SML 5 - Software
General Description

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1. Introduction

1.1. About AKTS-SML

Employing advanced numerical algorithms, migration modelling with the SML software [1] predicts the migrating amount of organic substance like residual monomers, additives, contaminants, reaction products, non-intentionally added substances from plastic multi-layer or multi-material multi-layer materials into the packed food or other contact media like pharmaceuticals, cosmetics, drinking water or environment. The presented method insures the compliance of plastic food contact materials and articles with specific migration limits according to EU Regulations [2,3] and Swiss Legislation [4].

The technique allows the specific migration assessment for complex materials, e.g. different geometries and any multi-layer structure. Simulation of the migration process is based on Fick’s 2nd law of diffusion under consideration of partitioning between adjacent layers or contact media in closed systems [1-4].

Temperature dependence of the diffusion process is considered by the Arrhenius equation. Diffusion coefficients of substances in polymer are estimated by generally recognised estimation procedures like the Piringer model based on polymer specific constants (A_P-values) [2] which are available for a limited number of polymers. Extension of the A_P value model by Brandsch [6] for estimation of diffusion coefficients based on the glass transition temperature of polymers opens modelling opportunities for any polymer or polymer mixture which is characterised by a glass transition temperature.

Estimation of partition coefficients between contact layer and contact medium (e.g. polymer and food simulant or water) is based on the migrants polarity expressed by the octanol/water partition coefficient of the substances [5].

Time dependent migration curves and the concentration profile inside all layers of multi-layer structures can be computed for both, migrant from the material and from the contact medium. Simulation of release of substances from multi-layer materials in extended temperature ranges and under temperature conditions is possible at which experimental investigation would be very difficult, e.g. when temperature fluctuates during the observation time occur. Complex surrounding temperature profiles can be considered such as stepwise, modulated, shock and additionally for temperature profiles reflecting real atmospheric temperature changes (yearly temperature profiles of different climates with daily minimal and maximal fluctuations).

NEW in SML 5:

- Migration modelling for a whole packaging structure build from multiple articles (e.g. lid and tray).
- Migration modelling for an unlimited number of layers.
- Migration modelling of an unlimited number of substances at once (batch process).
- database of 13’000 chemicals (additive, monomer, photoinitiator, pigment, solvent, polymer, etc.)
- Estimation of partition coefficients between contact layer and contact medium (e.g. polymer and food simulant or water) based on the polarity of migrants expressed by the octanol/water partition coefficient of the substances [5].
- Extension of the A_P-value model by Brandsch for estimation of diffusion coefficients based on the glass transition temperature of polymers which opens modelling opportunities for any polymer or polymer mixture which is characterised by a glass transition temperature [6].
- Proprietary estimation procedure by Brandsch for diffusion confidents in polymers based on the glass transition temperature of polymers and estimation of partition coefficients between polymers based on the solubility of substances in adjacent polymer layers.
- Probabilistic migration modelling and sensitivity analysis based on Gaussian distributions for all inputs with Monte Carlo, Sobol and FAST technique.
- New analytical methods
1.2. Exposure and Compliance

1.2.1. Exposure

Because consumers within the EU are likely to be exposed to a range of different products or articles containing substances (chemicals) with safety concerns, the total consumer exposure to these compounds from all identified pathways forms the basis for exposure assessment. The most important exposure pathways are food, indoor air, and dermal contact with different polymer materials.

Substances with safety concerns are present in final products and articles at a level to accomplish the required technical effect. Due to thermodynamic driving forces, interaction between materials and contacting media occurs, and these compounds are transferred by release (migration and emission) and/or distribution (partitioning) to food, the ambient air, or directly to the consumer through dermal contact. The amount of compounds transferred is determined by the conditions of use (time and temperature, area to volume ratio) of the final products or articles. Typically, exposure factors and/or thermodynamic parameters (partition coefficients, diffusion coefficients) are used to model exposure scenarios. Based on the consumer habits, consumption behaviour and anthropometrics exposure pathways result. The consumer is exposed only to a limited extent to the individual pathways, such that their specific contributions in terms of real exposure levels must be considered.
1.2.2. Interaction

Interaction between polymeric materials and contacting media means transfer of substances (chemicals) from the materials to the media in contact resulting in changes of its quality/properties due to this process. From the point of view of consumer protection the focus has to be on the health risks caused by substances possibly released from the final products and articles. However, migration may lead to a change of the contact media quality with time and therefore is one of the key topics for quality assurance.

Depending on factors like concentration, mobility and solubility in the polymeric material as well as on temperature and duration of the contact, substances inevitably migrate to a more or less extent, into the contacting medium. Migration causes a change of medium composition with time. Due to this fact the European regulation on food contact materials for example is based on a positive list of substances under exclusion of all others with specific migration limitations on the food side. Migration of a substance from complex materials and articles like multilayer materials or composites are considered as a succession of individual mass transfer processes from which the slowest one defines the overall time scale. In most cases of practical relevance the diffusion process within the contact material or an individual layer in the structure of the material is the rate determining step of the migration process. On the other hand the relationship between the solubility of a substance in the material and the contacting medium, i.e. the partitioning process, strongly influences the overall amount of a substance migrating into the medium and consequently the amount of migrant still left in the contact material.

1.2.3. Compliance

Realistic evaluation of the health risk associated with polymeric materials and articles is necessary. The risk-to-benefit ratio regarding the use of polymeric materials is negligible compared to not using them. Even though this is unarguable, care must be taken to ensure consumer safety. Thus every regulation should consider the following points: i) the transfer of substances from polymeric materials and articles to contacting media may be undesirable and ii) unavoidable mass transfer from state-of-the-art products should not be prohibited, if the substances do not constitute health hazard and are technical unavoidable in an optimized system. The principal optimization criteria for modern products are their technical properties, consumer safety, environmental compatibility, and low cost. Meeting these points benefits the consumer and encourages technological progress.

Beside the acute toxicological properties of substance, their chronic mutagenic and carcinogenic activity is most important. The application to humans of the results of “No Observed Adverse Effect Level” (NOAEL) experiments on animals and the validity of subsequently derived “Acceptable Daily Intake” (ADI) values may be uncertain. “Estimated Daily Intake” EDI levels have additional uncertainties arising from regional and temporal considerations. The relevant exposure varies with season, geography, and socioeconomic or ethnic background. The amount of substances transferred from the polymeric materials and articles contacting media and hence the consumer exposure can vary over a large range. The theory of diffusion can be used to estimate mathematically the quantity of substances transferred. However, many other complex factors affecting migration cannot be anticipated.

Compliance with world wide regulation like FDA's Code of federal Regulation, EU Regulations and Directives, German BfR Recommendations, etc. is compulsory for polymeric materials and articles regarding positive listing and associated limits. The permissible levels of components to which the consumer is exposed are a function of above considerations. As a consequence of these uncertainties, all substances can be divided into categories according to their health risk, which than can be used as a basis for regulation. One end of the spectrum consists of substances that poses no risk (those substances which are inert or naturally occurring and are toxicological inactive) and the other end are substances that must be excluded from use because they are recognized as toxicological dangerous. Between this two extremes are the remaining substances which in more or less detail require toxicological or migration studies from evaluation from which specific limits can be derived.

The verification of compliance of food contact materials by the application of recognised diffusion model was introduced 2001 in the European legislation [1].

1.3. Migration modelling

1.3.1. Introduction

Polymeric materials (Plastics, Coatings, Rubbers, etc.) transfer their components (low molecular weight substances like monomers, additives, etc.) to contacting media to more or less extent, due to thermodynamic driving forces. This phenomenon is called mass transfer and the common wording is migration and/or emission depending on the type of contacting medium, i.e. liquid or gaseous. Due to transfer of substances (chemicals) from the polymeric material to the contact medium the substance amount in the polymeric material decreases and a concentration profile is established. The amount of substance is depleted first at the material/medium interface. The release of the substances from polymeric materials to contacting media obeys in most cases the law of diffusion because the diffusion process is the rate determining step. In case of gaseous contact media the evaporation process may become under certain circumstances the rate determining step. It is obvious that mass transfer can occur as well from the contacting medium to the polymeric material.

The release of substances from the polymeric material was historically assessed by experimental testing under conventional test conditions. Due to advanced understanding of the mass transfer processes and translation into science based computational tools simulation became the method of choice.

1.3.2. Simulation & diffusion models

The complex migration process (mass transfer) is reduced to the rate determining step, i.e. the diffusion process. Correspondingly migration modelling is based on diffusion models. The migration process may be simulated according to real use or according to conventional test conditions. Modelling migration according to conventional test conditions makes a one to one comparison between simulation and experimental results possible.

From mathematical point of view the system polymeric material in contact with a medium is

![Mass transfer - diffusion](Image)

To simplify the mathematical problem it is assumed that the polymeric material and its individual layers as well as the contacting medium are ordered parallel to each other. The diffusion equation is a partial differential equation which can be solved with recognised numerical algorithms. For more details regarding the numerical algorithms employed the reader is referred to the help menu of the SML software.
With the numerical solution of the diffusion equation the migration kinetic, i.e. migration of substances from the polymeric material to the contacting medium with time and the concentration profile of the substance in the system can be calculated.

**Diffusion models**

- monolayer materials (monolayer)
  
  \[ \frac{D}{K} \]

- multilayer materials (multilayer)
  
  \[ (D/K)_n \]

\( D, K \) - mass transfer constants

**Diffusion models**

**polymeric materials in contact with ...**

**general diffusion model:**

\[ \frac{D}{K} / \ldots / \frac{D}{K} \]

\( D/K \) - polymer/liquid

\( D/K/D \) - polymer/solid

\( D/K/D/K \) - polymer/coating/liquid

\( \ldots \)

\( (D/K)_n/D \) - general

*Fig. 1.3 - Symbols for diffusion models (n - number of layers)*

One has to distinguish between monolayer and multilayer materials. If monolayer materials are in contact with a liquid medium the system is described by two mass transfer constants, the diffusion coefficient of the substance in the polymeric material and the partition coefficient of the substance between polymeric material and contacting medium.

If multilayer materials with \( n \) layers are in contact with a liquid medium, all mass transfer constants describing the system must be considered, i.e. \( n \) diffusion coefficients of the substance in each layer. As long as the contacting medium is a liquid or a gas the diffusion process in the medium is neglected.
because the diffusion rates are much lower compared to solids like polymeric materials. If the contacting medium is a solid like some foods or another polymeric material, the diffusion process in the medium must be considered accordingly.

The solution of the diffusion equation requires variables for the simulation of migration kinetics and concentration profiles:

- geometry related variables (thicknesses, contact area, volumes) as well as time and temperature, e.g. according to real use or conventional test conditions
- initial or residual concentration of the migrant in each layer including the contacting medium) e.g. residual amount of monomers or initial concentration of additives.
- mass transfer constants (diffusion- and partition coefficients). These are not available from the literature and must be estimated according to generally recognised and validated estimation procedures based on scientific evidence.

A model is valid if it describes precisely enough the behaviour of the real system. The comparison between time dependent experimental migration data and simulated data is suitable for the validation of diffusion models. This procedure was chosen in the frame of several EU-projects [1-4] as well as many publications in the scientific literature. It was shown that migration processes in the system polymeric material in contact with a medium can be well described by the solution of the diffusion equation.

1.3.3. Estimation of mass transfer coefficients

**Diffusion coefficients**

The diffusion coefficient is a time related mass transfer constant which specifies how fast a substance is released from a polymeric material to a contacting medium by diffusion.

![Diffusion coefficient](image)

\[ D = D_0 \cdot e^{-\frac{E_A}{RT}} \]

- **D** - diffusion coefficient [cm²/s]
- **D₀** - pre-exponential factor
- **E_A** - activation energy [J]
- **R** - gas constant [8.314 J/mol K]
- **T** - temperature [K]

*Fig. 1.4 - Diffusion coefficient (Arrhenius)*

**Partition coefficients**

The partition coefficient is a thermodynamic mass transfer constant which considers the equilibrium concentrations of a substance in the polymeric material and the contacting medium. The partition coefficient defines the maximum amount of substance which can be transferred from the polymeric material to the contacting medium.
For the estimation of diffusion- and partition coefficients there are several scientific approaches:

- **Partition coefficient (K**

\[ K_{P,M} = \frac{C_{P,\infty}}{C_{M,\infty}} \]

- **Estimation of mass transfer constants**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>(D_p)</td>
<td>diffusion coefficient</td>
</tr>
<tr>
<td>(D_0)</td>
<td>pre-exponential factor (Arrhenius)</td>
</tr>
<tr>
<td>(E_a)</td>
<td>activation energy (Arrhenius)</td>
</tr>
<tr>
<td>(T)</td>
<td>temperature [K]</td>
</tr>
<tr>
<td>(A_0)</td>
<td>polymer specific constant (Arrhenius)</td>
</tr>
<tr>
<td>(A_p')</td>
<td>polymer specific temperature constant (Piringer)</td>
</tr>
<tr>
<td>(\tau)</td>
<td>polymer specific temperature constant (Piringer)</td>
</tr>
<tr>
<td>(M)</td>
<td>molecular weight [g/mol]</td>
</tr>
<tr>
<td>(M_0)</td>
<td>relative molecular weight</td>
</tr>
<tr>
<td>(T_m)</td>
<td>glass transition temperature</td>
</tr>
<tr>
<td>(K_{PM})</td>
<td>partition coefficient</td>
</tr>
<tr>
<td>(V_p)</td>
<td>volume of polymer</td>
</tr>
<tr>
<td>(V_m)</td>
<td>volume of medium</td>
</tr>
<tr>
<td>(p)</td>
<td>vapour pressure of migrant</td>
</tr>
<tr>
<td>(S_p)</td>
<td>water solubility of migrant</td>
</tr>
<tr>
<td>(P_{OM})</td>
<td>octanol/water partition coefficient of migrant</td>
</tr>
</tbody>
</table>

**Diffusion coefficients (\(D_p\))**

- **Arrhenius**
  \[ D_p = f(D_0, E_A, T) \]
- **Piringer**
  \[ D_p = f(A_p', \tau, M, T) \]
- **Brandsch**
  \[ D_p = f(T_g, M, T) \] - new

**Partition coefficients (\(K_{PM}\))**

- **worst case**
  \[ K = 1; (V_p \ll V_m) \]
- **Piringer**
  \[ K = f(p, M_a, W_a, G_F) \]
- **Brandsch**
  \[ K = f(S_W) \]
  \[ K = f(P_{OM}) \] - new

For the estimation procedures of diffusion coefficients according to Arrhenius and Piringer experimental testing is required to determine material specific parameters like the pre-exponential factor, \(D_0\); the activation energy, \(E_A\); the polymer specific constant, \(A_0\) and the polymer specific temperature constant, \(\tau\) (corresponds to the deviation from the reference activation energy, \(E_A = E_A, \text{ref} + t \cdot R\) with \(R\) the gas constant). The influence of the migrant size to the diffusion rate may be considered by its molecular weight. The \(A_p'\)-value concept of Piringer was validate in the frame of an EU-project, refined in further EU activities and validated for migration modelling from plastics into food simulants (polymeric material in contact with liquids).
The estimation of diffusion coefficients according to Brandsch is an ab initio technique based on well known thermodynamic parameters like the glass temperature of polymeric materials. Validation of the new procedure is possible against the existing $A_P$-value approach as well as against experimental data.

The estimation of partition coefficients is less advanced. Nevertheless some scientific approaches exist based on a group contribution method developed by Piringer or an empirical approach developed by Brandsch in the frame of the EU-project “Foodmigrosure”. The empirical approach by Brandsch considers the polarity of the migrant by its octanol/water partition coefficients and sets it in relation to the partition coefficient between polymeric materials and real foods or food simulants. Knowledge of the water solubility may allow for the estimation of worst case partition coefficients between polymeric materials and aqueous media.

**$A_P$ value concept (Piringer)**

The estimation procedure for diffusion coefficients according to Piringer, the so called $A_P$-value concept, requires the experimental determination of the polymer specific constant, $A_P$-value and the polymer specific temperature constant, tau once for each polymer type. For each polymeric material a minimum of time dependent migration experiments must be run at different temperatures. From the experimental data diffusion coefficients are determined. These are translated into $A_P$-values according to the relationship developed by Piringer. From all available $A_P$-values an upper limit value for one polymeric material is calculated as the 95-percetntile of that data set. Provided the data set available is big enough, the $A_P$-value for that polymeric material is considered to be validated.

Experimental time dependent migration data, diffusion coefficients and $A_P$-values derived there from are collected and evaluated by the Modelling Task Force at the Joint Research Centre of the EU-Commission.

For most of the polymeric materials used in food contact materials upper limit $A_P$*-values and tau-values are listed in the JRC-Guideline supporting the Plastics Regulation (EU) No 10/2011 of the EU-Commission. Upper limit $A_P$*-values result in overestimated migration values in support of consumer safety.

**Overestimation and consumer protection**

It is in support of consumer safety to develop procedures for estimation of mass transfer constants which systematically overestimate the migration behaviour of real polymeric materials. Due to systematic overestimation the risk of underestimation compared to the real system is minimized. Due to simulation of one single migration cycle it is easy for food contact materials to implement overestimation. The use of upper limit $A_P$-values in the estimation procedure of diffusion coefficients and lower limit partition coefficients results in estimated migration value which are higher compared to the real ones.

**Repeated use**

Polymeric materials with repeated use or dynamic flow behaviour of the contacting medium need more specific considerations. The experimental conventional test conditions as well as migration simulations account for the repeated use or dynamic flow behaviour by implementation of several migration test cycles. Overestimating the migration in the first migration cycle may cause underestimation in later migration cycles. This can happen only if the overestimation based on diffusion and partitioning is very high and more than 50% of the substance migrates out of the polymeric material in the first migration cycle. In these special cases, which can be easily identified during simulation, only the first migration cycle can be used for comparison with a specific migration limit.

[1] EU-project "Recyclability" FAIR-CT98-4318
[3] EU-project "FOODMIGROSURE" QLK1-CT2002-2390
[4] EU-project "MIGGRESIVES" COLL-CT-2006-030309
1.4. Legal background

1.4.1. Use of simulation (introduction)

Polymeric materials are used in a variety of applications. Through all the following applications direct or indirect consumer exposure with substances (chemicals) from polymeric materials may occur.

- food contact materials and articles
- toys
- textiles
- child use and care articles
- medical devices
- drinking water applications
- household articles
- consumer goods
- construction materials
- automotive applications
- electronics applications
- other materials and articles

Due to interaction between polymeric materials and contacting media, and consumer exposure resulting there from, legal requirements are set at national and international level. For given applications like food contact materials or toys detailed legal requirements in terms of substance specific migration limits are set by the applicable legislation. Historically the experimental approach, i.e. experimental migration testing under conventional test conditions was used for compliance assessment.

Migration modelling is a valuable tool to estimate the type and extend of interaction between polymeric materials and contacting media. Estimating the mass transfer based on the relevant physical and chemical parameters, i.e. mass transfer constants, enable professionals to estimate consumer exposure at all stages of the production chain.

In the last years migration modelling got more and more accepted and was first introduced in legislation for plastic food contact materials and articles in 2001 allowing for compliance assessment with applicable legislation.

1.4.2. Food contact materials

EU legislation


Detailed information about the general recognised diffusion models based on scientific evidence can be found in the JRC Scientific and Technical Report, 2010; C. Simoneau, ed., "Application of generally recognise diffusion models for the estimation of specific migration in support of EU Directive 2002/72/EC."

In the new Regulation (EU) No 10/2011 the Migration Modeling approach was defined in Annex V as one of the so called "screening approaches" which can be used in support of compliance evaluation for food contact plastics. The Plastics Regulation states: "To screen for specific migration the migration potential can be calculated based on the residual content of the substance in the material or article applying generally recognised diffusion models based on scientific evidence that are constructed such as to overestimate real migration."

According to Article 18 of Regulation (EU) No 10/2011 migration modelling can be used to demonstrate compliance of food contact materials and articles with the applicable legislation. To demonstrate noncompliance, i.e. by official control, the experimental approach is compulsory.
1.4.3. Drinking water contact materials

**German Recommendation**

The German Recommendation "Leitlinie zur mathematischen Abschätzung der Migration von Einzelstoffen aus organischen Materialien in das Trinkwasser (Modellierungsleitlinie)" as of 7. October 2008 states: The mathematical estimation of migration can be used to evaluate the compliance with requirements of the "KTW-Leitlinie", "Beschichtungsleitlinie" or the "Schmierstoffleitlinie" regarding individual substances instead of an experimental proof.

1.4.4. Other applications

Strong efforts are made to get migration modelling accepted for all applications were polymeric materials are used like:

- toys
- textiles
- child use and care articles
- medical devices
- drinking water applications
- household articles
- consumer goods
- construction materials
- automotive applications
- electronics applications
- other materials and articles

Because interaction between plastic materials and contacting media, i.e. migration and emission processes follow the same laws independent from the application one can expect that this objective will be achieved in near future.

For organic materials in contact with drinking water this objective was reached with introduction of the migration modeling approach by the German Umweltbundesamt with the "Modellierungsleitlinie".
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Licensee of the PROGRAM must have knowledge of packaging, chemistry, physics and engineering. The PROGRAM should not be used as the exclusive determinant of any hypothesis. Where risk to life is involved, results obtained with the PROGRAM should be examined carefully before any conclusion or new experiments are made. The PROGRAM should only be used as support, or for screening, of new experiments that can be later used as the exclusive determinant of other experiments or hypotheses. Not the PROGRAM but only these additional separate new experiments should exclusively be designed, manufactured or intended for use as an exclusive determinant of on-line control equipment in hazardous environments requiring fail-safe performance, safety and security testing, such as in the operation of nuclear facilities, aircraft navigation or communication systems, air traffic control, direct life support machines, weapons systems, or other domains in which the failure of the PROGRAM and misinterpretation of the results could lead directly to death, personal injury, or severe physical or environmental damage ("High Risk Activities"). The LICENSOR and its suppliers specifically disclaim any express or implied warranty of fitness of High Risk Activities. The LICENSOR or anyone involved in the creation of this PROGRAM, takes no responsibility for any inconvenience, loss of time, property, or product damage, personal damage, or any other incidental or consequential damages from the use of the PROGRAM.

1.5.5. License fees and payment

In consideration of the license rights, the user is responsible for paying the license fees. The amount is payable without any deduction for taxes, assessments, fees, or charges of any kind.

The user is responsible for paying all (i) taxes, sales, use, excise, value-added or any other governmental charges imposed on the licensing or use of the PROGRAM, Derivative Products or Documentation, (ii) freight, insurance and installation charges, and (iii) import or export duties or like charges, resulting from this license.

The user may terminate the license at any time. The LICENSOR may terminate the user’s license if the user fails to comply with the terms and conditions of this license. In either event, the user must destroy all copies of the PROGRAM.

This license is governed by the laws of Switzerland. Venue is Sion (VS), Switzerland. This license gives the user specific legal rights; the user may have others which vary from state to state and from country to country. The LICENSOR reserves all rights not specifically granted by this license.
This License Agreement may only be modified by a written license addendum signed by both the user and the LICENSOR. Should the user have any questions concerning this License Agreement, please contact the LICENSOR.

If the user agrees with the terms of this license, he may use the PROGRAM.

Any information the user provides enables us to understand better how LICENSOR technology is being applied, and lets us notify the user of upgraded versions when they are available. The user's name, e-mail address and other information will be kept as part of our LICENSOR license record file. No personal information about the user will be given to any organization outside of LICENSOR.

1.6. Release Notes

List of the main modifications and corrections. This list is not exhaustive.

Version 2
Analytical solution.

Version 3
Numerical solution with the introduction of multilayer concept. The version 3 was developed in cooperation with BAG (Federal Office of Public Health - FOPH).

Version 4
Numerical algorithms improved by MDCTec. Introduction of the repeated use and mass balance check.

Version 5
- Migration modelling for a whole packaging structure build from multiple articles (e.g. lid and tray).
- Migration modelling for an unlimited number of layers.
- Migration modelling of an unlimited number of substances at once (batch process).
- Binding the software with a database of 13'000 chemicals (additive, monomer, photoinitiator, pigment, solvent, polymer, etc.)
- Estimation of partition coefficients between contact layer and contact medium (e.g. polymer and food simulant or water) based on the polarity of migrants expressed by the octanol/water partition coefficient of the substance.
- Extension of the $A_p$ value model by Brandsch for estimation of diffusion coefficients based on the glass transition temperature of polymers which opens modelling opportunities for any polymer or polymer mixture which is characterised by a glass transition temperature.
- Proprietary estimation procedure by Brandsch for diffusion confidents in polymers based on the glass transition temperature of polymers and estimation of partition coefficients between polymers based on the solubility of substances in adjacent polymer layers.
- Probabilistic migration modelling and sensitivity analysis based on Gaussian distributions for all inputs with Monte Carlo, Sobol and FAST technique.
- New analytical methods
2. Installation and Maintenance

2.1. Minimal Configuration

Minimal required computer configuration for AKTS-SML software:

Microsoft Windows XP, Vista or 7
Intel Pentium 2 CPU 1.00 GHz
512 Mb of RAM

AKTS-SML software can handle a lot of data, a computer with more RAM memory is recommended when performing calculations with complex packaging.

2.2. AKTS-SML Installation

2.2.1. Preliminary remarks

The Windows account used for installing AKTS-SML does not need to have administrator rights. The installation simply consists in copying files from an installation support onto a computer.

Although it is also possible to manually copy the files, the installation wizard simplifies this procedure and adds shortcuts on the desktop and in the Windows Start Menu.

Once the software is installed, it must be activated.

2.2.2. Installation diagram

![AKTS-SML installation diagram]

AKTS-SML can be installed from the external storage media (CD-ROM, USB key, etc.) or downloaded from Internet.
2.2.3. Installation

After downloading AKTS-SML

**From the Internet**

- Simply unzip the downloaded files in the folder of your choice;
- No further installation is needed. AKTS-SML is ready to use!
- You can now activate the software

**From the external storage media**

- Insert the AKTS-SML installation support (CD-ROM, USB key, etc.);
- If the automatic execution of your support is not activated, launch the installation program `start.exe`, otherwise it will be automatically executed;

![AKTS-SML installation screen](image)

Fig. 2.2 - AKTS-SML installation screen

- Click on **Install now** to start installing AKTS-SML. The main window allows you choosing the folder where the files will be copied;
• When the files copying is finished, you can add shortcuts (Fig. 3):
  • Place a shortcut for AKTS-SML on the desktop;
  • Add AKTS-SML to Windows start menu;
• To close Installation click on Finish.

• After installation, the user may use the shortcuts or launch AKTS-SML software directly from the folder where it has been installed;
• You can now activate the software
2.3.   AKTS-SML Activation

2.3.1. Activation procedure

- The activation of AKTS-SML is required only once, when the first time the software is launched.
- Each computer on which AKTS-SML is installed needs a different license. Please activate AKTS-SML on each computer separately.
- The activation creates a license file "akts.lic" which is placed in the same folder where AKTS-SML is installed.
- The activation is automatic if the computer is connected to Internet, otherwise sending an activation number to AKTS is necessary in order to get the license file.

2.3.2. Online activation

If the computer on which SML Software is installed is connected to Internet, you can directly activate the software online.

On the login screen, use the menu Activation → Online Software Activation.

After having accepted the license agreement, it is necessary to introduce to the Activation Window the required activation information.

![Online Activation Window](image)

*Fig. 2.5 - Online Activation Window*

Username and password  Enter the username and password you have received to activate the software. Note: it is not "admin / admin".
2.3.3. Offline activation

If the computer on which SML Software is installed is not connected to Internet, the user must send manually an activation number which is used to create the license file.

Use the menu **Activation → Offline Software Activation**.

After having accepted the user agreement, the activation number will be displayed in the Offline Activation Window.

The activation number must be sent to the e-mail address shown in the window (Fig. 2). **Please send also your username and password.**

You will receive your license file generated with the information you have sent.

Place the license file "akts.lic" into the folder where SML software is installed. The software is activated as soon as the license file is placed into the folder.

**Important Note**

When you send the activation number, please be sure to submit your username and password.

2.4. Software Upgrades

Upgrade your SML software version in order to benefit from the latest developments, improvements and corrections of the software.

2.4.1. Upgrading with an Internet connection (automatic)

When the computer on which SML software is installed, is connected to Internet, click on the menu **Administration → Automatic upgrade**.

An information message appears if a new version is available. If you click on **Upgrade now**, the new version will automatically be downloaded and installed.

2.4.2. Upgrading without an Internet connection (manual)
Check if a new upgrade is available

It the computer is not connected to Internet, we advise you to periodically check if a new version is available.

To check if you have the latest version, compare the version number of your current software which can be found under "?" ➔ About... with the version number posted on the AKTS (www.akts.com) website.

Upgrading the software

To upgrade the latest version of the software manually, download the latest version from the internet.

Once downloaded, move the installation file to the folder where SML software is installed. Then open the zip files and overwrite the old ones: the upgrade will replace the *.EXE files of SML software and the help files *.CHM.

2.5. Maintenance

2.5.1. Principles of Maintenance

- The software licenses are perpetual, meaning that it is still possible to use the software once the maintenance date has expired.

What happens after the maintenance date has expired?

- Once the maintenance date has expired, it is not possible to upgrade the software to the next so-called "major" version.
- However, the new minor versions may still be downloaded even if they are released after the expiration of the maintenance date.

2.5.2. Major and minor versions

In the software version number, the first digit indicates the major version number, while the second decimal indicates the minor version. A major release contains mainly new features, while a minor release contains mainly bug fixes.

Fig. 2.7 - In red the major version number, in blue the minor version number

2.5.3. Support and Maintenance Information

At AKTS AG, we know that time is critical when it comes to your research, development and production. That is why AKTS AG Support is organized to respond quickly and accurately to meet your needs. Our support engineers help resolve your difficulties you may have with our products and suggest efficient ways of achieving your development objectives. In addition, we offer optional consulting services for those needing special tools or libraries for « AKTS-Software » and your specific operating system/environment. Each AKTS AG Support and Maintenance Contract Offers:

- Support response in two business days or less.
- Access to the web site for maintenance releases and patches, and unlimited email support.
- Free upgrades to the latest version of AKTS-Software when released.
- Each support and maintenance contract is limited to support up to 2 engineers on one project.

This guide introduces you to the support services available from AKTS AG and instructions on how to use them. Specifically, it tells you how to access these services, and how to make the most effective
use of them. Purchasing AKTS AG Support is assurance in having access to the AKTS-Software support engineers when you need them the most – meeting a critical deadline, needing help through a tough problem, finding work-arounds or fixing tool bugs.

How to Request Support

Internet email and telephone help desk are the two ways to contact AKTS AG.

- info_contact@akts.com
- phone: +41 848 800 221

If AKTS AG received a question by email, an engineer will follow-up with a telephone call or email (usually within one business day or less), depending on workload and nature of the question. The customer will be notified as to an estimated time for problem resolution.

Escalation of Problem Reporting

- Normally most questions are resolved through user assistance and initial collaboration.
- If the problem cannot be resolved during the initial contact, it is escalated to an SPR (Software Problem Report). An SPR is opened and referred to a subject matter expert who is specifically equipped to deal with support issues in his product area. He will continue to work the SPR to resolution, or until a software problem is identified.
- If not resolved at the SPR level (i.e., a defect is identified), the support engineer issues a Software Change Request (SCR).

AKTS AG engineering evaluates the nature of the software issue, to determine the optimum nature of resolution for the SPR. Depending on severity, level of urgency, and schedule, AKTS AG engineering may recommend one or more of the following options:

- **Workaround.** A specific methodology for mitigating the impact of the software problem, which may be implemented on an expedient basis to allow customer development to proceed.
- **Version Patch or Build.** If the software problem can be isolated / diagnosed to a small region of code that is easily modifiable, AKTS AG may elect to provide the customer with a custom rebuild of the effected software component(s). This also provides an expedient path for resumption of customer development. Normally these SCRs will be fed into the normal software engineering upgrade cycle, such that fixes are automatically incorporated into future maintenance releases.
- **Custom/ECP.** In some cases, software enhancements are proposed by customer. If the proposed software enhancements can be easily implemented, these new features will be fed into the normal software engineering upgrade cycle and incorporated into future maintenance releases. However new features that will require major software development effort to implement (typically this implies development scope requiring many source lines of code). In such cases AKTS AG will develop an Engineering Change Proposal (ECP) outlining the cost, resources, and schedule requirements for implementing the new features. This ECP will serve as the basis of negotiations between AKTS AG and our development partners for cost (and benefit) sharing of the proposed software enhancements.

Summary of Escalation Levels

- Internet email and telephone help desk
- Software Problem Report (SPR)
- Software Change Request (SCR)
  - Workaround
  - Patch/Build
- Custom Development via Engineering Change Proposal (ECP)
Web Site Support Features

AKTS AG has a web site with support pages that gives you access to the following features:

- On-Line Documentation
- Knowledge Base
- Maintenance Releases
- Downloads/Upgrades

By registering an AKTS AG product, the customer receives access to all of the web site support features for free. Purchasing support gives the customer the added benefits of help desk support and problem resolution. The AKTS AG web site is continually evolving. Information is update, and new features are added regularly. We encourage you to visit the site frequently to see new features.

Help Us Help You

Making an Inquiry

Each customer should designate per license one person as technical contact per AKTS AG terms and conditions for Support and Maintenance. When a question or problem comes up, your technical contact should be the person directing the inquiry to Support. AKTS AG support maintains a list of customer technical contacts. We understand that personnel may change. Please keep us informed of your current technical contact by contacting AKTS AG.

How to Get Answers, Fast!

When you call, we want to help you use time efficiently. If you have the following information at your fingertips, it will help us to help you more quickly:

- AKTS AG Product
- AKTS AG Version
- Host Platform
- Upgrade question
- AKTS-Software question

You can help us resolve your question more quickly if you’re also prepared with a clear description of the problem and any associated problems you encountered in a test case (some screen captures or a quick approach to reproducing the problem may be helpful).

Your Feedback

AKTS AG is committed to responding to customers quickly and accurately. We welcome your comments regarding our support services, and we encourage your feedback. If you have suggestions or concerns, please let us know. As part of our commitment to providing you with the best support possible, if you are contacted, please take the few minutes to answer questions. Your response will help us maintain the highest level of service.

2.5.4. Terms and Conditions

These terms and conditions apply to each Support and Maintenance Contract. Your purchase of a Support and Maintenance Contract is an acceptance by you of these terms and conditions.

Support

This Agreement entitles you to obtain technical support services ("Support") from AKTS AG. Support means answers to questions, guidance, and assistance as determined by AKTS AG. Support excludes configuration of hardware, software, and networking equipment and software that are not products of AKTS AG. It excludes general computer system maintenance and consulting services that
are not in direct relation with AKTS-Software. You are responsible for performing operations on your computer system, and AKTS AG shall have no responsibility to perform operations on your computer system. You agree to provide AKTS AG all information reasonably requested by AKTS AG to enable AKTS AG to provide Support. Such information may include, but not be limited to, the type of hardware you are using, a description of the problem for which you seek Support, and additional software you are using that falls outside the subject matter scope of coverage. You understand and agree that the completeness and accuracy of the information you provide to AKTS AG pursuant to this section may affect AKTS AG’s ability to provide Support.

**Subject Matter Scope of Coverage**

AKTS AG will provide Support for the official customer site where AKTS-Software product has been licensed and installed. AKTS AG will provide Support for AKTS-Software only and for other customer sites where AKTS-Software product has been licensed. You understand and agree that AKTS-Software may not function with certain hardware systems and components. Such hardware is unsupported hardware. AKTS AG shall have no obligation to provide Support for any system that is or that includes unsupported hardware.

**Availability of Coverage**

You are entitled to seek Support from 9:00 AM till 12:00 AM and from 1:00 PM till 5:00 PM Central Europe Time Monday through Friday, excluding holidays, throughout the term of this agreement. Holidays include, but may not be limited to, the Swiss holidays. In the event that one of these holidays falls on a Saturday, the preceding Friday shall be a holiday. In the event that one of the holidays falls on Sunday, the following Monday shall be a holiday.

**Who May Seek Support**

Only the official sites where AKTS-Software has been licensed may seek Support from AKTS AG. You are responsible for all persons who seek Support pursuant to this agreement. AKTS AG shall have no responsibility for any unauthorized use of Support.

**Response Times**

AKTS AG shall respond to requests for Support within two business days of receipt of your request for Support. A response to a request for Support may consist of a receipt of and acknowledgment by AKTS AG of your request for Support. You acknowledge and understand that no software is perfect or error free, and that despite its commercially reasonable efforts, AKTS AG may be unable to provide answers to or resolve some or all requests for Support. AKTS AG makes no promises, guarantees or assurances of any kind that it will be able to provide the support services you seek. We do promise to do our best to satisfy each customer, whether it be complete software fixes, upgrades or workarounds to a problem.

**Termination**

Either party may terminate this agreement at any time. Termination of this agreement does not relieve your payment obligation for Support provided to you by AKTS AG.

**Payment**

Any and all payments made by you pursuant to this agreement shall be nonrefundable. There shall be no refunds or credits for any unused Support or other unused services upon the termination of this agreement for any reason or at any other time. In the event that you fail to pay AKTS AG pursuant to this agreement, AKTS AG’s obligations to provide Support shall be suspended until AKTS AG receives full payment for all fees, including late fees and interest, due to AKTS AG.
General description of the new SML software

No Transfer

Any reuse, transfer, assignment, or distribution of Support without the prior written permission of AKTS AG is prohibited. Any attempt to transfer, assign, or redistribute Support in violation of this section shall be a violation of this agreement and shall immediately terminate this agreement and all your rights under it.

No Warranty

Support, other services, information, and software provided to you by AKTS AG are provided “as is” without warranty of any kind, express, or implied, including, but not limited to, the implied warranties of merchantability, fitness for a particular purpose, and non-infringement.

Limitation on Liability

Neither you nor AKTS AG shall be in breach of this agreement due to any failure of performance that arises out of causes beyond its reasonable control. AKTS AG shall not be liable to you or to any third party for any indirect, special, incidental, or consequential damages in connection with or arising out of this agreement, including, but not limited to, lost profits or lost data in connection with this agreement, even if AKTS AG had been advised of the possibility of such damages. AKTS AG will not be liable to you on account of errors, omissions, delays or losses.

General

This contract is governed by the laws of Switzerland. Venue is Sion (VS), Switzerland. This contract gives you specific legal rights; you may have others which vary from state to state and from country to country. AKTS reserves all rights not specifically granted by this contract. Any dispute arising out of this contract shall be adjudicated solely in the applicable federal or state courts within Switzerland.

This contract, including all schedules, constitutes the entire understanding of the parties. This contract supersedes and terminates all prior representations, warranties, and agreements, written or oral, regarding the subject matter of this agreement. Any modification to this contract must be in writing signed by both parties.
3. The Mathematical Model

3.1. Introduction

Computer programs are available to predict, for consumer protection purposes, the migration of additives from a polymeric material or article during its contact with food. However most of these programs were developed to estimate migration only from single layer polymeric packaging under isothermal conditions. In this work a diffusion model was developed to simulate the migration from multilayer packaging and under non-isothermal temperature conditions too.

3.2. General description of the model

Simulation of the diffusion processes of migrant and simulant occurring in packaging layers can be reduced to the analysis of a single layer.

\[ \frac{\partial C}{\partial t} = D \left( \frac{\partial^2 C}{\partial x^2} \right) \]

**Fig. 3.1 - Scheme of the packaging**

Considering one layer inside the packaging, it can be demonstrated that the mass of the layer which is taken for calculation of the diffusion of both migrant and simulant can be treated as an ‘infinite’ surface of thickness ‘d’ (i.e. ‘infinite’ in two directions and of wall thickness ‘d’ in the third, see eqs. 3.7, 3.8). To calculate the amount of the migrating substance that reaches the food after a certain time all package geometries are reduced to a simple case: a plane of several sheets with only one surface in contact with the food. It can be assumed that diffusion obeys Fick’s law and that the diffusion of the species in the y and z direction is negligible as compared to x direction. The presented model enables calculations of the concentration gradients using finite element methods, considering the diffusion progresses of both species (migrant and simulant) in the multi-layers. The Arrhenius, Piringer and Brandsch equations can be applied in order to evaluate a magnitude for the diffusion coefficient in the different layers. The equations have been developed using coordinates (x and t) where the whole surface of the packaging will be derived from the different packaging shapes.
3.3. Concentration distribution in the layers

3.3.1. Generalized mass balance over a layer volume element

In order to consider the change of the concentration of the migrant (and/or simulant) diffusing inside the layer, a mass balance over a volume element can be made as following:

\[
\begin{align*}
\text{Input} &= \text{Output} + \text{Accumulation} + \text{Reaction} \\
\int n_x \, dydz + \int n_y \, dxdz + n_z \, dxdy &= \\
\left( n_x + \frac{\partial n_x}{\partial x} \right) dydz + \left( n_y + \frac{\partial n_y}{\partial y} \right) dxdz + \left( n_z + \frac{\partial n_z}{\partial z} \right) dxdy + \frac{dM}{dt} + R \cdot dV \\
\text{(3.1)}
\end{align*}
\]

with

\[
\begin{align*}
\text{dM} &= c \, dV \\
\text{dV} &= dx dy dz \\
\Rightarrow \frac{dC}{dt} \, dx dy dz &= \left( \frac{\partial n_x}{\partial x} + \frac{\partial n_y}{\partial y} + \frac{\partial n_z}{\partial z} \right) dx dy dz - R \, dx dy dz \\
\text{(3.4)}
\end{align*}
\]

where

\[
\begin{align*}
n_x &= -D \frac{\partial C}{\partial x}, \quad n_y = -D \frac{\partial C}{\partial y}, \quad n_z = -D \frac{\partial C}{\partial z} \\
\Rightarrow \frac{dC}{dt} &= D \left( \frac{\partial^2 C}{\partial x^2} + \frac{\partial^2 C}{\partial y^2} + \frac{\partial^2 C}{\partial z^2} \right) - R \\
\text{(3.5)}
\end{align*}
\]

Considering cylindrical coordinates and generalizing the above equation we can write for a recipient
\[
\frac{\partial C}{\partial t} \gg \frac{\partial^2 C}{\partial z^2} \gg \frac{\partial^3 C}{\partial z^2} \frac{\partial C}{\partial z^2} \tag{3.7}
\]

\[
\frac{dC}{dt} = D \left( \frac{\partial^2 C}{\partial z^2} + \frac{J \partial C}{\partial t} \right) - R^* \tag{3.8}
\]

where \( J \) is a geometry factor which is dependent on the type of recipient:

\( J=0 \) for the infinite plate
\( J=1 \) for the infinite cylinder
\( J=2 \) for the sphere

Without chemical reaction

\[
R^* = 0 \tag{3.9}
\]

the mass balance for a migrant 'M' reads for an infinite plate:

\[
\frac{dC_M}{dt} = D_{M,Layer_U} \frac{\partial^2 C_M}{\partial x^2} \tag{3.10}
\]

Similarly, the mass balance for a simulant S' reads:

\[
\frac{dC_S}{dt} = D_{S,Layer_U} \frac{\partial^2 C_S}{\partial x^2} \tag{3.11}
\]

with the following possible boundary conditions:

- **Boundary (I):** Symmetry axis (if perfect insulation):

  \[
  \frac{\partial C}{\partial x} \bigg|_U = 0 \tag{3.12}
  \]

  If a layer is insulated on its left or right side, the boundary condition is derived from the symmetrical properties of the concentration distribution at the wall surface of a layer \( U \).

- **Boundary (II):** Considering the ‘left’ and ‘right’ sides of one interface, we can write at the interface between two layers \( U \) and \( U+1 \).

  \[
  n_x \bigg|_{Layer_U} = n_x \bigg|_{Layer_U+1} \leftrightarrow D_{Layer_U} \frac{\partial C}{\partial x} \bigg|_U = D_{Layer_U+1} \frac{\partial C}{\partial x} \bigg|_{U+1} \tag{3.13}
  \]

  This boundary condition is derived from comparison of fluxes at the interface between the different layers.

In the above scheme, the initial concentration of the migrant and solubility have to be set for each layer. To solve the problem we essentially make use of equation (3.8) under consideration of the boundary conditions. The solubility in each layer to ‘control’ the effect of the partition coefficient at the interface between two layers is also considered in the calculation procedure. A mass balance can be established similarly for both migrant and/or simulant.

### 3.3.2. Discretization of the layer domain

The packaging mass which is taken for the diffusion expressions can be treated as an ‘infinite’ surface of thickness ‘\( d \)’ (i.e. infinite in two directions -\( y \), \( z \) directions- and of layer thickness ‘\( d \)’ in the third -\( x \) direction-).

Using the generalized mass balance eq. 3.8 over one layer element in the packaging wall, we can relate the diffusion of e.g. a migrant 'M' in each layer. The scheme of the grid-point distribution applied for calculating the concentration distribution in each layer is presented below.
Fig. 3.3 - Description of a layer ‘domain’. The grid-point distribution is chosen with variable step lengths in the diffusion direction \( x \) as well as in the time direction.

The functions of the mass balance (eq. 3.8) are singular at the interface of the different layers and at the beginning of the diffusion process (times around \( 0 \)). Therefore the grid-point distribution must be chosen with variable step lengths (see Fig. 3.3). The generation of adaptive meshes allow the achievement of a desired resolution in localized regions and decreases by orders of magnitude the calculation time. Grid points are added in regions of high gradients to generate a denser mesh in that region and subtracted from regions where the solution is decaying or flattening out.

Discretization: Let us choose \( n \) for satisfying following conditions:

\[
\begin{align}
\lambda &\leq 1 \\
\lambda &= 1 \\
\end{align}
\]

describes with arbitrary units the length of a desired thickness inside one layer.

After computing a series expansion of the above equations with respect to the variable ‘\( k \)’, we obtain:

\[
\begin{align}
1 + k + k^2 + k^3 + \ldots + k^n &= \frac{k^{n+1} - 1}{k - 1} \\
\Rightarrow h \frac{k^{n+1} - 1}{k - 1} &< \lambda
\end{align}
\]

Taking the natural logarithm, we can solve the inequality 3.17 for ‘\( n \)’ and round the obtained value to the nearest integers towards minus infinity:

\[
n = \left\lfloor \ln \left( \frac{k - 1}{h} + 1 \right) \ln(k) \right\rfloor - 1
\]
The partial pressure profile for the migrant may now be expressed by substituting finite-difference approximations. Taylor series expansions of the second derivates are computed, with respect to the variable $x$, up to the order three. The series data structure represents an expression as a truncated series in one indeterminate node, expanded about the particular point $(i,j)$ (see Fig. 3.3). The detailed presentation of analysis is upon the scope of this help.

### 3.3.3. Programming

Using the boundary conditions expressed by eqs. 3.12-13 and eq. 3.8 which describes the diffusion in the bulk, the concentration distribution inside all layers can be computed for both migrant and the simulant. The initial concentrations of the migrant (in mg/kg units) have to be introduced for all layers at $t = 0$. The strong internal gradients are calculated very precisely due to the variable step lengths.
4.AKTS-SML

4.1. Basics
The use of AKTS-SML software can be described in four steps:

1. Define the package by creating the different articles of the package and filling their properties.
2. Predict the migration using different temperature profiles (iso, non-iso, worldwide climate, etc.).
3. Analyze the calculated outputs.
4. Check the conformity of the results with different legislations.

4.2. Package Structure
A package is a group of different articles, each article having different layers properties. For instance a bottle can be divided into two articles: the bottle cap and the bottle itself.

An article is composed of one or more layers of different sizes and properties.
Fig. 4.3 - An article is composed of multiple layers

Fig. 4.4 - Chemicals can be found in all layers

Chemicals can be found in one or more layers.

4.3. Creating packages and articles

Fig. 4.5 - The package panel for packaging and article creation
The package panel allows changing the geometry and the size of the package. The surface of each article can be defined in the grid.

4.4. The Wizard

When creating an article, many information and properties have to be filled. The role of the Article Creation Wizard is to help filling all this information step by step.

1. Surface: The surface of the article has to be entered first.
2. Layers: Then enter the number of layers and fill the information for each of them.
3. Chemicals: Enter the number of chemicals and fill the information for each of them.
4. Data: First fill the concentration of each substance in each layer, then the diffusion coefficients and finally the partition coefficient.

The package being fully created, it is possible to start calculating predictions by clicking on the ‘Run Prediction’ button.

Note: the Wizard is optional.
4.5. Article Properties

The article grid

![The article grid](image)

The article grid displays the layers (which can include the contact medium) and the substances. In the grid it is possible to customize the concentration, the diffusion coefficient and the partition coefficient for all chemicals and layers.

The button **Add layer** adds a new layer represented as a column in the grid. The button **Add substances** adds a new chemical represented as a row in the grid.

See more about:

- The layer properties ;
- The chemical properties ;
- The data (concentration and coefficients).

When all the properties of the article are filled, click on **Run Prediction...** to start a calculation process. See the Predictions chapter for more information.

Layers

![Layer properties](image)

The layer properties panel allows defining the properties of the current selected layer. **Type (of layer)** defines if the layer is a contact medium (typically food) or a polymer.
General description of the new SML software

Material specific constants for estimation of diffusion coefficients according to Piringer:

- Upper limit: $A'p: 2.21$, Tau: 0
- Realistic case: $A'p: 13.1$, Tau: 1577

Layer details:
- Molecular weight (g/mol): 1000000
- Glass transition temperature (°C): 53
- Electronegativity: 10

**Fig. 4.10 - Additional properties for polymer type layer**

**Database** allows browsing for a known polymer.

**Fig. 4.11 - Polymer database**

**Contact medium**

**Fig. 4.12 - Contact medium database**
Set to user defined allows customizing the properties of the polymer. When the polymer is set to user defined, it is possible to enter the properties of the polymer. Otherwise if the polymer is loaded from the database, its properties are filled automatically.

Reset layer allows setting the default values.

4.6. Substances properties

The substance properties panel allows defining the properties of the current selected substance. When the substance is set to user defined, it is possible to enter the properties of the substance. Otherwise if the substance is loaded from the database, its properties are filled automatically.

Database allows browsing for known substances (13'000 chemicals: additive, monomer, photoinitiator, pigment, solvent, etc.).
4.7. Data – concentration, diffusion and partition coefficients

The tab Data allows defining:
- the concentration;
- the diffusion coefficient;
- the partition coefficient.

**Diffusion coefficient**

The diffusion coefficient values can be entered manually when known, or it is possible to load a value from the database, to use an Arrhenius, Piringer or Brandsch calculation and even to enter a customized equation.

![Diffusion coefficient](image)

*Fig. 4.15 - Determination of the diffusion coefficients. The data properties shown are based on the current selected tab of the article grid.*

The diffusion coefficient values can be entered manually when known, or it is possible to load a value from the database, to use an Arrhenius, Piringer or Brandsch calculation and even to enter a customized equation.
**Partition coefficient**

![Partition coefficient interface](image)

**Fig. 4.16 - Determination of the partition coefficients. The data properties shown are based on the current selected tab of the article grid.**

The partition coefficient value can be entered manually when known. In case of liquid contact media the solubility can be entered, or the Pow.
5. Predictions and temperature profiles

When all properties of an article are filled, it is possible to proceed with prediction calculations by clicking on the prediction button.

![Run Prediction...](image)

*Fig. 5.1 - The prediction button*

Different types of predictions are available:

- Isothermal
- Non-Isothermal
- Stepwise
- Modulated
- Shock
- Worldwide
- STANAG
- Customized

5.1. Isothermal

In the isothermal conditions mode, it is possible to set a number of isotherms and the temperature difference ($\Delta T$) between each isotherm.

<table>
<thead>
<tr>
<th>Temperature</th>
<th>20 °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Delta T$</td>
<td>10 °C</td>
</tr>
<tr>
<td>Number of isotherms</td>
<td>5</td>
</tr>
<tr>
<td>Final Temperature</td>
<td>60 °C</td>
</tr>
</tbody>
</table>

*Fig. 5.2 - Isothermal conditions*

5.2. Non-Isothermal

In the non-isothermal conditions, the starting temperature and different heating rates can be defined.

<table>
<thead>
<tr>
<th>Starting temperature</th>
<th>20 °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heating rate (°C/min)</td>
<td></td>
</tr>
<tr>
<td>1 K/min</td>
<td></td>
</tr>
<tr>
<td>2 K/min</td>
<td></td>
</tr>
<tr>
<td>4 K/min</td>
<td></td>
</tr>
<tr>
<td>8 K/min</td>
<td></td>
</tr>
</tbody>
</table>

*Fig. 5.3 - Non-Isothermal conditions*
5.3. **Stepwise**

The stepwise conditions are a combination between isothermal and non-isothermal temperature modes. A number of cycles can be also fixed.

![Fig. 5.4 - Stepwise conditions](image)

5.4. **Modulated**

In the modulated conditions, it is possible to set an oscillatory temperature mode, i.e. a day/night cycle.

![Fig. 5.5 - Modulated conditions](image)

5.5. **Shock**

The shock temperature conditions simulate a rapid temperature raise. The frequency of the temperature shocks can be also defined.

![Fig. 5.6 - Shock conditions](image)
5.6. Worldwide

Fig. 5.7 - Worldwide conditions

5.7. STANAG

STANAG 2895 is a NATO Standardisation Agreement describing the principal climatic factors which constitute the distinctive climatic environments found throughout the world.

Fig. 5.8 - STANAG conditions
5.8. Customized

The customized prediction mode allows loading a file with a custom temperature profile, i.e. when using a datalogger.

![Customized conditions](image)

Fig. 5.9 - Customized conditions
6. Outputs

The output window shows the results of the prediction calculations. The window is divided in three parts:

- The results grid;
- The c(t) chart;
- The c(x, t) chart.

Moving the mouse pointer over the c(t) chart will update the results grid and the c(x, t) chart based on the time pointed on the c(t) chart.

6.1. The results grid

The grid shows the values of the concentration, the diffusion coefficients and the partition coefficients for all substances in all layers.

6.2. The c(t) chart

The c(t) chart shows the migration of the chemicals over time. The chemicals and layers to be displayed can be selected by using the checkboxes in the results grid.
6.3. The c(x,t) chart

The c(x,t) chart shows the migration of the chemicals into the different layers, the dotted line being the average concentration of a chemical inside a layer.

Fig. 6.3 - The c(x, t) chart
6.4. Comparison Output

The comparison output window allows comparing the calculation results of different outputs. To add an output to the comparison, drag and drop the output from the list on the left to the dedicated zone in the comparison output window.

*Fig. 6.4 - The comparison output window*
6.5. Sum Output

The sum output window allows adding the calculation results of outputs of same substances. To add an output to the comparison, drag and drop the output from the list on the left to the dedicated zone in the comparison output window.

Fig. 6.5 - The sum output window
In the last years migration modelling got more and more accepted and was introduced in legislation for plastic food contact materials and articles allowing for compliance assessment with applicable specific migration limits stipulated by legislation.

ADIPIC ACID - ADIPIC ACID

Properties
   Density (g/cm^3) : 1
   Molecular weight (g/mol) : 146.14
   POW : 0.08

Initial concentration
   POLYVINYL BUTYRAL : 450mg/kg

Partition coefficient
   POLYVINYL BUTYRAL / Primer : 1 (Solubility based)
   Primer / Aluminium : 1 (Known)
   Aluminium / HS Lacquer : 1 (Known)
   HS Lacquer / Contact Medium : 0.1397 (POW based)

Diffusion coefficient
   POLYVINYL BUTYRAL : 1.025E-12 cm^2/s ()
   Primer : 4.320E-11 cm^2/s ()
   Aluminium : 2.844E-35 cm^2/s ()
   HS Lacquer : 7.990E-09 cm^2/s ()
   Contact Medium : 1.000E-04 cm^2/s (Known)

BADGE - 2,2-BIS(4-HYDROXYPHENYL)PROPANE BIS(2,3-EPOXYPROPYL) ETHER

Properties
   Density (g/cm^3) : 1
   Molecular weight (g/mol) : 340.42
   POW : 3.84

Initial concentration
   Primer : 230mg/kg

Partition coefficient
   POLYVINYL BUTYRAL / Primer : 1.546 (Solubility based)
   Primer / Aluminium : 1 (Known)
   Aluminium / HS Lacquer : 1 (Known)
   HS Lacquer / Contact Medium : 0.6288 (POW based)

Diffusion coefficient
   POLYVINYL BUTYRAL : 1.077E-13 cm^2/s ()
   Primer : 4.538E-12 cm^2/s ()
   Aluminium : 2.908E-36 cm^2/s ()
   HS Lacquer : 8.393E-10 cm^2/s ()
   Contact Medium : 1.000E-04 cm^2/s (Known)
General description of the new SML software

**STYRENE - STYRENE**

**Properties**
- Density (g/cm$^3$) : 1
- Molecular weight (g/mol) : 104.15
- POW : 0

**Initial concentration**
- HS Lacquer : 100mg/kg

**Partition coefficient**
- POLYVINYL BUTYRAL / Primer : 0.00683 (Solubility based)
- Primer / Aluminium : 1 (Known)
- Aluminium / HS Lacquer : 1 (Known)
- HS Lacquer / Contact Medium : 0.1353 (POW based)

**Diffusion coefficient**
- POLYVINYL BUTYRAL : $1.927E-12$ cm$^2$/s
- Primer : $8.121E-11$ cm$^2$/s
- Aluminium : $5.347E-35$ cm$^2$/s
- HS Lacquer : $1.802E-08$ cm$^2$/s
- Contact Medium : $1.000E-04$ cm$^2$/s (Known)

**OCTADECYL 3-(3,5-DI-tert-BUTYL-4-HYDROXYPHENYL) PRO...**

**Properties**
- Density (g/cm$^3$) : 1
- Molecular weight (g/mol) : 530.38
- POW : 13.41

**Initial concentration**
- HS Lacquer : 350mg/kg

**Partition coefficient**
- POLYVINYL BUTYRAL / Primer : 5.675 (Solubility based)
- Primer / Aluminium : 1 (Known)
- Aluminium / HS Lacquer : 1 (Known)
- HS Lacquer / Contact Medium : 28.9 (POW based)

**Diffusion coefficient**
- POLYVINYL BUTYRAL : $1.971E-14$ cm$^2$/s
- Primer : $8.302E-13$ cm$^2$/s
- Aluminium : $5.470E-37$ cm$^2$/s
- HS Lacquer : $1.536E-10$ cm$^2$/s
- Contact Medium : $1.000E-04$ cm$^2$/s (Known)

**Time/Temperature conditions**
- Iso 20°C

**Migration**
- SML (mg/kg of contact medium): Specific Migration Limit
- QM (mg/kg of packaging): Quantity Maximum
- QMA (mg/dm$^2$ of packaging): Quantity Maximum per Area
- DL (mg/kg of contact medium): Detection Limit
- Green : Compliant
- Red: Not compliant

Fig. 7.1 - Legislation and compliance report (calculated migration values)
**General description of the new SML 5 software**

<table>
<thead>
<tr>
<th>Substance</th>
<th>Regulation</th>
<th>Migrant Limit</th>
<th>Migrant Concentration</th>
<th>Compliant</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADIPIC ACID</td>
<td>EU No 10/2011</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Swiss</td>
<td>SR 817.023.21</td>
<td>60</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>European Union</td>
<td>2002/72/EC</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>OCTADECYL 3-(3,5-DI-tert-BUTYL-4-HYDROXYPHENYL) PROPYL</td>
<td>EU No 10/2011</td>
<td>5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Swiss</td>
<td>SR 817.023.21</td>
<td>5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>European Union</td>
<td>2002/72/EC</td>
<td>5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>BADGE</td>
<td>EU No 10/2011</td>
<td>0.000E+00</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Swiss</td>
<td>SR 817.023.21</td>
<td>1.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>European Union</td>
<td>2002/72/EC</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>STYRENE</td>
<td>EU No 10/2011</td>
<td>1.663E-01</td>
<td>1.5</td>
<td>-</td>
</tr>
<tr>
<td>Swiss</td>
<td>SR 817.023.21</td>
<td>60</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>European Union</td>
<td>2002/72/EC</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Fig. 7.2 - Legislation and compliance report (migration limits)**
8. Sensitivity Analysis Methods

8.1. Introduction

Sensitivity analysis studies how the uncertainties in the model inputs \((X_1; X_2; \ldots; X_k)\) affect the model’s response \(Y\), which (for simplicity) we assume to be a scalar:

\[ Y = f(X_1; X_2; \ldots; X_k); \]

where \(f\) describes the implemented model.

A sensitivity analysis attempts to provide a ranking of the model’s input assumptions with respect to their contribution to model output variability or uncertainty. The difficulty of a sensitivity analysis increases when the underlying model is nonlinear, nonmonotonic or when the input parameters range over several orders of magnitude. Many measures of sensitivity have been proposed. For example, the partial rank correlation coefficient and standardized rank regression coefficient have been found to be useful. Scatter plots of the output against each of the model inputs can be a very effective tool for identifying sensitivities, especially when the relationships are nonlinear. In a broader sense, sensitivity can refer to how conclusions may change if models, data, or assessment assumptions are changed, see [1] for more details on the subject.

The analysis methods available in SML software are:

- Monte Carlo
- Fourier Amplitude Sensitivity Test (FAST)
- Sobol

8.2. Monte Carlo Simulation (MCS)

Monte Carlo Simulation (MCS) is a widely used method for uncertainty or sensitivity analysis. It involves random sampling from the distribution of inputs and successive model runs until the desired accuracy of the outputs is reached. Not only the means and variances but also the distributions of input parameters are required to run the MCS. In the present version of SML only Gaussian (normal) distribution have been implemented for the different input parameters.

![Random sampling from the distribution of inputs (Gaussian (normal) distribution).](image)

Fig. 8.1 - Random sampling from the distribution of inputs (Gaussian (normal) distribution).
The main advantage of the MCS is its general applicability. MCS suffers for its computational requirements since thousands of repetitive runs of a model are required to reach convergence. High-speed personal computers have minimized the computational challenges. Another limitation of MCS is the need for user-specified rules for determining the number of simulations required, see [2-4] for more information and recommendation on the subject.

Sensitivity measures based on the MCS approach include regression-based measures (Standardized Regression Coefficients (SRC), Partial Correlation Coefficients (PCC), Standardized Rank Regression Coefficients (SRRC), Partial Rank Correlation Coefficients (PRCC)). Some of them have been implemented in the present version of SML and are described below.

8.2.1. Correlation coefficient (CC) and partial correlation coefficients (PCC)

The correlation coefficient (CC) usually known as Pearson's product moment correlation coefficients, provide a measure of the strength of the linear relationship between two variables $x$ and $y$ and is denoted by $\text{corr}(x; y)$, see for example [5] for more information on the definition of CC.

The correlation coefficient measures the extent to which $y$ can be approximated by a linear function of $x$, and vice versa.

In particular if exactly $y = a + bx$, then $\text{corr}(x; y) = 1$, if $b = 1$ and $\text{corr}(x; y) = -1$, if $b = -1$.

CC only measures the linear relationship between two variables without considering the effect that other possible variables might have.

When more than one input factor is under consideration, as it usually is, the partial correlation coefficients (PCCs) can be used instead to provide a measure of the linear relationships between two variables when all linear effects of other variables are removed. PCC between an individual variable $x_i$ and $y$ can be written in terms of correlation coefficients, see for example [5]. It is denoted by $pcc(x_i; y)$. PCC characterizes the strength of the linear relationship between two variables after a correction has been made for the linear effects of the other variables in the analyses.
**Fig. 8.3** – Correlation coefficients (CC) providing a measure of the strength of the linear relationship between two variables \(x\) (variable parameters in the article) and \(y\) (migration).

**Fig. 8.4** - Scatter plots illustrating relationships between the input factor \(X_i\) (variable parameters in the article) and the output \(Y\) (migration).
A plot of the points \([X_i, Y_j]\) for \(j = 1, 2;...;N\) usually called a scatter plot can reveal nonlinear or other unexpected relationships between the input factor \(X_i\) and the output \(Y\). Scatter plots are undoubtedly the simplest sensitivity analysis technique and is a natural starting point in the analysis of a complex model. It facilitates the understanding of model behavior and the planning of more sophisticated sensitivity analysis.

### 8.2.2. Rank correlation coefficient (RCC) and partial rank correlation coefficients (PRCC)

Since the correlation coefficient and partial rank correlation coefficient methods are based on the assumption of linear relationships between the input-output factors, they will perform poorly if the relationships are nonlinear. With SML-Software, rank transformation of the data is possible too. This concept can be used to transform a nonlinear but monotonic relationship to a linear relationship. When using rank transformation the data is replaced with their corresponding ranks. The usual correlation procedures are then performed on the ranks instead of the original data values. Spearman rank correlation coefficient (RCC) are corresponding CC calculated on ranks and partial rank correlation coefficients (PRCC) are PCC calculated on ranks.

Rank transformed statistics are more robust, and provide a useful solution in the presence of long tailed input-output distributions. A rank transformed model is not only more linear, it is also more additive. Thus the relative weight of the first-order terms is increased on the expense of higher-order terms and interactions see for example [5].

### 8.3. Variance based methods for sensitivity analysis

The main idea of the variance-based methods is to quantify the amount of variance that each input factor \(X_i\) contributes with on the unconditional variance of the output \(V(Y)\).

We are considering the model function: \(Y = f(X)\), where \(Y\) is the output and \(X = (X_1;X_2;...;X_k)\) are \(k\) independent input factors, each one varying over its own probability density function. The values of the input parameters are not exactly known. We assume that this uncertainty can be handled by using random variables \(X_j\), \(j = 1;...;k\) of known distributions. Then the model output is also a random variable \(Y = f(X_1;...;X_k)\).

The first order effect for the input factor \(j\) is the fraction of the variance of the output \(Y\) which can be attributed to the input \(X_j\) and is denoted by \(S_j\), see for example [5].

To estimate the value of \(S_j\) we require realizations of the input distributions and the associated model evaluations. The ratio \(S_j\) was named first order sensitivity index by Sobol [6]. The first order sensitivity index measures only the main effect contribution of each input parameter on the output variance. It doesn't take into account the interactions between input factors. Two factors are said to interact if their total effect on the output isn't the sum of their first order effects. The effect of the interaction between two orthogonal factors \(X_i\) and \(X_j\) on the output \(Y\) can be computed (see for more details [5]) and is known as the second order effect. Higher-order effects can as well be computed, see for example [5].

A model without interactions is said to be additive, for example a linear one. The first order indices sums up to one in an additive model with orthogonal inputs. For additive models, the first order indices coincide with what can be obtained with regression methods. For non-additive models we would like to know information from all interactions as well as the first order effect. For non-linear models the sum of all first order indices can be very low.

The sum of all the order effects that a factor accounts for is called the 'total' effect [7]. So for an input \(X_i\), the total sensitivity index \(ST_i\) is defined as the sum of all indices relating to \(X_i\) (first and higher order).

There are different techniques to obtain these sensitivity indices, such as Sobol's indices, Jansen's Winding Stairs technique, (Extended) Fourier Amplitude Sensitivity Test ((E)FAST).

In the present software, two methods are implemented, the FAST method and the Sobol's indices based on Jansen's Winding Stairs technique.
8.4. **Fourier Amplitude Sensitivity Test (FAST)**

The Fourier Amplitude Sensitivity Test (FAST) was proposed already in the 70's [8-10] and was at the time successfully applied to two chemical reaction systems involving sets of coupled, nonlinear rate equations.

The Fourier Amplitude Sensitivity Test (FAST) is a sensitivity analysis method which does not use a Gaussian distribution. Rotating vectors are assigned to each variable, and each has a unique frequency and an amplitude of the "mean". A lot of input sets are generated, making the variables oscillating. A Fourier analysis is then applied on the results. The number of runs depends only on the number of variables, but it is not linear.

Note that the graphs of the FAST method are the same than the graphs of Sobol, except that FAST shows only the local sensitivity.

![Figure 8.5 - Quantification based on FAST analysis of the amount of variance that each input factor Xi (all variables of the articles) contributes with on the unconditional variance of the output V (Y).](image1)

![Figure 8.6 - FAST analysis results. Sensitivity S(v) of each variable (influence of each examined variable on the migration results).](image2)
8.5. Sobol's indices via Winding Stairs

Chan, Saltelli and Tarantola [11] proposed the use of a new sampling scheme to compute both first and total order sensitivity indices in only $N \times k$ model evaluations. The sampling method used to measure the main effect was called Winding Stairs, developed by Jansen, Rossing and Deemen in 1994 [12].

A first set of variables simply comes from the Gaussian distribution. Then a lot of other set of input of variables are generated from the first set and will be used in complex mathematics analysis afterward (For example: if one enters 10 runs and has 1 substance with 4 variables, it will run the simulations $(4+1) \times 10$ times).

The above figures illustrate the total sensitivity $S_t(v)$ of the variables (influence of all variables on the migration results) and the evolution of the total sensitivity as a function of time. In some cases there are "unexplained" values. This situation can happen when the percentage calculation doesn't reach 100%. Two cases are possible:

- The number of runs chosen to perform the calculations is not sufficient;
- Not enough variables are chosen to apply the method correctly.

Comments about our example:

All methods clearly demonstrate for our examined article that the initial concentration of the migrant (OCTADECYL 3-(3,5-DI-tert-BUTYL-4-HYDROXYPHENYL) PROPIONATE) plays the most important role concerning its migration from the article to the contact medium. The other parameters such as the thickness of both layers and the solubility of migrant in the contact medium have in comparison a negligible influence on the migration.
General description of the new SML software