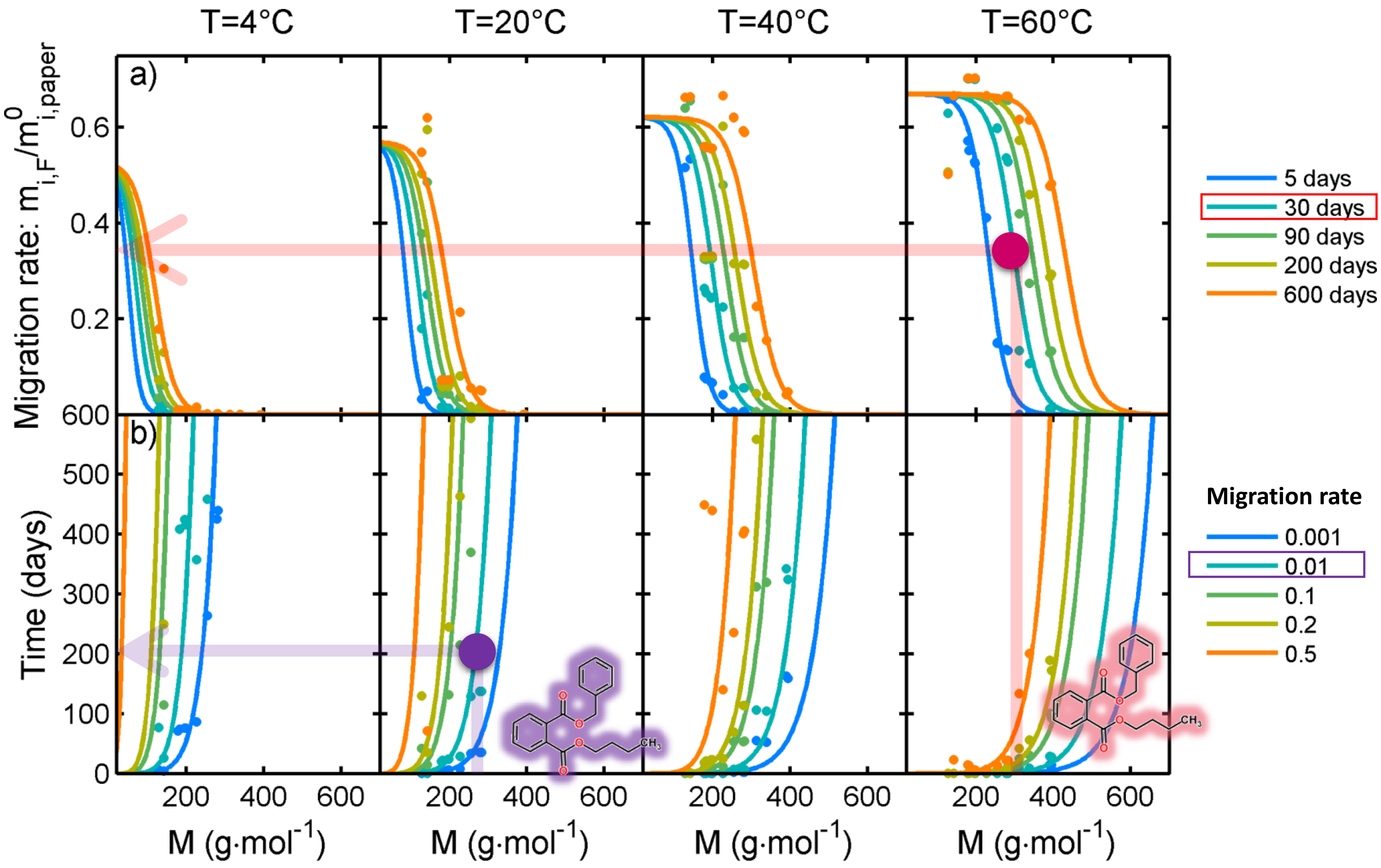
Experimental results at 60°C, *i*=1…15 → **Detailed modeling** with FMECAengine → $\widehat{C_F}(T,t,i)$ *i* = 1..15 solutes at any temperature → **Simplified modeling** Solute independent → $\widetilde{C_F}(T,t,M)$ simplified at any temperature

Nguyen et al. Food Additives and Contaminants. 2017;34:1703-20.

CONTAMINATION THROUGH THE GAS PHASE

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

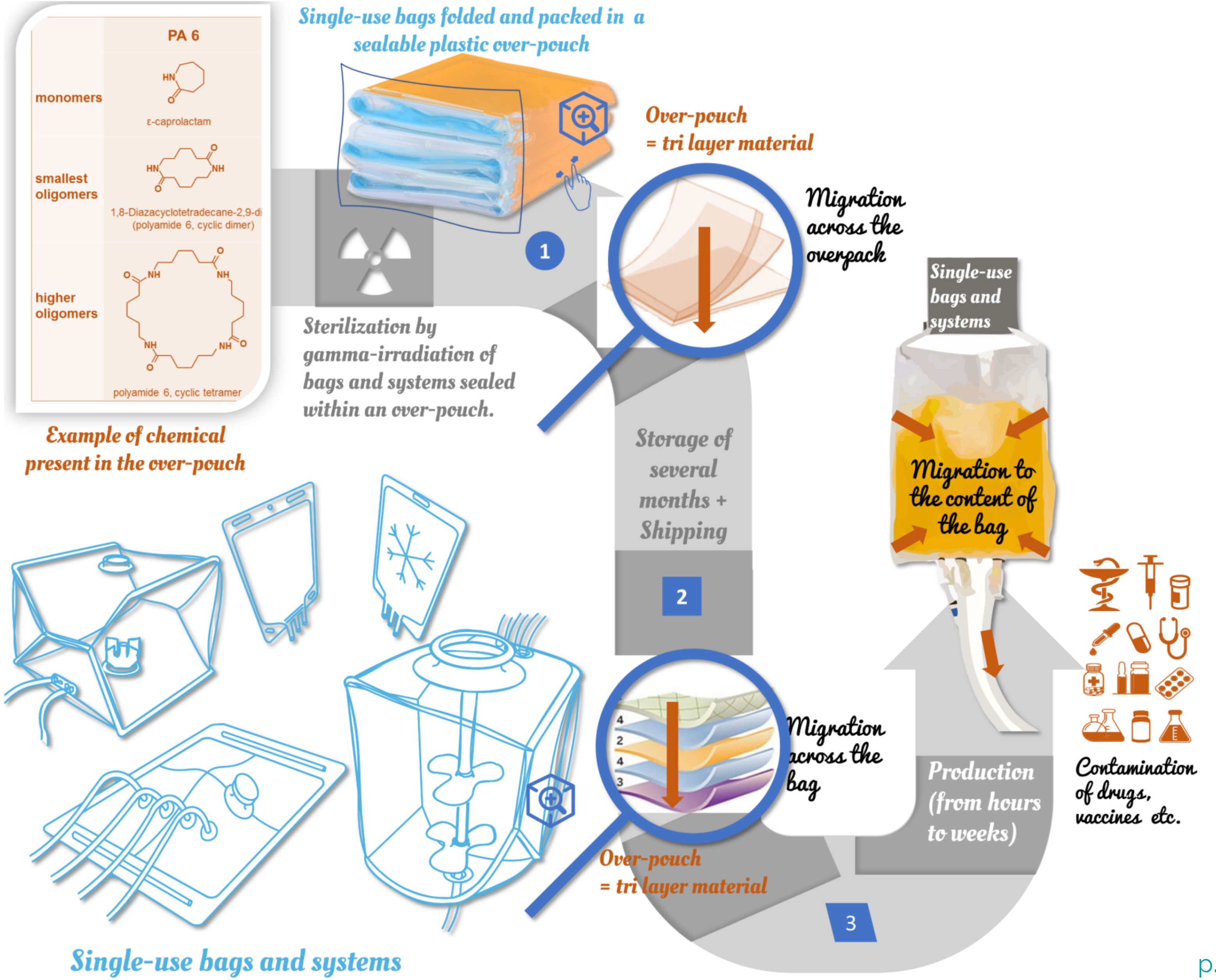




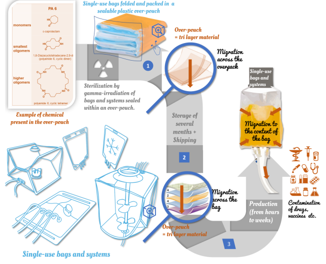
UBIQUITOUS CROSS-CONTAMINATION IN SINGLE-USE APPLICATIONS

Five key steps

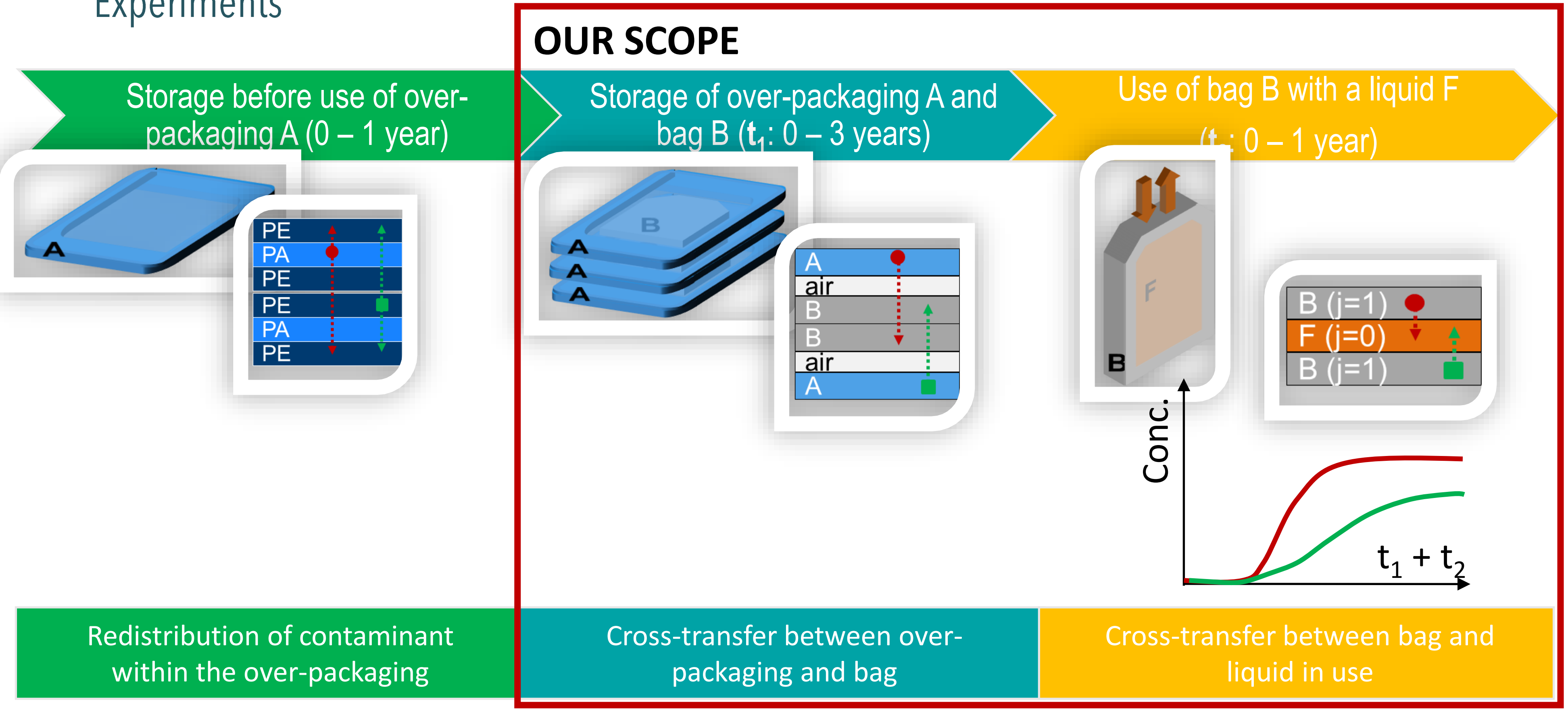
1) Overpouch containing monomers (e.g. from PA6)
2) Storage for several months before shipping
3) Mass-transfer across the bags (folded or not)
4) Migration in the culture medium
5) Ubiquitous contamination of lots



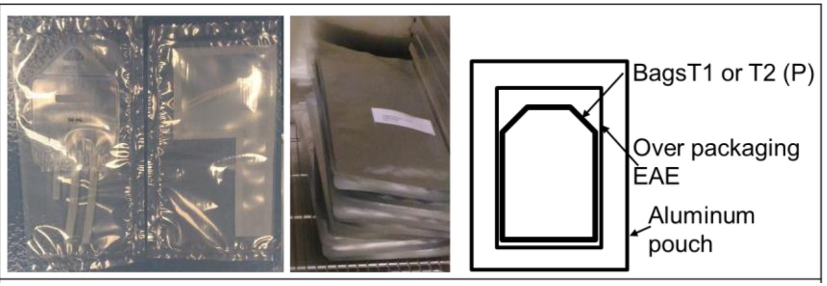
UBIQUITOUS CROSS-CONTAMINATION IN SINGLE-USE APPLICATIONS



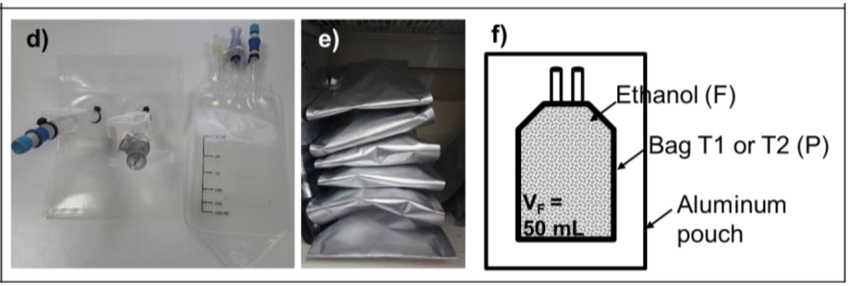
Experiments



STEP 1 STUDY “LOADING”

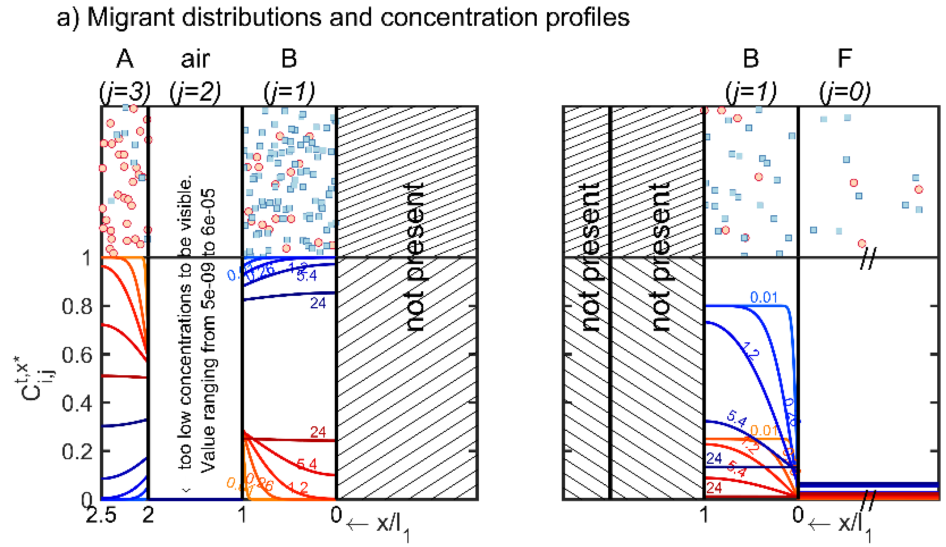


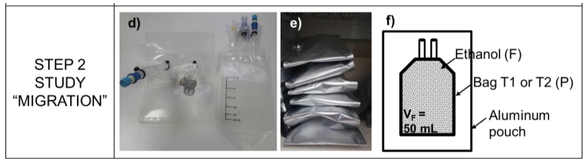
STEP 2 STUDY “MIGRATION”

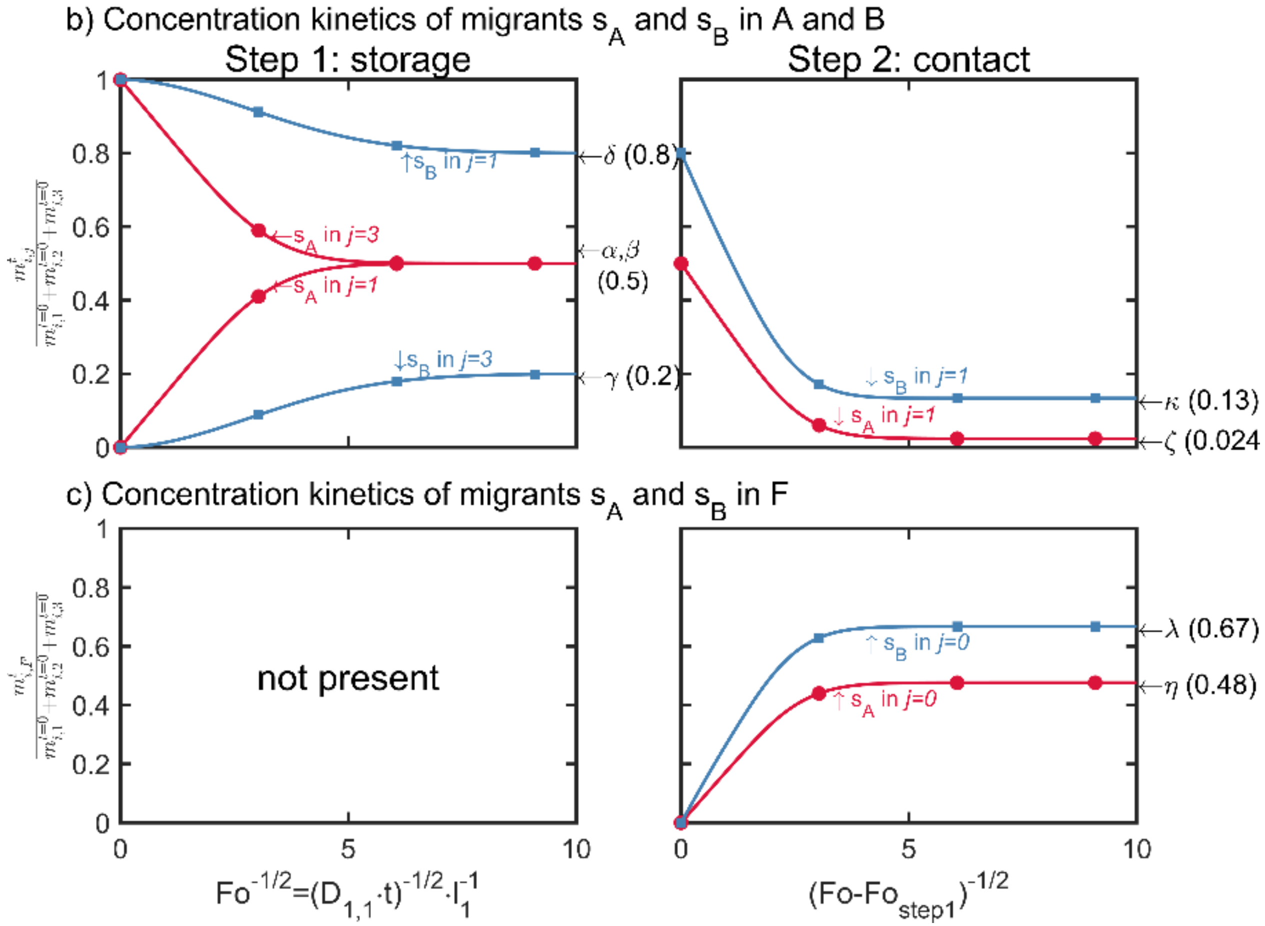


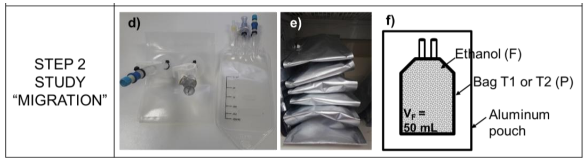
UBIQUITOUS CROSS-CONTAMINATION IN SINGLE-USE APPLICATIONS

Modeling





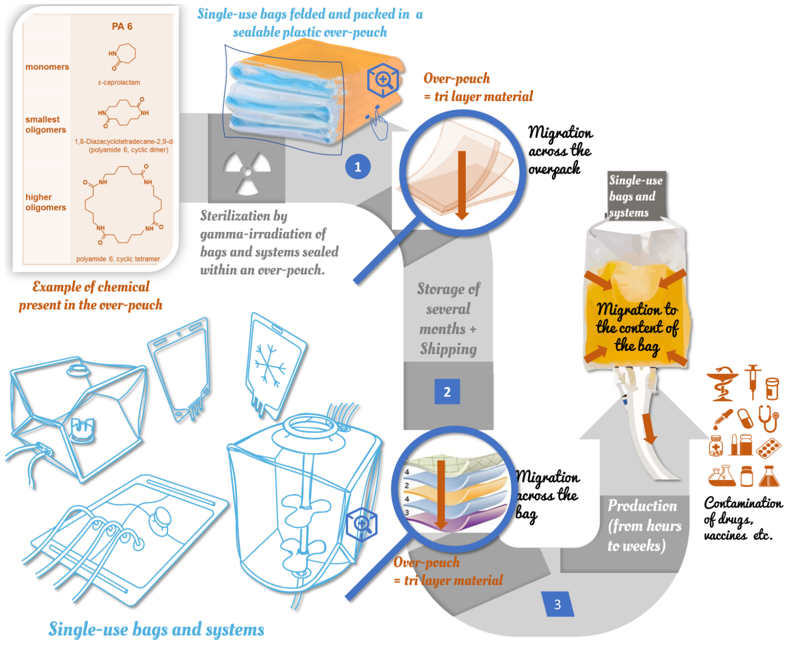


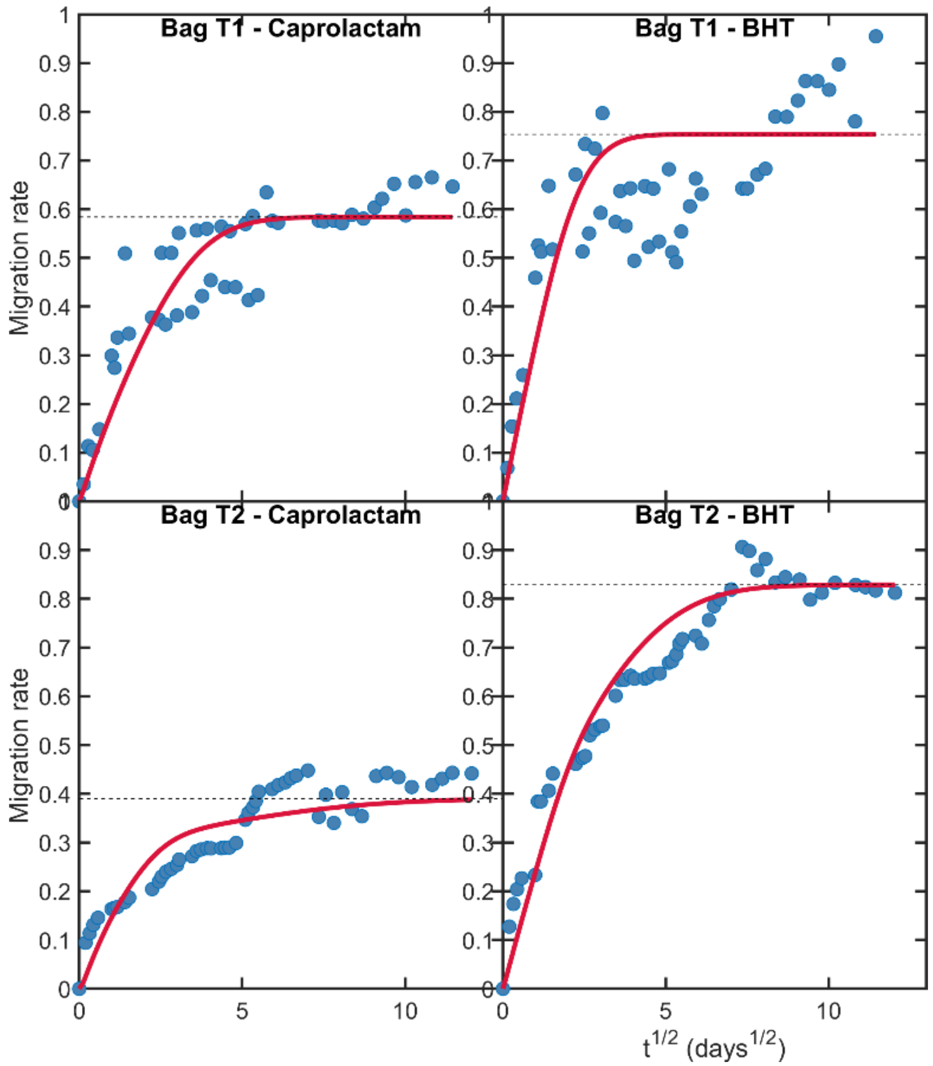


COMPARISON BETWEEN PREDICTION AND EXPERIMENTS

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.



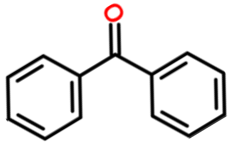


Nguyen P-M, Dorey S, Vitrac O. The Ubiquitous Issue of Cross-Mass Transfer: Applications to Single-Use Systems. *Molecules. 2019;24:3467.*

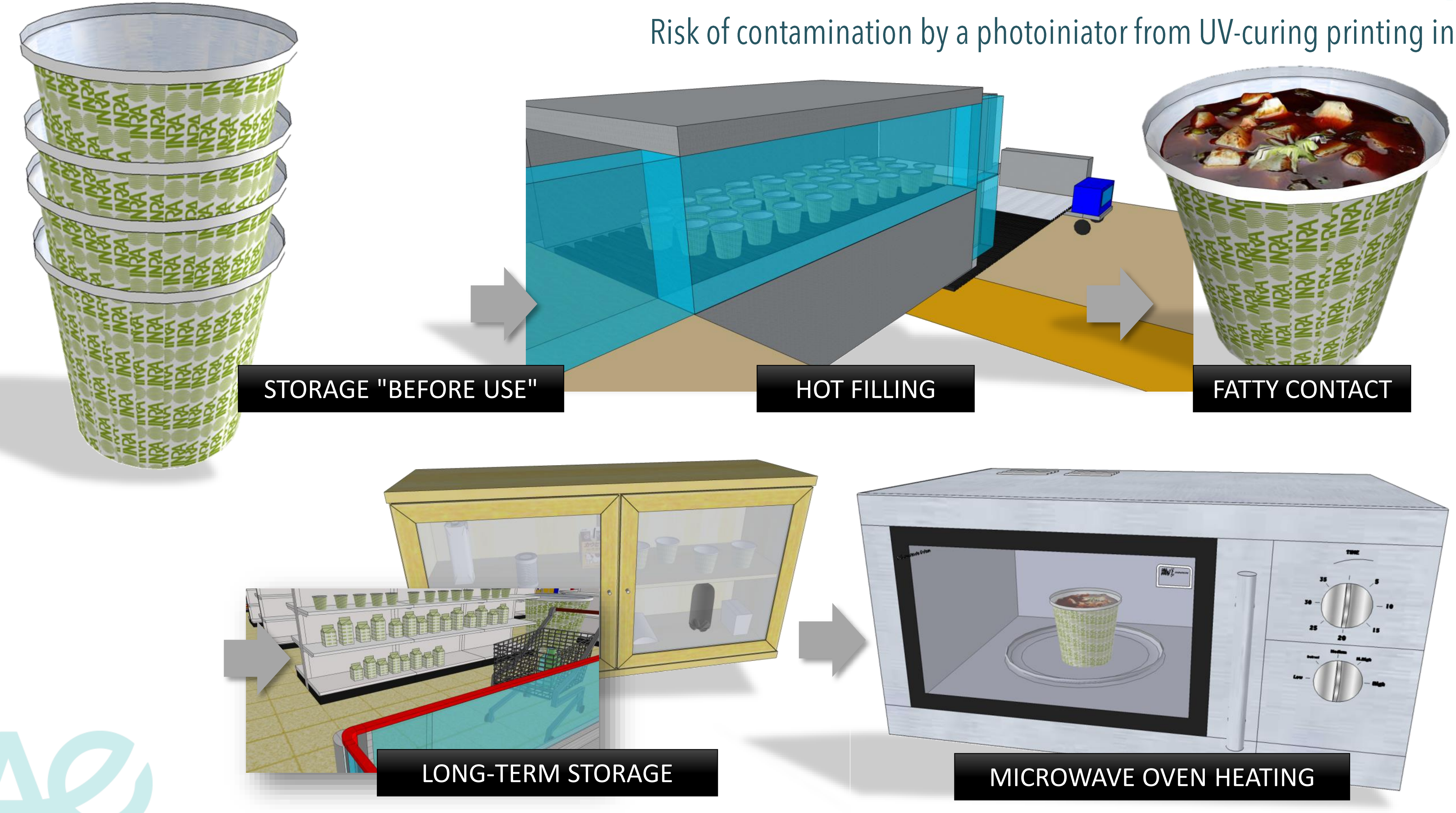
Preventive Approaches

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

CHAINED STEPS: where is the critical step?



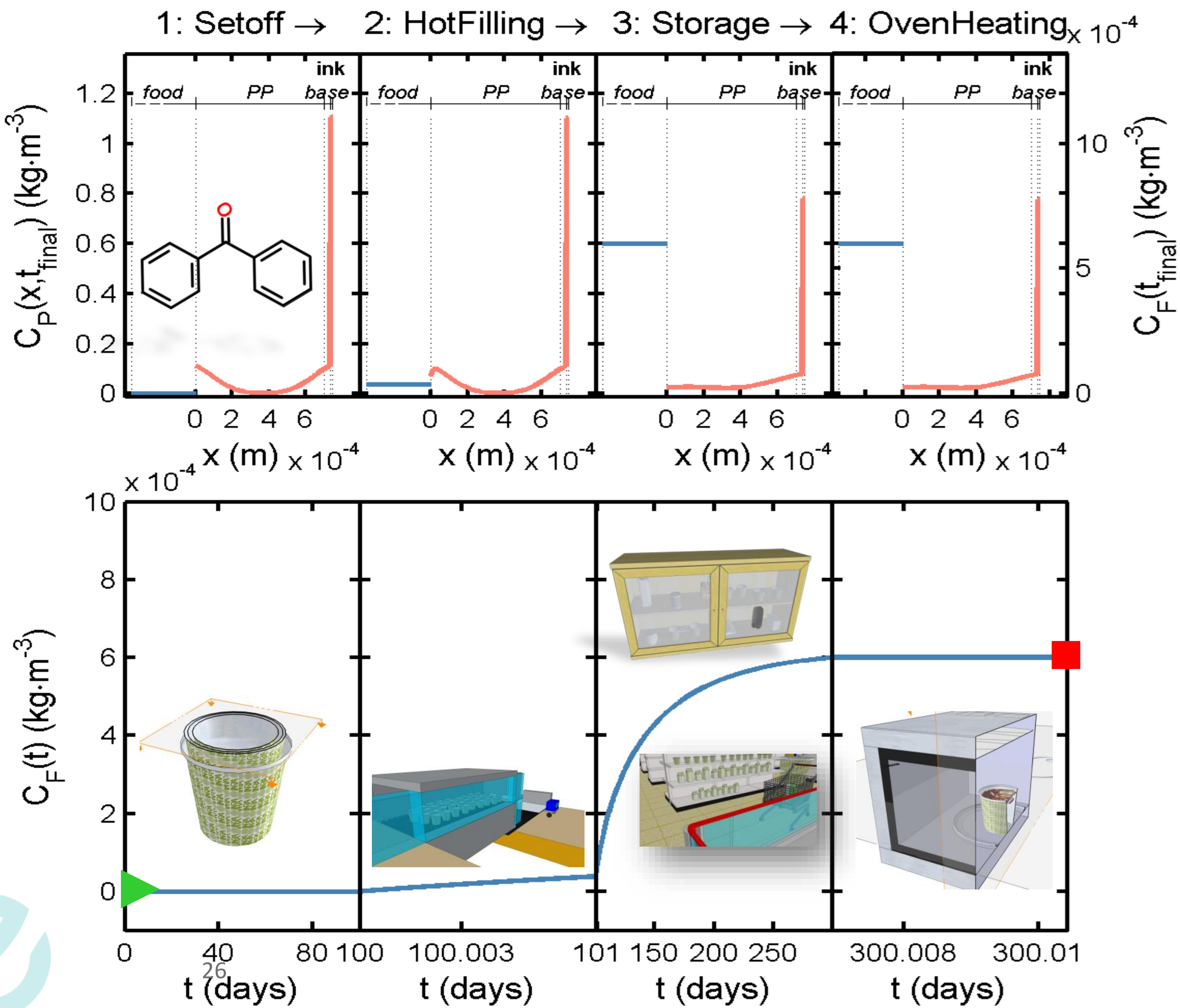
Risk of contamination by a photoiniator from UV-curing printing ink

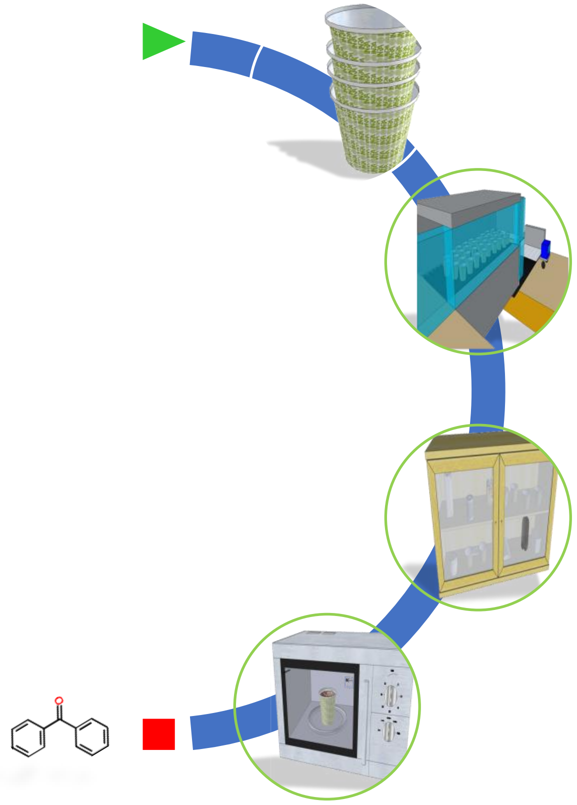


Nguyen, P.-M., Goujon, A., Sauvegrain, P., et Vitrac, O. (2013). A Computer-Aided Methodology to Design Safe Food Packaging and Related Systems. AIChE Journal, 59(4), 1183-1212.

CHAINED STEPS

UV-curing printing ink

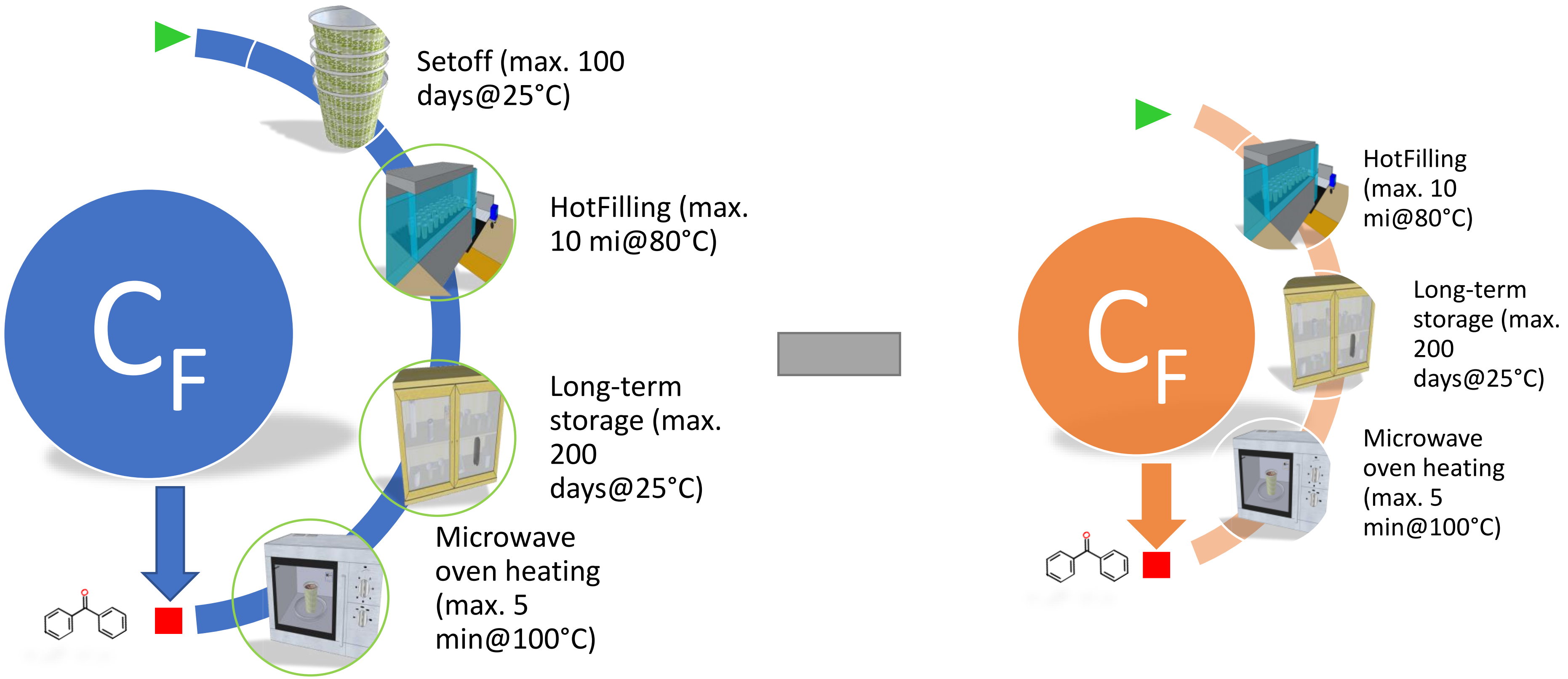




AIChE Journal, 59(4), 1183-1212

ASSESSING THE SEVERITY OF A SINGLE STEP

CASE OF "SETOFF" STEP



comparison with step i alone

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

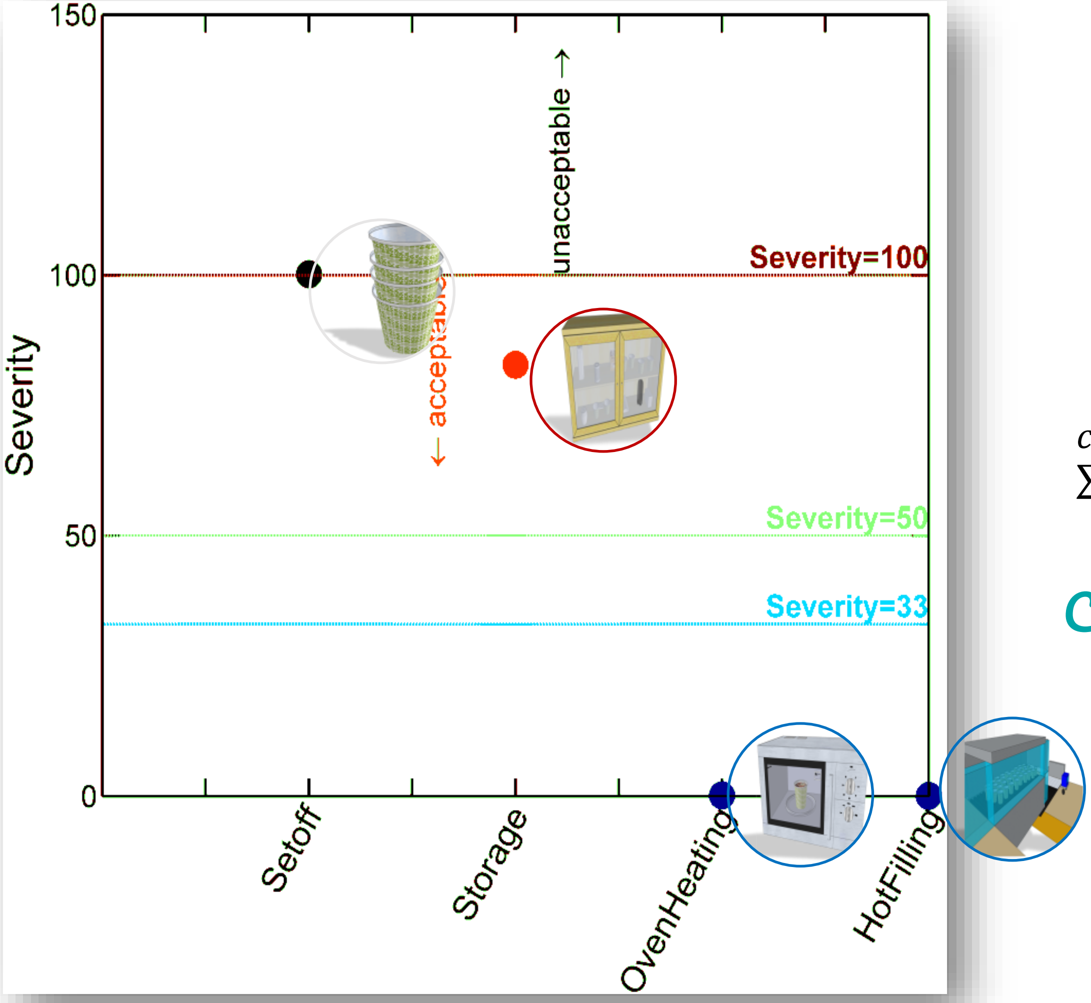
comparison with step i removed

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

AIChE Journal, 59(4), 1183-1212

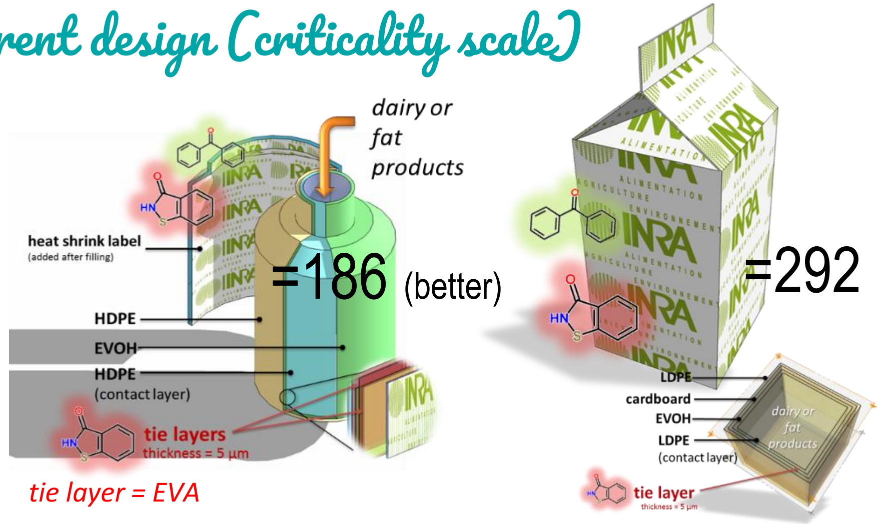
Critical step (severity scale)

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



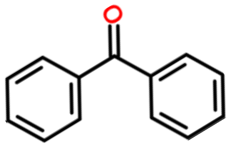
Unacceptable when $severity > 100$

Concurrent design (criticality scale)

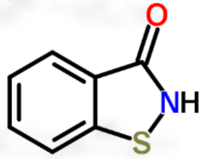


$$criticality = \sum_{all\ components} \sum_{all\ substances} \sum_{all\ modalities} pr(modality) \times severity$$

Critical substance



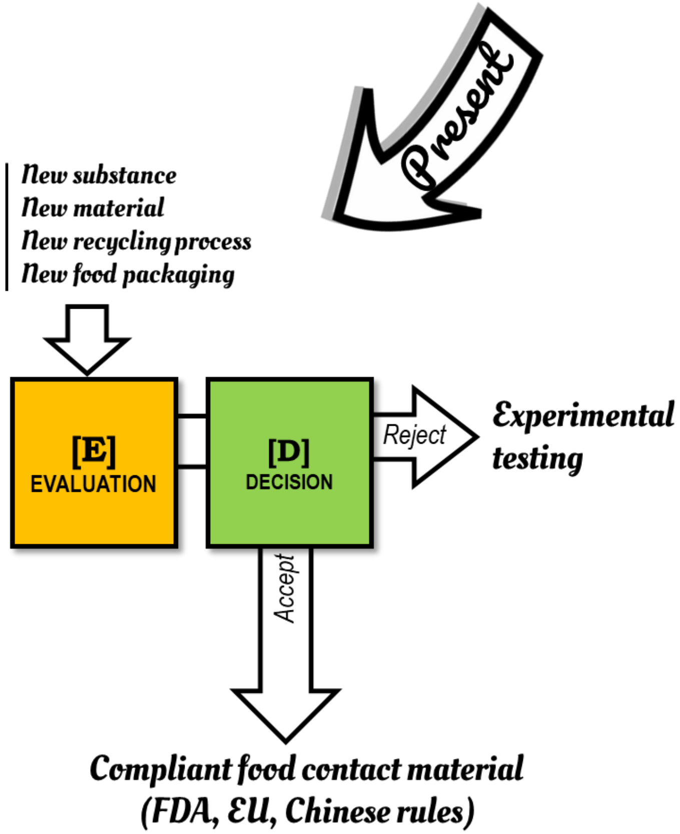
=115
(almost acceptable)

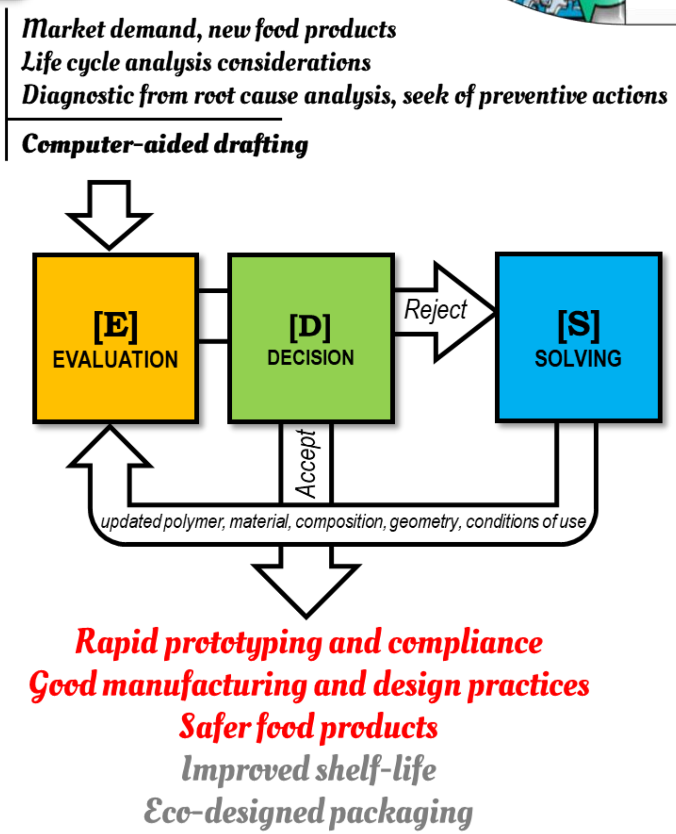


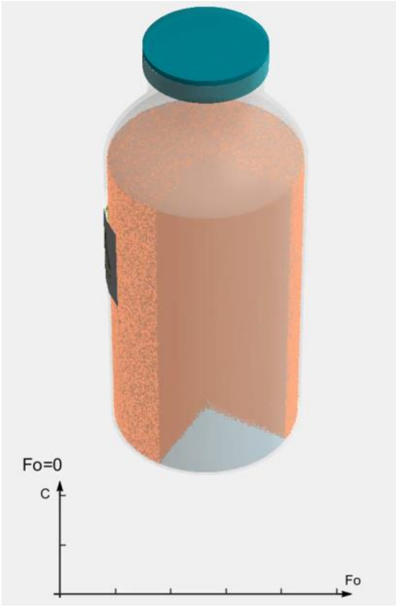
=124

Beyond concurrent design, integrated engineering

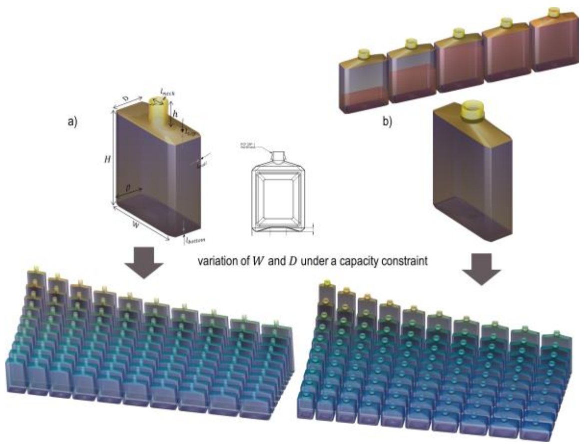
Multicriteria optimization





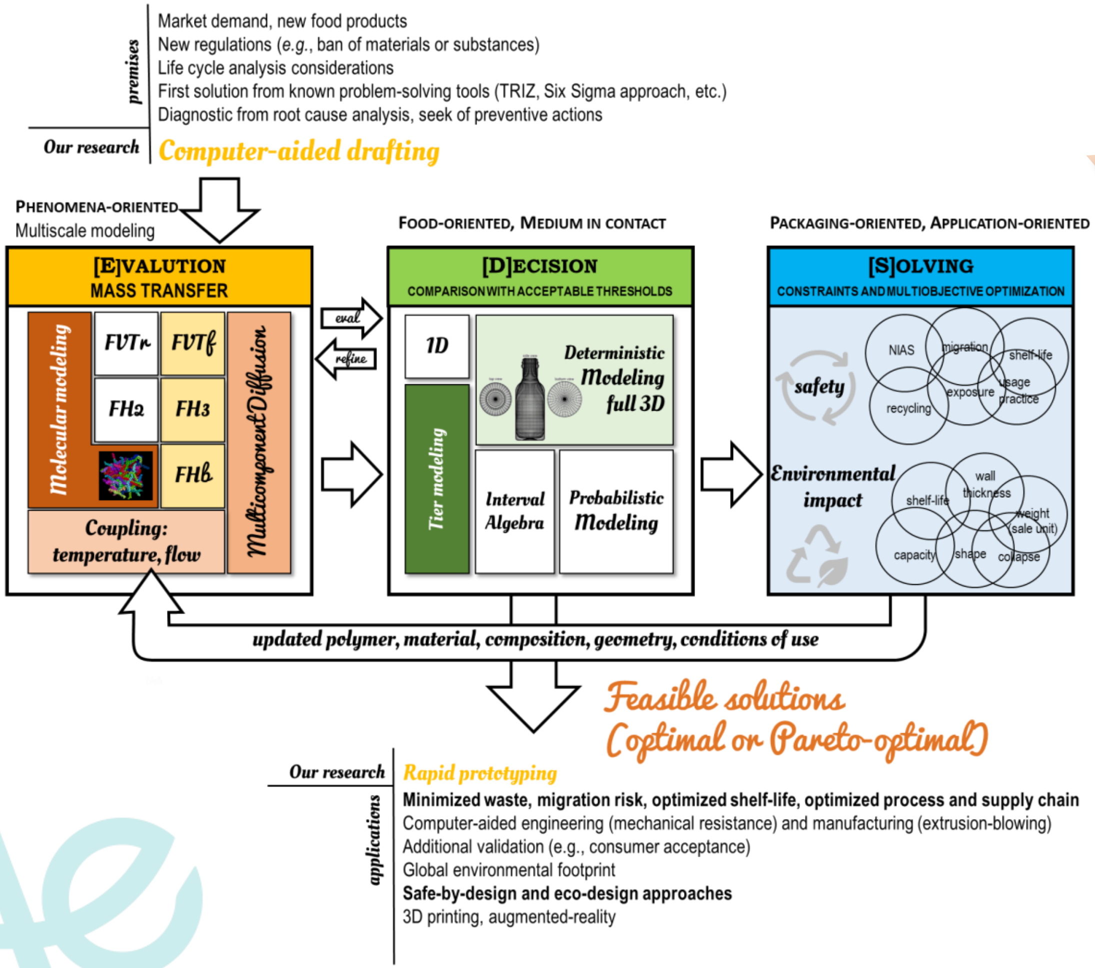


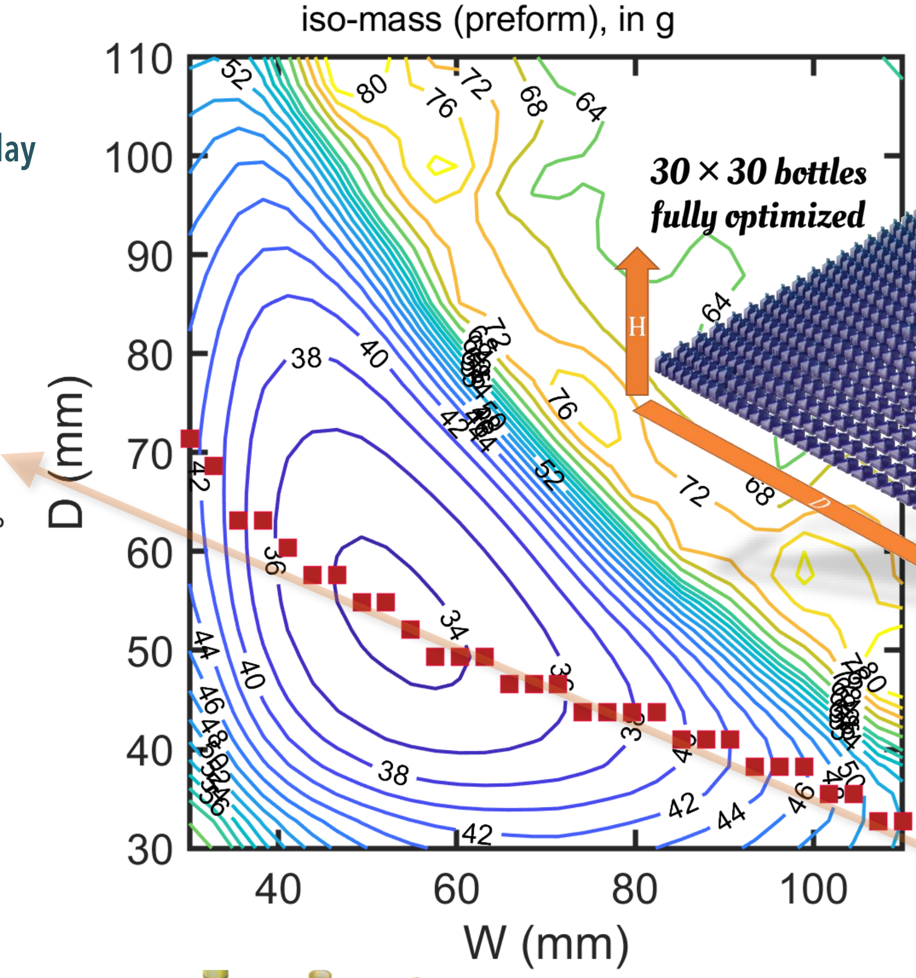
Integrated engineering

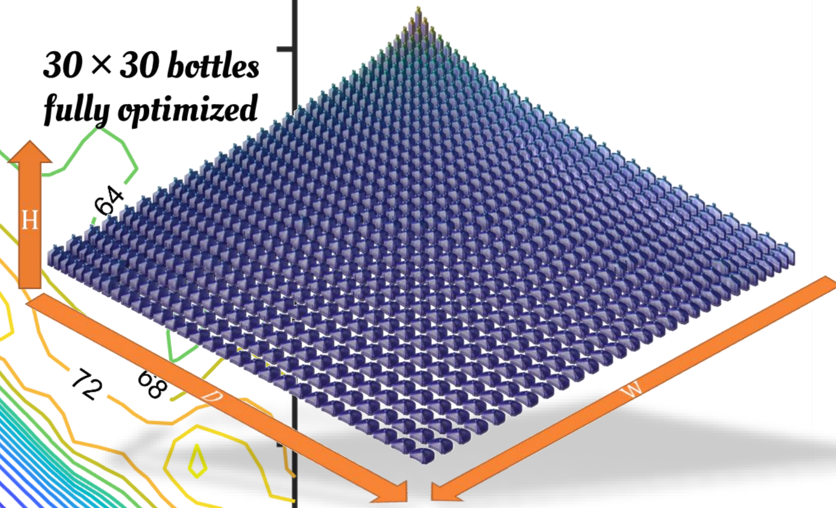


Example: redesign of PET bottle for alcoholic beverages (optimized shape, recycled content, reduced weight, improved shell-life)

3D prototype printed the same day







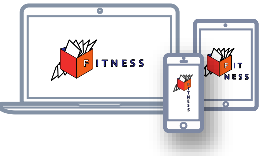
shelf-life=1 year with minimal weight, higher safety

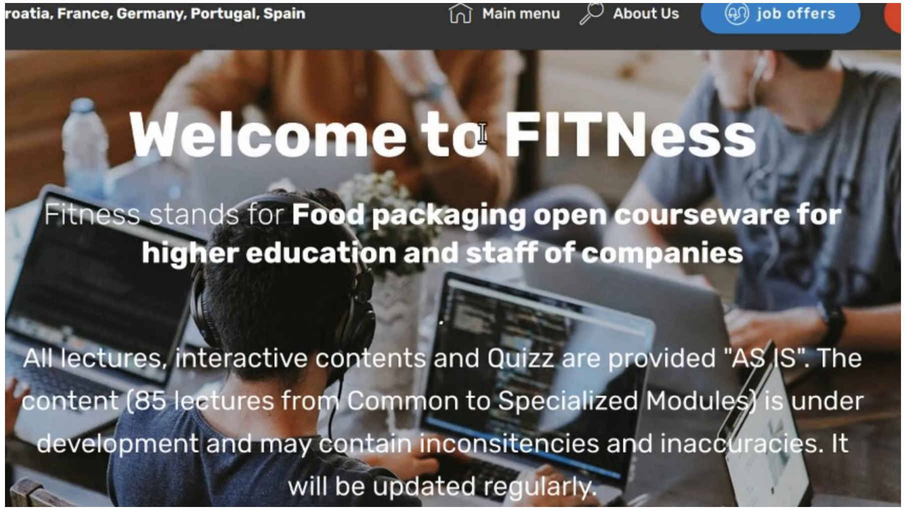
Zhu, Y., Guillemat, B., et Vitrac, O. (2019). Rational Design of Packaging: Toward Safer and Ecodesigned Food Packaging Systems. *Frontiers in Chemistry, 7(349).*

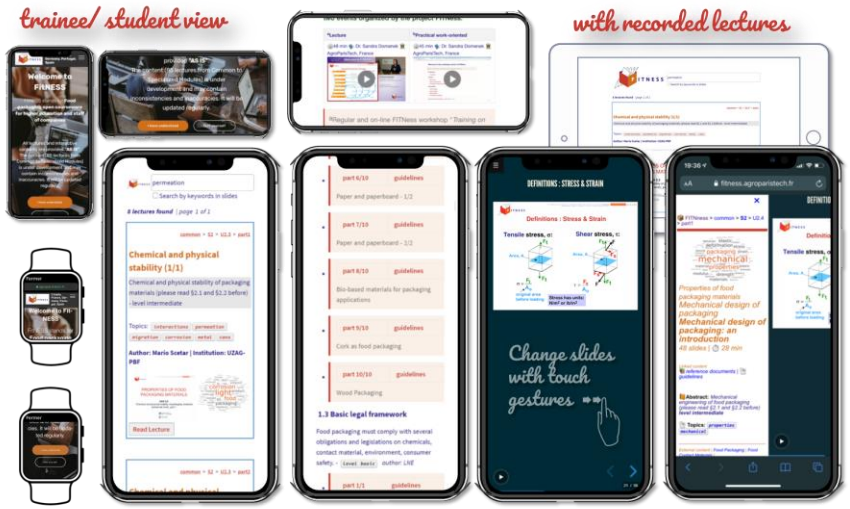
Train yourself to become green

Three months online curriculum on packaging design

https://fitness.agroparistech.fr/







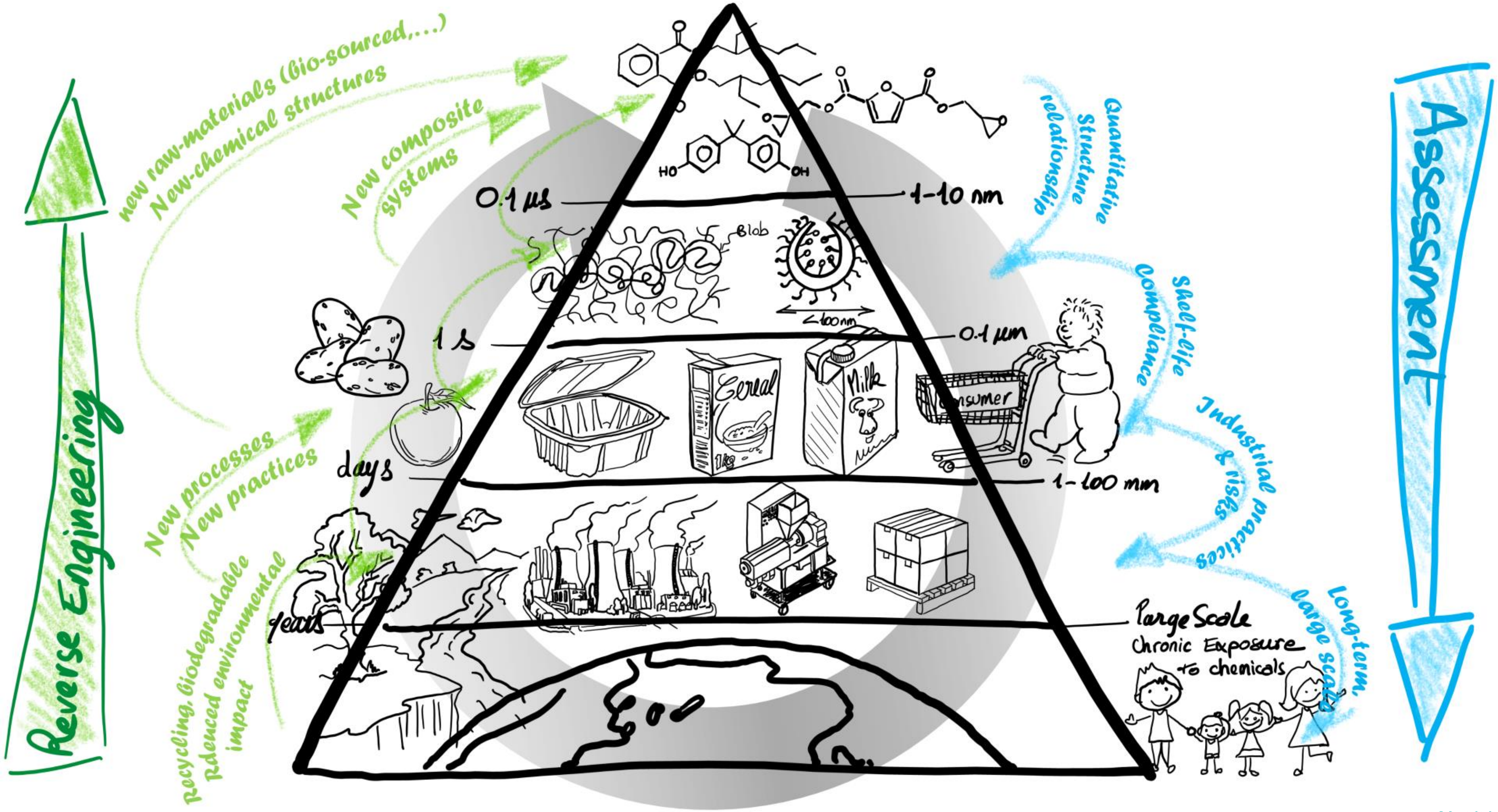
Co-funded by the Erasmus+ Programme of the European Union

Conclusions & Perspectives

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

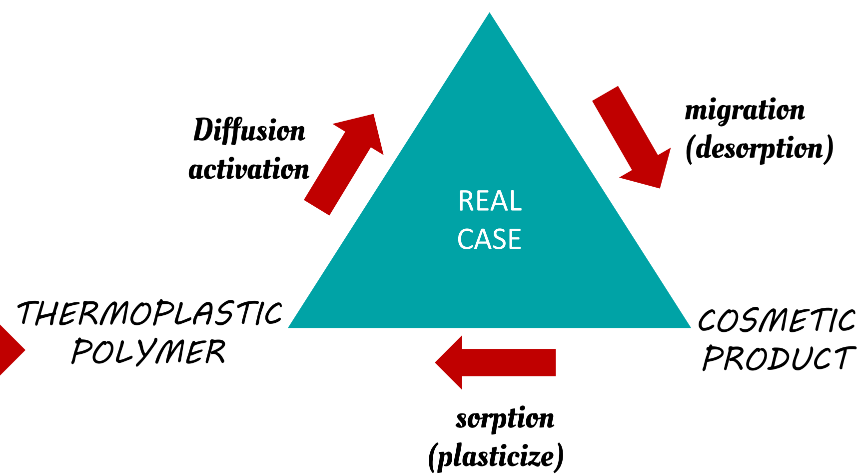
Future of packaging design = safe-by-design + ecodesign

Think
BIG
with engineering



PROJET COSMETOPACK

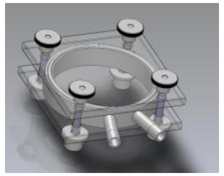
a) Real case



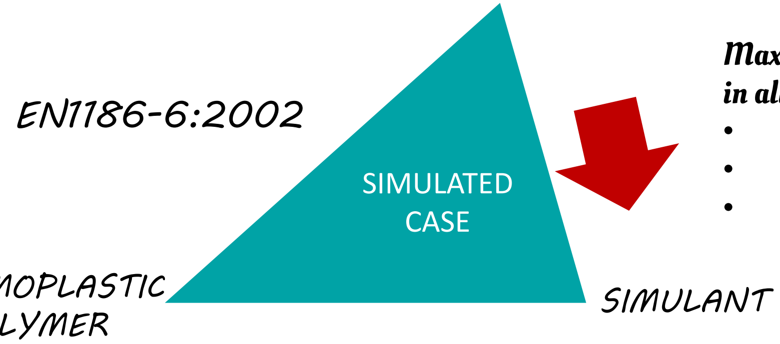
Migration is affected by:

- *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)



EN1186-6:2002



Maximize migration in all conditions

- *whatever the substance*
- *whatever the polymer*
- *whatever the storage temperature*

Migration is overestimated by:

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

For any question, contact: olivier.vitrac@agroparistech.fr