f3.0.2

FACET Exposure Assessment Tool

Technical Documentation

Version 3.0.2

March 2017

1: Introduction

This document provides an outline of the exposure algorithms used in the FACET 3.0.2 prototype. The document is divided into four sections.

Section 2 provides a description of how the exposure algorithm works in general for flavouring substances. Dietary exposure due to added and natural flavourings is dealt with in separate sections.

Section 3 provides a description the exposure algorithm for additives, including the treatment of Maximum Permitted Levels (MPLs), ingredient fractions, and data provided by industry.

Section 4 provides a description of how the exposure algorithm works for food packaging migrants. This section also describes how packaging is decomposed within the FACET project, the requirements for the packaging migration model, and how this information is linked to the food consumption diaries.

2: FACET Exposure Algorithm for Flavourings

Overview

In FACET, two sources of dietary exposure to flavouring substances are considered; exposure to added flavourings and exposure to naturally occurring flavourings. Total dietary exposure is considered as the sum of the two sources.

FACET employs a diary driven approach to determine the population distribution of exposure to flavourings in foods. This requires two basic inputs:

A Diary of food consumption events.

A Substance Concentration table of the concentrations of the flavourings of interest in the foods that are consumed in the Diary.

With this information as input, the *basic* algorithm to determine the population profile of exposure is in Figure 1 .

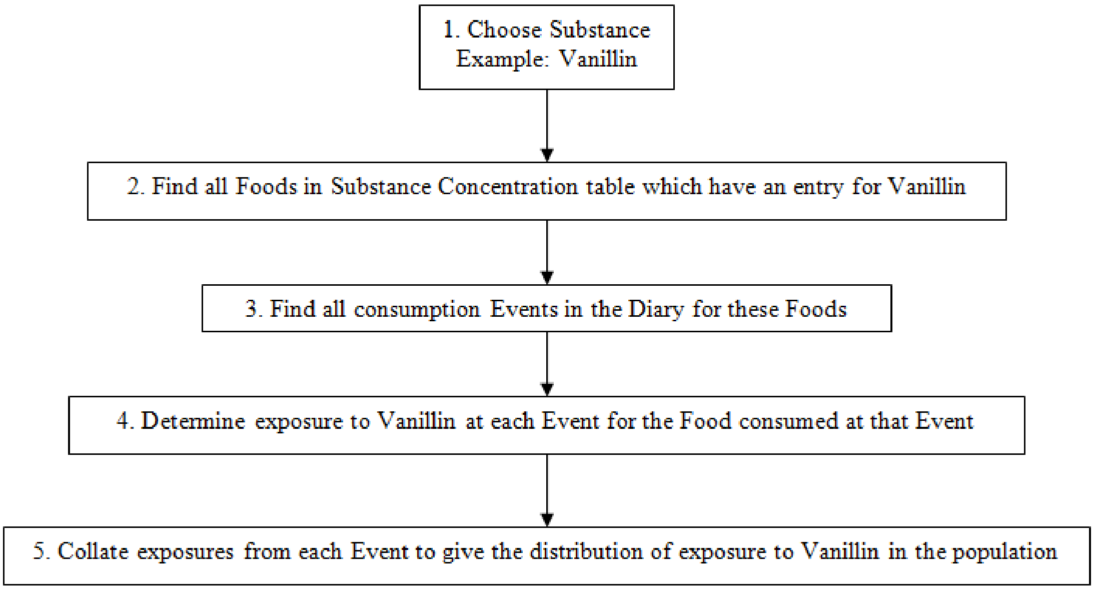

Figure 1: Basic overall algorithm to determine population profile of flavouring exposure

This document details this approach for flavourings, as implemented in FACET 3.0.2

Exposure Algorithm for Added Flavourings

In this section we outline the exposure algorithms for added Flavourings. There are approximately 2750 flavouring substances that the FACET software needed to be able to choose from. 41 of these substances are target flavourings as decided by WP2, for which there were more detailed concentration data available via the flags system. This allowed for a more refined determination of exposure for each of these 41 substances.

Screening Methods

A number of screening techniques have been implemented in FACET to estimate dietary exposure to flavourings. These are rough calculations of exposure based on some standard parameters. The following screening methods have been implemented:

- Theoretical Added Maximum Daily Intake (TAMDI)
- Modified Theoretical Added Maximum Daily Intake (mTAMDI)
- Single Portion Added Technique (SPET)
- Added Portions Exposure Technique (APET)

TAMDI and mTAMDI

The underlying assumption of the TAMDI and mTAMDI calculations is that a person consumes a standard portion of flavoured foods and beverages per day. The consumption amounts are multiplied by the use levels of the flavouring of interest and summed. For TAMDI, average use levels of the flavouring are considered, and for mTAMDI upper use levels of the flavouring are considered.

The formula to calculate TAMDI is given by:

TAMDI (mg /day) = (324 × UUL) + (133.4 × UUL) + (27 × UUL) + (20 × UUL) + (20 × UUL) + (20 × UUL) + (2 × UUL)

where

UUL = Upper Use Level of flavouring

mTAMDI (mg /day) = (324 × AUL) + (133.4 × AUL) + (27 × AUL) + (20 × AUL) + (20 × AUL) + (20 × AUL) + (2 × AUL)

where

AUL = Average Use Level of flavouring.

Standard Portions and food groups for the TAMDI calculation can be seen in Table 1.

Table 1: Standard Portions for the TAMDI and mTAMDI calculations

Food Groups	TAMDI Consumption (g/day)
Food	133.4
Beverages	324
Exceptions:	
a) Candy, confectionary	27
b) Condiments, seasonings	20
c) Alcoholic beverages	20
d) Soups, savouries	20
e) Other exceptions	2

APET and SPET

The SPET calculation is also based on multiplying average use levels by standard portion sizes in given food categories. For flavouring substances with use levels in multiple food categories, only the food category resulting in the highest potential dietary exposure is considered. The calculated figure is divided by 1000 and by a standard body weight of 60kg to find exposure in mg /kg body weight in adults.

The APET calculation is similar to SPET, based on slightly different food groupings and same portion sizes. It is calculated by summing the highest potential dietary exposure within each of the two groups (beverage and food). The calculated figure is divided by 1000 and by a standard body weight of 60kg to find the exposure in mg /kg body weight in adults. The calculation can be performed for children by multiplying the adult portions by 0.63 and dividing the result by 15kg for the bodyweight. The technique can also be applied to infants, by using another set of food categories and portion sizes and summing potential dietary exposure of all categories, and dividing by a body weight of 10kg.

Refined Exposure

Refined exposure to flavouring substances is found via the use of national food consumption survey and a database of flavouring concentrations. Two important features of the exposure calculation for Flavourings:

- There were eight different sources of concentration data that the user can choose from. These are:
    - IOFI JECFA 2006 - International Organisation of the Flavour Industry
    - IOFI JECFA 2007
    - IOFI JECFA 210
    - IOFI DG SANCO 2007
    - FEMA - Flavour and Extract Manufacturers Association
    - CoE – Council of Europe
    - EFFA - European Flavouring and Fragrance Association
    - Young et al.

  Each of these sources uses a different food coding system; some at a very aggregated level, others at a more refined level. Depending on the database used, the exposure assessment can have typical use levels, upper use levels, or both. If both typical and upper use levels are present, the option of using a fitted parametric distribution for the flavouring concentration is also available to the user. These different sources have been recoded into the FACET food categories for use in FACET software.
- There are three different levels of refinement for the exposure calculation. These are explained in greater detail below.

The overall exposure algorithm is the same as outlined in the overview, but with one added stage as mentioned above:

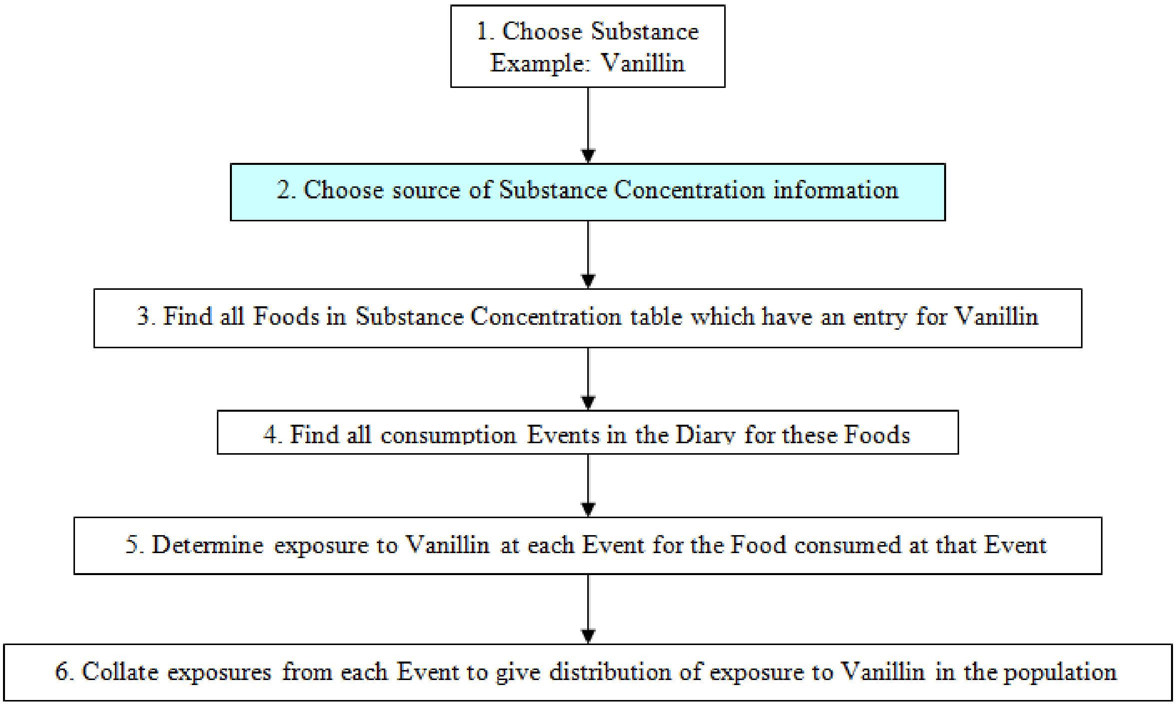

Figure 2: Basic overall algorithm to determine population profile of substance exposure for flavourings

The core part of the exposure algorithm is now step 5. Furthermore, for flavourings there are three possible levels of exposure calculation that can be undertaken. As mentioned previously, the range of options available to the user depend on the choice of database and flavouring. For a given assessment and flavouring, the user has the option of calculating exposure with typical use levels, upper use levels, or a fitted parametric distribution, and with or without probability of addition data. Note that in call cases where a parametric distribution is used, a concentration is allocated by random sampling.

Level 1: Basic Assessment Level. This level of exposure assessment can be undertaken for any of the 2750 + substances in the list of flavouring substances.

All eating events involving foods with a non-zero concentration value for that substance are used in the determination of exposure.

Level 2: More Refined Level. This level of exposure assessment can be undertaken for any of the 2750 + substances in the list of flavouring substances. The following options are possible:

All eating events in Level 1 are used, except events marked with a FACET flavouring flag “Without Added Flavourings”.

All eating events in Level 1 are used, except events marked with a FACET packaging flag “Unprocessed” in the food category “F.3 Fruits, nuts and seeds”.

All eating events in Level 1 are used, except events marked with a FACET flavouring flag “Without Added Flavourings” and eating events with a FACET packaging flag “Unprocessed” in the food category “F.3 Fruits, nuts and seeds”.

Level 3: Most Refined Level. This level of exposure assessment can only be undertaken for one of the 41 target flavouring substances of the FACET project.

All eating events in Level 1 are used, and the full FACET flavouring flag system is used in the determination of exposure. This is detailed further below. Note that the options presented at Level 2 are available here too.

The assessment level available depends on the substance and database chosen, and the particular options the user selects.

In order to illustrate these three levels of assessment, consider the following example:

Five consumption events in the Diary for one food category, F14.4.1 – “Gaseosa: non-alcoholic water-based drinks with added carbon dioxide, sweeteners and flavourings”

Entries in the Substance Concentration table for two flavourings: Raspberry Ketone and Vanillin. Note that in this example, both typical and upper concentrations are available for use in the assessment.

Table 2: Food Diary

Event	Subject	Day	Food	Amt(g)	Flag 6	Flag 7	Flag 8	Flag 9
1	1324	1	F14.4.1	100	1:Without	-3:NFI	-3:NFI	-3:NFI
2	1011	1	F14.4.1	250	2:With	-3:NFI	-3:NFI	-3:NFI
3	2422	2	F14.4.1	150	19:Raspberry	18:Strawberry	-3:NFI	-3:NFI
4	1056	2	F14.4.1	150	6:Vanilla	-3:NFI	-3:NFI	-3:NFI
5	1066	2	F14.4.1	200	-3:NFI	-3:NFI	-3:NFI	-3:NFI

Table 3: Substance Concentration

Food	Substance	Typical Conc (mg/kg)	Upper Conc (mg/kg)
F14.4.1	Raspberry Ketone	0.05	0.1
F14.4.1	Vanillin	0.1	0.15

Note: In both the Food Diary and Substance Concentration tables (Table 2 and Table 3, respectively), the abbreviated flag settings are:

1:Without = Without Added Flavourings

2:With = With added flavourings (not precisely known or not in the list of specific flags)

-3:NFI = No Further Information.

Level 1 Assessment:

- Flag settings are not used.
- In this example, all 5 eating events have an exposure to both Raspberry Ketone and Vanillin.
- The exposure to each substance in each event is calculated as in Figure 2.
- For example, in eating event 1, the exposure to Raspberry Ketone is 0.005 mg, and the exposure to Vanillin is 0.01mg, if typical concentration values are used.

Level 2 Assessment:

- Events with a flag value "Without Added Flavourings" are ignored, events with a flag value "Unprocessed" in the food category "F.3 Fruits, nuts and seeds" are ignored, or both types of events are ignored. These options depend on what is chosen by the user.
- In this example, event 1 can be ignored, and only eating events 2-5 inclusive have an exposure to both Raspberry Ketone and Vanillin.
- For these 4 eating events the exposure to both Raspberry Ketone and Vanillin is exactly as in the Level 1 calculation.
- The overall population exposure is changed because there are fewer eating events that contribute to the exposure.

Level 3 Assessment:

This level only applies to substances that are in the list of 41 target substances of the FACET project. The substances in the present example, Raspberry Ketone and Vanillin, are both in this list.

This level requires a further table of probability of addition values for each of the 41 target substances in each FACET food category for each possible value of the FACET flavouring flags, as well as refined concentration levels when these are available. Currently there are 43 values of the FACET flavouring flag. See Table 4 for an example of these entries

Table 4: Probability of Addition

Substance	Food	Flag Value	Probability of Addition	Refined concentration level (mg/kg)
Raspberry Ketone	F14.4.1	9:Fruit, fresh and dry	0.6	
Raspberry Ketone	F14.4.1	10:Tropical Fruits	0.1	
Raspberry Ketone	F14.4.1	11:Forest Fruits	0.9	
Raspberry Ketone	F14.4.1	18:Strawberry	0.5	
Raspberry Ketone	F14.4.1	19:Raspberry	0.8	
Vanillin	F14.4.1	5:Coffee	0.01	
Vanillin	F14.4.1	6:Vanilla	0.7	0.12
Vanillin	F14.4.1	7:Caramel	0.45	
Vanillin	F14.4.1	8:Cola Flavour	0.8	
Vanillin	F14.4.1	10:Tropical Fruits	0.07	
Vanillin	F14.4.1	18:Strawberry	0.36	

All Presence Probability values are in the range [0,1], and have been assigned by expert judgement. In FACET 3.0.2, only isopentyl acetate (Flavis number 9024) has this kind of data assigned.

At this level of exposure assessment:

Only eating events with a non-zero probability of addition value for one of the flags associated with it are used in the exposure calculation.

In this example, eating event 2 has an exposure to both Raspberry Ketone and Vanillin, and event 3 has an exposure to Vanillin.

The concentration values used are the same as in Level 1 and Level 2 assessments, but now they are moderated by the values in the Probability of Addition table.

In cases where refined concentration is available, this data is used in preference to typical concentration levels from the selected database. Thus in the above example, 0.12 mg/kg is selected as the concentration for exposure in event 4, if typical concentration levels are being used in the assessment. If the assessment is being performed using upper use levels, then the maximum value between the upper and refined level is used. Thus in the above example, 0.15 mg/kg is used to estimate exposure at event 4, if upper use levels were used in the assessment. If the exposure assessment is being performed using a fitted distribution, the refined concentration level is used in preference to a random sample from the distribution.

It may happen that a consumption event has more than one flavouring flag assigned to it, giving rise to more than one possible match from the Probability of Addition table. This is the case for consumption event 3 in the above example.

Table 5: Probability of Addition

Substance	Food	Flag Value	Probability of Addition
Raspberry Ketone	F14.4.1	18:Strawberry	0.5
Raspberry Ketone	F14.4.1	19:Raspberry	0.8

In this case, the larger of the two probabilities of addition values is taken into account. If the case arose that there were two possible concentrations and two possible probabilities of addition values, the largest expected value across the possible values are taken into account. This rule extends to multiple combinations, and is explained in Appendix A. In the example in Table 5, the value of 0.8 is used to estimate exposure for consumption event 3.

Probability of addition values are interpreted as Bernoulli distributions in FACET, meaning they take a value of 1 or 0 with a given probability.

Exposure Algorithm for Natural Flavourings

In addition to considering dietary exposure to added flavourings, natural sources of exposure may also be considered for the 41 target flavourings in the FACET project. For this purpose, a database of natural occurrence levels has been developed, using the TNO database. The following considerations are necessary for estimating dietary exposure to natural flavourings in FACET:

- The TNO database does not consider all possible sources of natural concentration for all FACET food codes. Thus, it may be necessary to consider concentration values calculated from the likely presence of ingredients in different food categories.
- Some consumption events have flags that have a generic description, e.g. “Fruit, fresh and dry”. Calculations can be made based on this description.
- The natural concentration of flavouring in a food can due to multiple components, e.g. plain yoghurt with strawberries. Both plain yoghurt and strawberries may have the same naturally occurring flavouring, so the final concentration can be found by summing.
- Correction factors are needed to transform the concentration of a flavouring into the concentration in the food as consumed, e.g. concentration measured in coffee beans.
- In general, average estimates of flavouring concentrations are used.

Four tables are used to assign natural concentration data to the FACET food categories. Each of these is explained in detail below.

Natural Occurrence Concentration Data

This table contains natural concentration data and for a number of flavouring/FACET Food category combinations. For a given pair, either a fixed value, or a minimum and a maximum concentration value is presented. The table also contains correction factors to be applied to each flavouring/food concentration. The following rules applying when selecting a concentration from this table:

- If minimum and maximum concentrations are both present, use mid-range of two values.
- If the typical value is present, use that value.
- If only the maximum is present, use half that value.
- The correction factor is used in all cases. If a mid-range is used, multiply mid-range by correction factor.

An example of entries in the table can be seen below, showing two food codes; “F14.5.1.2: Coffee and coffee extracts” and “F3.3.2: Pineapple”.

Table 6: Natural Occurrence Concentration Data

Substance	Food Code	Min (mg/kg)	Max (mg/kg)	Fixed Value (mg/kg)	Correction Factor
Furanone	F14.5.1.2	25	50		0.375
Furanone	F3.3.2			0.01	1

Natural Occurrence Food Category Table

For a given food code, this table shows what other food codes can be contained in this food and in what proportions. A simplified extract from the table is shown below. For each food code, the other foods that were considered in the calculation are indicated by a “0” value, as well as their proportions and how to combine multiple values.

Table 7: Natural Occurrence Concentration Data

Food Code	Type of Estimation	F1.1.1	F1.1.2	F18	Min Proportion (%)	Max Proportion (%)
F1.1.1					100	100
F1.1.2		0	0		85	90
F1.1.3			0			
...	...	...	...	...	...	...
F18						

The “Type of Estimation” column contains the following calculation types:

- “Mid-range of unique value” - use the single value from concentration data table. This should only apply when there are no multiple “0” values.
- “Mean of mid-range and 0 values” - use the mean of all possible mid-range values present.
- “Median of mid-range” - use the median of the possible concentration values present.

Natural Occurrence Flag Setting Table

For a given flag, this table shows what foods are used to calculate a concentration value for a particular flag setting. A simplified extract from the table is shown below. For each flag, the other foods that have to be considered in the calculation are indicated by a "0" value, as well as how to combine multiple values.

Table 8:Natural Occurrence Concentration Data

Flag Code	Type of Estimation	F1.1.1	F1.1.2	...	F18
5: Coffee				...	
6: Vanilla		0	0	...	
...			0	...	
...	...	...	...	...	...
43: NFI				...	

The "Type of Estimation" column contains the following calculation types:

- "Mid-range of unique value" - use single value from concentration data table. This should only apply when there are no multiple "0" values.
- "Mean of mid-range and 0 values" - use the mean of all possible mid-range values presented.
- "Median of mid-range" - use the median of the possible concentration values present.

Natural Occurrence Recipe Data

This table shows, for a given flag and FACET food category, the minimum and maximum ingredient fraction, and the rule for combining the different contributions to natural exposure. A simplified extract from the table is shown below. The mean of the minimum and maximum ingredient fractions is used in all calculations.

The “Action” field contains two possibilities:

Sum - sum the various ingredients with the other contributions to give the total concentration in food.

Substitute - substitute the value from the recipe table for the value previously calculated.

Table 9: Natural Occurrence Recipe Data

Food Code	FACET Flag	Min Proportion (%)	Max Proportion (%)	Action
F1.1.1	3	0	9	Sum
	4	0	9	Sum
	5	0	9	Sum
...	...	...	...	...
F18	12	12	35	Substitution
	13	12	35	Substitution
	14	12	35	Substitution

For eating occasions with multiple flags that can all contribute to exposure, the mean of the contributions is used to calculate the total concentration.

Calculating Exposure to Natural Flavourings

1. Estimate exposure where concentration data is given directly- use consumption events in the diary for foods that have an entry in the Natural Occurrence Concentration Data table.

2. Estimate exposure by finding the concentration of a substance in foods in the diary using the Natural Occurrence Food Category Table.

3. Use dietary events with flags. Recipe proportions can be estimated from the Natural Occurrence Recipe Data table, and what foods are used with what flags can be estimated from the Natural Occurrence Flag Setting table.

4. Estimate overall exposure to flavourings by combining estimates from steps 2 and 3 by using the rule indicated in the Action column from the Natural Occurrence Recipe Data table.

Total Dietary Exposure to Flavourings

In order to assess total dietary exposure to a flavouring substance, both added and natural sources of exposure must be considered. Total dietary exposure is given by the sum of both sources of exposure, per eating event.

Matching Information at Different Food Levels

An issue arises when it has only been possible to describe a food at a higher level in the FACET food categorisation hierarchy. In this discussion, “higher” means fewer dots in the food category code, “lower” means more dots, e.g. F14.4 is a “higher” level than F14.4.1, which is at a “lower” level.

Consider eating events of the following foods:

- F17.1.4 = “Milk analogues”
- F17.1.4.1 = “Soy and other vegetable milk”
- F17.1.4.2 = “Beverage whiteners”
- F14.3 = “Fruit and vegetable nectars”
- F14.3.1 = “Fruit nectar”

and the corresponding concentration information for a single Flavouring, Raspberry Ketone.

Table 10: Diary

Event	Subject	Day	Food	Amount (g)
101	1043	2	F17.1.4	150
102	2458	2	F17.1.4.1	100
103	2349	2	F17.1.4.2	110
104	3142	2	F14.3	250
105	1113	2	F14.3.1	250

Table 11: Substance Concentration

Food	Substance	Presence Probability	Concentration
F17.1.4.1	Raspberry Ketone	0.15	0.1
F17.1.2.2	Raspberry Ketone	0.75	0.3
F14.3	Raspberry Ketone	0.95	0.2

If we want to determine the exposure to Raspberry Ketone in these eating events, we immediately see that there is a problem at Events 101 and 105:

- Event 101: there is no entry in the Substance Concentration table for F17.1.4. However, there are entries for foods at the *next lowest* level in the food categorisation hierarchy (F17.1.4.1 and F17.1.4.2).

- Event 105: there is no entry in the Substance Concentration table for F14.3.1. However, there is an entry for the food at the *next highest* level in the food categorisation hierarchy, F14.3.

In general there are 4 possible scenarios when matching foods between the Diary and the Substance Concentration table:

Scenario	Food Level in Diary	Food Level in Substance Concentration
1	Low	Low
2	High	High
3	Low	High
4	High	Low

With reference to the example eating events:

- Events 102 and 103 are both in Scenario 1
- Event 104 is in Scenario 2
- Event 105 is in Scenario 3
- Event 101 is in Scenario 4

There is no difficulty with Scenarios 1 and 2 – each one uses a straightforward match between the Diary and Substance Concentration tables. The issue is how to deal with Scenarios 3 and 4.

Scenario 3: Low level in Diary, High level in Substance Concentration

This is the more straightforward of the two scenarios. If we have no concentration information at the low level, but we do have concentration information at the high level, we simply use the high level information.

In our example, for exposure to Raspberry Ketone at Event 105, we use the Substance Concentration entry for F14.3.

Scenario 4: High level in Diary, Low level in Substance Concentration

In this scenario, we need to specify concentration information for the higher level food, but where we only have concentration information for foods at a lower level. In order to do this we need to know the distribution of foods in the next level lower in the hierarchy. This requires the information in the following table:

Table 12: Food Level Proportions

FACET Food Code	FACET Food Codes at next lowest level	Proportion
F17.1.4	F17.1.4.1	0.30
F17.1.4	F17.1.4.2	0.70

Note that the proportions must sum to 1.0 for each food at the higher level. This table generalises to matching at any two adjacent levels in the hierarchy, e.g. the table can define the probabilities of a set of level 2 food categories for its level 1 food category. This table is populated using the distribution of known consumption events in the diary; i.e. the frequency with which consumption events are reported at the lowest level. In the absence of the distribution of this data, the exposure algorithm randomly sampled from the different foods in the lower tier, assuming that each food is equally likely.

Flag Settings

When determining the distribution of food codes for a given food category, a combination of food code and flag settings is considered to be a unique food. The distribution of food codes at the lowest level is always calculated, with weightings assigned to all lower level food groups and flag settings reported in the diary. If a higher level food category is reported with a particular flag set, it is assumed that the lower food groups inherit that flag set and have equal weighting.

Examples

Diary:

F14.3.1 – “Fruit nectar” reported 10 times with flag set (i).

F14.3.2 – “Vegetable nectars” reported 20 times with flag set (i).

Total consumption events in F14.3 – “Fruit and vegetable nectars” = 30.

Assumption:

Consumption events described as F14.3 – “Fruit and vegetable nectars” with flag set (i) are assigned to F14.3.1 – “Fruit nectar” with flag set (i) with a weighting of 10/30, and assigned to F14.3.2 – “Vegetable nectars” with flag set (i) with a weighting of 20/30.

Diary:

F14.3 – “Fruit and vegetable nectars” reported with flag set (i).

Assumption:

F14.3.1 – “Fruit nectar” and F14.3.2 – “Vegetable nectars” are both equally likely, both having flag set (i).

Consumer Loyalty

The user has the option of performing an exposure assessment either with or without the consumer loyalty model. The consumer loyalty model is most relevant to assessments where a concentration is allocated randomly, i.e. for assessments with probability of addition and a distribution for concentration. The default setting is that subjects in an exposure assessment are 0% loyal to the flavouring concentration they are initially allocated; i.e. there is no loyalty. If an exposure assessment is performed with the consumer loyalty model invoked, the user has to select what food categories consumers will be loyal to. Then, it is assumed that every subject in the assessment is 100% loyal to the flavouring concentration, additive concentration, or migrant concentration they are initially allocated, within the selected food categories. Thus, all subsequent consumption events involving the same subject and the same food category are allocated the same flavouring concentration, additive concentration, or migrant concentration. In all cases, the implicit assumption is that the concentration allocated to the subject represents the concentration associated with a particular brand.

The hierarchical food coding system in FACET also has to be taken into account. Thus, if the user specifies that consumers at loyal to a food at a higher tier, it is assumed that this loyalty applies to the lower tiers also.

The consumer loyalty model applied when the concentration data for flavourings in foods is in the form of a fitted distribution (based on the maximum and typical use levels of flavouring substances in industry). This is the case regardless of whether the flavouring is one of the 41 target flavourings (for which more detailed concentration data is available) or one of the other 2700+ flavourings.

Determining exposure to a flavouring at a consumption event involving a given food requires sampling from this distribution. For the consumer loyalty model, a subject is initially allocated a random sample from the concentration distribution for a particular food/flavouring concentration. All subsequent consumption events for the same food for the same subject is then allocated the same concentration.

Exposure Calculations

The following are the principal values calculated and outputted by the software:

- Substance exposure per kilogram of bodyweight per day
- Absolute substance exposure per day
- Food intake per kilogram of bodyweight per day
- Absolute food intake per day

The above values are presented by the FACET Food Categories. Statistics on these values are presented along with estimates of the error on the statistic in each case, as described in the next section.

Monte Carlo Sampling and Statistics

In order to accurately determine exposure to a substance in a population, Monte Carlo sampling is used. Re-simulation of consumption events in the food consumption diaries is used to build up a profile of exposure in the population, which captures the variability and uncertainty in the various inputs, for example chemical concentration data.

Once the desired number of iterations is achieved, statistics can be calculated over the simulated events (mean, standard deviation, percentiles, min, max etc). Statistics (for example the mean exposure per kilogram bodyweight per day) are calculated over the period of the consumption diary only. Bootstrapping is then used to estimate the standard error and confidence intervals on these statistics, whereby subsets of the simulated population are sampled with replacement a large number of times.

Statistics are calculated for two population types; “Food Consumers” and “Total Population”. The “Total Population” statistics are statistics calculated over all the subjects of interest in the assessment. The “Food Consumers” statistics are statistics over the subset of the subjects of interest in the diary that consumed the particular food in question.

3: FACET Exposure Algorithm for Additives

Overview

FACET employs a diary driven approach to determine the population distribution of exposure to additives in foods. This requires two basic inputs:

- A Diary of food consumption events
- A Substance Concentration table of the concentration of the substances of interest in the foods that are consumed in the Diary

With this information as input, the *basic* algorithm to determine the population profile of exposure is as follows:

1. Choose Substance
Example: E211

↓

2. Find all Foods in Substance Concentration table which have an entry for E211

↓

3. Find all consumption Events in the Diary for these Foods

↓

4. Determine exposure to E211 at each Event for the Food consumed at that Event

↓

5. Collate exposures from each Event to give distribution of exposure to E211 in the population

Figure 3: Basic overall algorithm to determine population profile of substance exposure

The core of the algorithm is Step 4 in Figure 1 above. In the following sections we outline this core step in detail for additives.

Concentration Data

There are two possible sources of concentration data for additives. One is a database of Maximum Permitted Levels (MPLs), and the other is a database of additive concentrations for 32 priority additives provided by industry.

The MPL database has MPL values for all additives in FACET in all food categories for which the additive has not been designated QS (*Quantum Satis*). These values are linked to various combinations of FACET food categories and flag settings. In some cases, the MPL value is in an ingredient in the food, indicated by the flag setting (e.g. the MPL is in chocolate, and a flag indicates that a food item has a chocolate topping). In these cases, the MPL values were linked to a distribution of possible ingredient fractions for that MPL value, each with a given weighting.

The industry data is in the form of four point estimates for the concentration of each of the priority additives in each food category; an extreme minimum, a typical minimum, a typical maximum, and an extreme maximum. Each of these point estimates can be used in an exposure assessment in FACET 1.9.1. In addition, a fitted distribution to these data points can be used to assess exposure.

There is also a database of occurrence data for additives in FACET; i.e. the presence probability of each additive occurring in each food category. The database is created using a combination of targeted market survey data from WP6 and the Oqali database. Presence probabilities, like the probability of addition value for flavourings, are interpreted as Bernoulli distributions in FACET, meaning they take a value of 1 or 0 with a given probability.

Exposure Algorithm

Consider the following example of eating events and substance concentrations:

- Three consumption events in the Diary for one food category, A1.1.3 – "Dairy based drinks"
- Entries in the Substance Concentration table for three Additives in this food category: Aspartame, Sodium Benzoate, Xanthan Gum

Table 13: Diary

Event	Subject	Day	Food	Amount(g)	Flag10	Flag 11	Flag 12
11	1012	2	A1.1.3	100	-3:NFI	-3:NFI	-3:NFI
12	1235	2	A1.1.3	150	1:Sugar Reduced	-3:NFI	-3:NFI
13	1759	2	A1.1.3	86	1:Sugar Reduced	2:Low Fat	-3:NFI

NFI = “No Further Information”;

Table 14:Substance Concentration

Food	Substance	P.P.	Conc. (mg/kg)	Flag10	Flag 11	Flag 12
A1.1.3	Sodium Benzoate	0.85	450	-3:NFI	-3:NFI	-3:NFI
A1.1.3	Aspartame	0.85	240	1:Sugar Reduced	-3:NFI	-3:NFI
A1.1.3	Aspartame	0.40	120	2:Low Fat	-3:NFI	-3:NFI
A1.1.3	Aspartame	0.15	200	1:Sugar Reduced	2:Low Fat	-3:NFI
A1.1.3	Xanthan Gum	0.90	165	2:Low Fat	-3:NFI	-3:NFI

P.P. = Presence Probability; Conc. = Concentration

In this example we only use the nutritional flags for additives (flags 10 - 12) for clarity and simplicity – the treatment of topping, coating and filling flags (flags 13 - 18) is functionally identical. Also, one concentration value is given for simplicity. In practice, this could be a distribution, either fitted or parametric.

We make the following assumptions in the additive exposure algorithm:

1. Only flags 6-18 were used in the additive concentration table (flags 10-18 are officially additive flags, but flavouring flags 6-9 were used to encode some additional information).

2. There were no flags with the setting -1 (unknown) in the additive concentration table. The flag -1 is only used in the food consumption diaries, when data cannot be attributed to a food category based on its description.

3. If, for a particular set of flags (e.g. 13-15, Topping) one of the flags is set to -2 (not applicable), then all of the flags in that group were set to -2 as well. This should apply to both the diary and the additive concentration table

4. There is no weighting between the groups of different flags; i.e. when matching flags 10-12 have no more importance than flags 13-15.

Also, some flag values have been added to certain categories, to cover the case "No Further Information" case, i.e. a null value that covers all flag settings in that category (Table 15).

Table 15: Flags Table

	Name of flag	Flag	Flag value
10 to 12	Nutritional information	Sugar reduced or without added sugar	1
		Low fat	2
		Enriched (vitamins, minerals, other)	3
		Gluten free	4
		Other (unsalted)	5
		Regular	6
		No other nutritional information	-3
		Not applicable	-2
		Unknown	-1
13 to 15	Topping (syrup, sauces)	Chocolate topping	1
		Fruit based topping	2
		Other topping	3
		No further information	-4
		No topping	-3
		Not applicable	-2
		Unknown	-1
16	Coating	Chocolate coating	1
		Other coating	2
		No further information	-4
		No coating	-3
		Not applicable	-2
		Unknown	-1
17 to 18	Filling	Chocolate filling	1
		Fruit filling	2
		Other filling	3
		No further information	-4
		No filling	-3
		Not applicable	-2
		Unknown	-1

The value “-4” has been added to a number of categories for use in the substance concentration table.

In words, the entries in the above Substance Concentration table mean:

- Sodium Benzoate occurs in all foods in category A1.1.3 with a Presence Probability of 0.85. Flag values are all -3:NFI for Sodium Benzoate in the Substance Concentration table, and hence the exposure algorithm ignores these flags in the Diary when determining the exposure to Sodium Benzoate.

- Aspartame only occurs in A1.1.3 at those eating events where the nutritional flags have values “Sugar Reduced”, “Low Fat” or both.

- Xanthan Gum only occurs in A1.1.3 at those eating events where the nutritional flags have the value “Low Fat”.

So, with reference to the three eating events in this example:

- There is a probable exposure to Sodium Benzoate in all three events

- There is no exposure to Aspartame in Event 11

- There is a probable exposure to Aspartame in both Events 12 and 13

- There is no exposure to Xantan Gum in both Events 11 and 12

- There is no exposure to Xantan Gum in Event 13

For Sodium Benzoate, the core of the exposure algorithm (Step 4 in Figure 1) works as follows for each of the eating events:

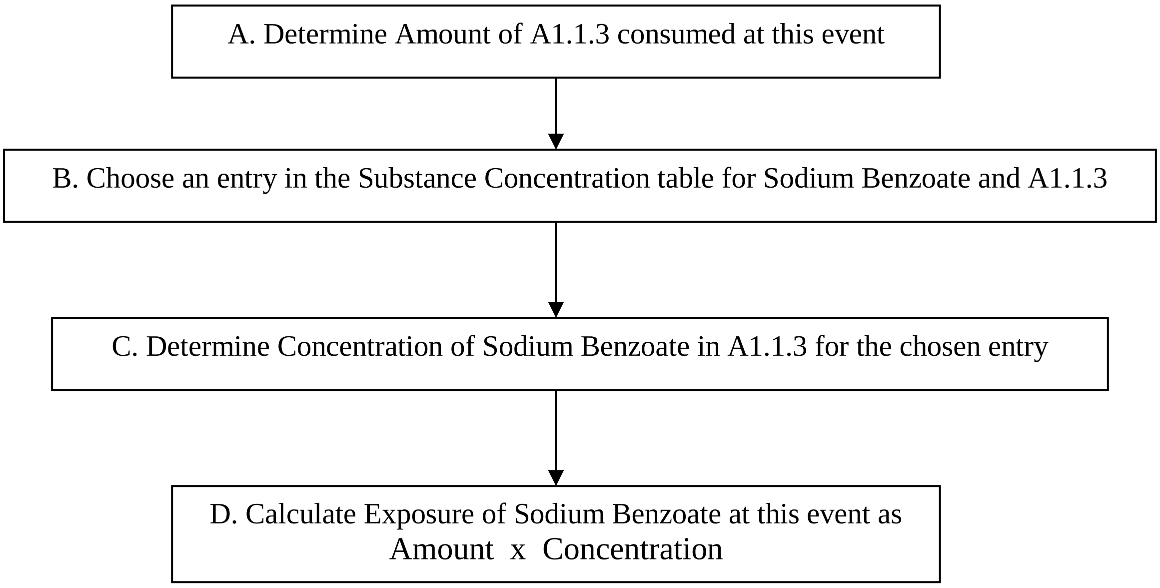

Figure 4: Determination of Exposure to a substance at a single eating event

These steps in greater detail:

A. In the given example the Amount consumed is a single value (100 g) and this step is straightforward in this case.

B. In this step we choose the entry according the presence probability: the given concentration value for Sodium Benzoate is picked 85% of the time, and a zero value is picked 15% of the time.

C. Suppose we have chosen the non-zero entry for concentration at Step B, then this gives the concentration of Sodium Benzoate in A1.1.3 as 450 mg/kg. This step is straightforward in this case.

D. Multiply the Amount of food consumed (Step A) by the Concentration of the substance (Step C) to get the Exposure at this eating event. In this example for this event the exposure is 45 mg.

Note that the Amount and Concentration fields in this example contained regular numbers (100g and 450 mg/kg respectively). In general, these fields could contain probability distributions. If the fields contain distributions the software samples this distribution to pick a single value for each of the Amount and Concentration that is used in Step D.

In the remaining examples in this document we will continue to just use single value numbers for Amount consumed and substance Concentration. However, it should be understood that probabilistic descriptions of these values can also be used as input.

For Aspartame and Xanthan Gum, the core of the exposure algorithm is slightly different at Step B. Taking the example of Aspartame at Event 12:

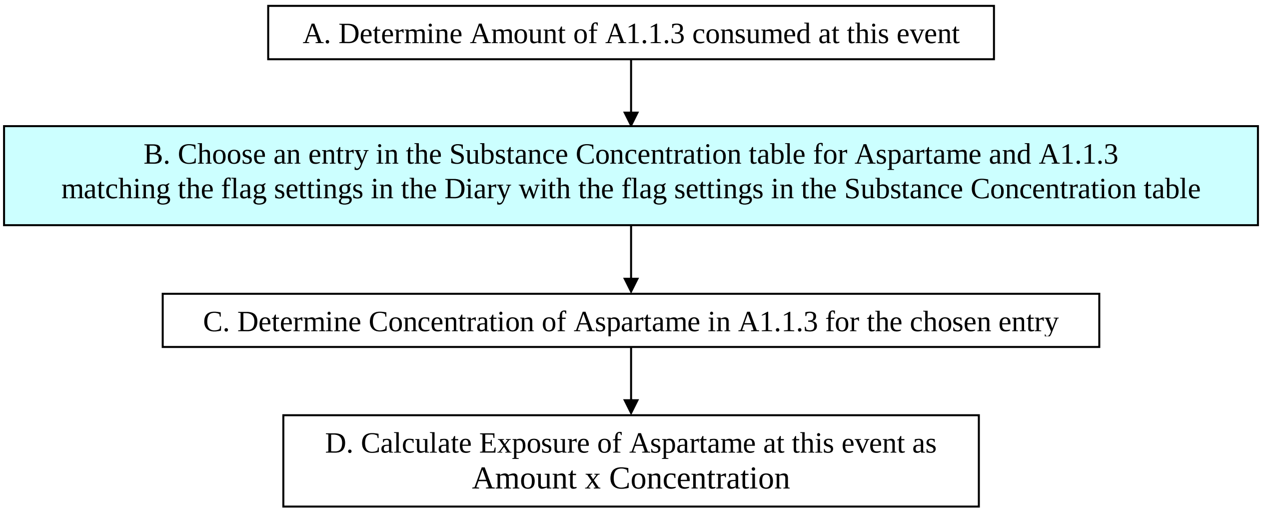

Figure 5: Determination of exposure to a substance at a single eating event, using FACET flags for additives

These steps in greater detail:

A. In the given example the Amount consumed is a single value (150 g) and this step is straightforward in this case.

B. In this step we choose the entry according the presence probability and the additive flags.

   - First, there is only one additive flag set for this eating event, with value “Sugar Reduced”.

   - The only entry in the Substance Concentration table for Aspartame with ONLY flag value “Sugar Reduced” is the first entry (pp=0.85, conc=240 mg/kg).

   - The given concentration value for Aspartame at this entry is picked 85% of the time, and a zero value is picked 15% of the time.

A. Suppose we have chosen the non-zero entry for concentration at Step B, then this gives the concentration of Aspartame in A1.1.3 as 240 mg/kg. This step is straightforward in this case.

B. Multiply the Amount of food consumed (Step A) by the Concentration of the substance (Step C) to get the Exposure at this eating event. In this example for this event the exposure is 32 mg.

There are several important points to note:

- The default flag entry is "No Further Information" (with a value of -3 or -4). This is ignored in matching between the Diary and Substance Concentration tables.
- The order of the flag settings is not important for both the Diary and the Substance Concentration table. Therefore the following entries are equivalent:
  - Flag 10 = "Sugar Reduced", Flag 11 = "Low Fat", Flag 12= "NFI"
  - Flag 10 = "Low Fat", Flag 11 = "Sugar Reduced", Flag 12 = "NFI"
- The location of the flag settings is also not important in both tables. Therefore the following settings are equivalent:
  - Flag 10 = "NFI", Flag 11 = "NFI", Flag 12= "Low Fat"
  - Flag 10 = "Low Fat", Flag 11 = "NFI", Flag 12 = "NFI"

The software takes these factors into account when checking for a match between the entries in the Diary and the Substance Concentration tables.

Events with multiple flag values need to be handled with care in the model. In the current example, Event 13 has a positive setting for both Flags 10 and 11, "Sugar Reduced" and "Low Fat" respectively. For Aspartame, we could logically take the concentration information from any of the three entries in the Substance Concentration table. The exposure model used the following approach to deal with this:

- If there is a positive match on all flags between the Diary and Substance Concentration table, the algorithm used this entry in the Substance Concentration table. In this example, for Event 13 and Aspartame, we use the entry in the Substance Concentration table where Flag 10 = "Sugar Reduced" and Flag 11 = "Low Fat". The entries in the Substance Concentration table with only Flag 10 = "Sugar Reduced" or only Flag 10 = "Low Fat" is ignored.
- However, if this exactly matching entry is not present in the Substance Concentration table, the algorithm has to check for partial matches. Again for Event 13 and Aspartame, we have partial matches on the two entries where only Flag 10 = "Sugar Reduced" and only Flag 10 = "Low Fat". In absence of additional these

When not to match flags

There are certain scenarios where it is not logically consistent to match consumption events with additives concentration data based on the FACET flag settings.

Consider the following scenarios when matching flags. Again, flags 10-12 are used for simplicity, but the examples apply to all flags. The consumption diaries and additive concentration tables are simplified in order to focus on the flag settings.

Scenario 1:

We have an event in the diary with the following flag settings:

Diary:

Food	Flag 10	Flag 11	Flag 12
A.5.3.2	1	3	2

We have the following two entries in the additive concentration table for a particular additive:

Additive Concentration Table:

Entry	Food	Flag 10	Flag 11	Flag 12
1	A.5.3.2	1	2	4
2	A.5.3.2	1	2	-3

There is **no** match for entry 1 with flag as there is a mismatch on the flag 11 = 3 in the diary and flag 12 = 4 in the concentration table. There is a match for entry 2, as there are two exact matches and a -3, which implies no further information is required to match that concentration entry to a diary entry with two of flags 10-12 set to values 1 and 2.

Scenario 2:

Here, we consider an event in the diary with the following flag settings:

Diary:

Food	Flag 10	Flag 11	Flag 12
A.5.3.2	1	4	-3

And we have the following two entries in the additive concentration table for a particular additive:

Additive Concentration Table:

Entry	Food	Flag 10	Flag 11	Flag 12
1	A.5.3.2	1	2	4
2	A.5.3.2	2	1	-3

Here, there is **no** match for entry 1 in the concentration table as the flag settings imply that the concentration only applies to eating events where the flags 10-12 are set to values 1, 2, and 4. Also, there is **no** a match for entry 2, as the flag settings imply that the concentration only applies to entries where flags 10-12 have the settings 1 and 2, and anything else.

Matching Information at Different Food Levels

An issue arises when it has only been possible to describe a food at a higher level in the FACET food categorisation hierarchy. In this discussion, “higher” means fewer dots in the food category code, “lower” means more dots, e.g. A14.2 is a “higher” level than A14.2.3, which is at a “lower” level.

Consider eating events of the following foods:

- A1.1.3 = “Dairy based Drinks”
- A1.1.3.1 = “Chocolate and Malt based drinks”
- A1.1.3.2 = “Chocolate Milk”
- A1.1.3.3 = “Other Dairy based drinks”
- A14.2 = “Fruit and Vegetable Juices”
- A14.2.1 = “Pineapple Juice”

and the corresponding concentration information for a single Additive, Sodium Benzoate.

Table 16: Diary

Event	Subject	Day	Food	Amount(g)
101	1043	2	A1.1.3	150
102	2458	2	A1.1.3.1	100
103	2349	2	A1.1.3.2	110
104	3142	2	A1.1.3.3	250
105	1113	2	A14.2	250
106	1012	2	A14.2.1	250

Table 17:Substance Concentration

Food	Substance	Presence Probability	Concentration
A1.1.3.1	Sodium Benzoate	0.15	0.1
A1.1.3.2	Sodium Benzoate	0.75	0.3
A1.1.3.3	Sodium Benzoate	0.95	0.2
A14.2	Sodium Benzoate	0.95	0.2

If we want to determine the exposure to Sodium Benzoate in these eating events, we immediately see that there is a problem at Events 101 and 106:

- Event 101: there is no entry in the Substance Concentration table for A1.1.3. However, there are entries for foods at the *next lowest* level in the food categorisation hierarchy (A1.1.3.1, A1.1.3.2, A1.1.3.3).
- Event 106: there is no entry in the Substance Concentration table for A14.2.1. However, there is an entry for the food at the *next highest* level in the food categorisation hierarchy, A14.2.

In general there are 4 possible scenarios when matching foods between the Diary and the Substance Concentration table:

Scenario	Food Level in Diary	Food Level in Substance Concentration
1	Low	Low
2	High	High
3	Low	High
4	High	Low

With reference to the example eating events:

- Events 102,103, 104 are all in Scenario 1
- Event 105 is in Scenario 2
- Event 106 is in Scenario 3
- Event 101 is in Scenario 4

There is no difficulty with Scenarios 1 and 2 – each one uses a straightforward match between the Diary and Substance Concentration tables. The issue is how to deal with Scenarios 3 and 4.

Scenario 3: Low level in Diary, High level in Substance Concentration

This is the more straightforward of the two scenarios. If we have no concentration information at the low level, but we do have concentration information at the high level, we simply use the high level information.

In our example, for exposure to Sodium Benzoate at Event 106, we use the Substance Concentration entry for A14.2.

Scenario 4: High level in Diary, Low level in Substance Concentration

In this scenario, we need to specify concentration information for the higher level food, but where we only have concentration information for foods at a lower level. In order to do this we need to know the distribution of foods in the next level lower in the hierarchy. This requires the information in the following table:

Table 18: Food Level Proportions

FACET Food Code	FACET Food Codes at next lowest level	Proportion
A1.1.3	A1.1.3.1	0.10
A1.1.3	A1.1.3.2	0.70
A1.1.3	A1.1.3.3	0.20

Note that the Proportions must sum to 1.0 for each food at the higher level. This table generalises to matching at any two adjacent levels in the hierarchy, e.g. the table can define the probabilities of a set of level 2 food categories for its level 1 food category. This table is populated using the distribution of known consumption events in the diary; i.e. the frequency with which consumption events are reported at the lowest level. In the absence of the distribution of this data (i.e. when the lower food codes are never recorded in the diary), the exposure algorithm randomly sampled from the different foods in the lower tier, with the assumption that each food is equally likely.

Flag Settings

When determining the distribution of food codes for a given food category, a combination of food code and flag settings is considered to be a unique food. The distribution of food codes at the lowest level is always calculated, with weightings assigned to all lower level food groups and flag settings reported in the diary. If a higher level food category is reported with a particular flag set, it is assumed that the lower food groups inherit that flag set and have equal weighting.

Examples

Diary:

A14.3.1 – “Fruit nectar” reported 10 times with flag set (i).

A14.3.2 – “Other fruit nectars” reported 20 times with flag set (i).

A14.3.3 – “Vegetable nectars” reported 20 times with flag set (i).

Total consumption events in A14.3 – “Fruit and vegetable nectars” = 50.

Assumption:

Consumption events described as A14.3 – “Fruit and vegetable nectars” with flag set (i) are assigned to A14.3.1 – “Fruit nectar” with flag set (i) with a weighting of 10/30, assigned to A14.3.2 – “Other fruit nectars” with flag set (i) with a weighting of 20/30, and assigned to A14.3.3 – “Vegetable nectars” with flag set (i) with a weighting of 20/50.

Diary:

A14.3 – “Fruit and vegetable nectars” reported with flag set (i).

Assumption:

A14.3.1 – “Fruit nectar”, A14.3.2 – “Vegetable nectars” are both equally likely, both having flag set (i).

Exposure Calculations

The following are the principal values calculated and outputted by the software:

- Substance exposure per kilogram of bodyweight per day
- Absolute substance exposure per day
- Food intake per kilogram of bodyweight per day
- Absolute food intake per day

The above values are presented by the FACET Food Categories. Statistics on these values are presented along with estimates of the error on the statistic in each case, as described in the next section.

Monte Carlo Sampling and Statistics

In order to accurately determine exposure to a substance in a population, Monte Carlo sampling is used. Re-simulation of consumption events in the food consumption diaries is used to build up a profile of exposure in the population, which captures the variability and uncertainty in the various inputs, for example chemical concentration data.

Once the desired number of iterations is achieved, statistics can be calculated over the simulated events (mean, standard deviation, percentiles, min, max etc). Statistics (for example the mean exposure per kilogram bodyweight per day) are calculated over the period of the consumption diary only. Bootstrapping is then used to estimate the standard error and confidence intervals on these statistics, whereby subsets of the simulated population are sampled with replacement a large number of times.

Statistics are calculated for two population types; “Food Consumers” and “Total Population”. The “Total Population” statistics are statistics calculated over all the subjects of interest in the assessment. The “Food Consumers” statistics are statistics over the subset of the subjects of interest in the diary that consumed the particular food in question.

4: FACET Exposure Algorithm for Food Packaging Migrants

This section provides an outline of the proposed exposure algorithm being implemented by Creme in FACET, with specific emphasis on Food Contact Materials (FCMs). In particular, this section deals with substances that require the migration model (as developed by WP4.2) in order to estimate the concentration of packaging migrants in foods. The section does not deal with packaging that can be linked directly to concentration estimates in foods (e.g. can coatings), as this type of exposure is not modelled using the migration model. In this case, the level of migration is in the form of concentration data for the migrants in foods, in units of weight over the contact area. The document touches on on some of the probabilistic aspects of the exposure model, but does not deal explicitly with WP4.2.5 ("Probabilistic modelling of concentration of FCM constituents in packed foods and link to exposure modelling in WP8").

Overview

In order to determine the population distribution of exposure to packaging migrants we use a diary driven approach. For this we require:

- A diary of food consumption events
- The concentration of packaging migrants in foods

A mathematical model of the movement of a migrant into food has been developed that provides quantitative estimates of the concentration of migrants in food. In order to run the model and determine exposure to migrants at each consumption event we need to know:

- What packaging foods are packed in (pack types, shapes, sizes and structures)
- What makes up the packaging that foods are packed in (components, layers, materials)
- What conditions do the foods in the packaging undergo (filling conditions, storage conditions, use conditions; by condition we mean time and temperature)
- What substances are in the materials that make up the packaging (migrant occurrence and concentration)
- What migration parameters are appropriate for the migrant/material/layer/component/conditions combination (migration modelling information)

In practice in the exposure software, the link between foods and packaging migrants will be made starting with the migrant:

- The user chooses the migrant of interest
- The software then determines
    - What packaging the migrant is in
    - What foods are packed in this packaging
    - The concentration of the migrant in those foods using the migration model
    - The estimated exposure to the migrant at each consumption event
    - The total exposure for a given population

In order to have a consistent framework for determining exposure to FCMs, several definitions are required whose meanings were consistent throughout this document. These are described in the next section.

Packaging Definitions

In FACET, packaging is decomposed in a very specific way. The following terms are very important and have specific meanings in the FACET project.

Pack Type: This is a basic description of what a food is packaged in, and may be recorded by Flag 5 in the consumption diaries. Example values are “Bottle: plastic” “Aluminium tray/foil”, “Canned/Tinned” and “Paper/board rigid box”.

Pack Components: These make up the specific pack types. There are four possible components:

- **“Mainpack” component**. This is the part which provides the majority of the contact with the food.
- **“Closure” component.** E.g. a cap, lid or sealed membrane. Note that ends for food cans are counted within this category.
- **“Outer Pack” component.** E.g. a carton which holds an open tray, or a flexible overwrap of an unlidded tray. This may have some potential contact with the food.
- **“Insert” component.** This is a two dimensional sheet which can either act as a base for the pack (e.g. the base board found in many smoked salmon pouches, the drip pad sometimes used under meat and fish products) or can act as interleaving between layers of the food (e.g. sheets of film separating slices of cured meats, glassine sheets in a box of chocolates). In the latter case, there may be multiple sheets per pack.

Component Type: Each pack component is of a given type. For example, a Mainpack may have the Component Type “plastic bottle”, and a Closure may have the Component Type “plastic screw thread”.

Component Structures: Each Component Type can be of more than one possible construction. An example is a 500ml bottle with many different lid types – it is one Pack Type, with two Pack Components, with the lid Component having several possible Component Structures. The distribution of these Component Structures for a given Component comes from data collected by the relevant packaging industry sector.

Materials: Each Component Structure is in turn made of a layer or layers of materials. Note that all materials in FACET have been predefined and have a specific *Material Code*, acting as a unique identifier for each material. The number, order and thickness of each layer are crucial in defining each component structure.

Migrants: Finally, each material can contain a number of potential migrants. Migrant occurrence and concentration data are collected by each packaging industry sector.

Exposure Algorithm for Food Packaging Migrants

In the FACET software tool, the user specifies the migrant and population of interest. The *basic* form of the algorithm is shown below.

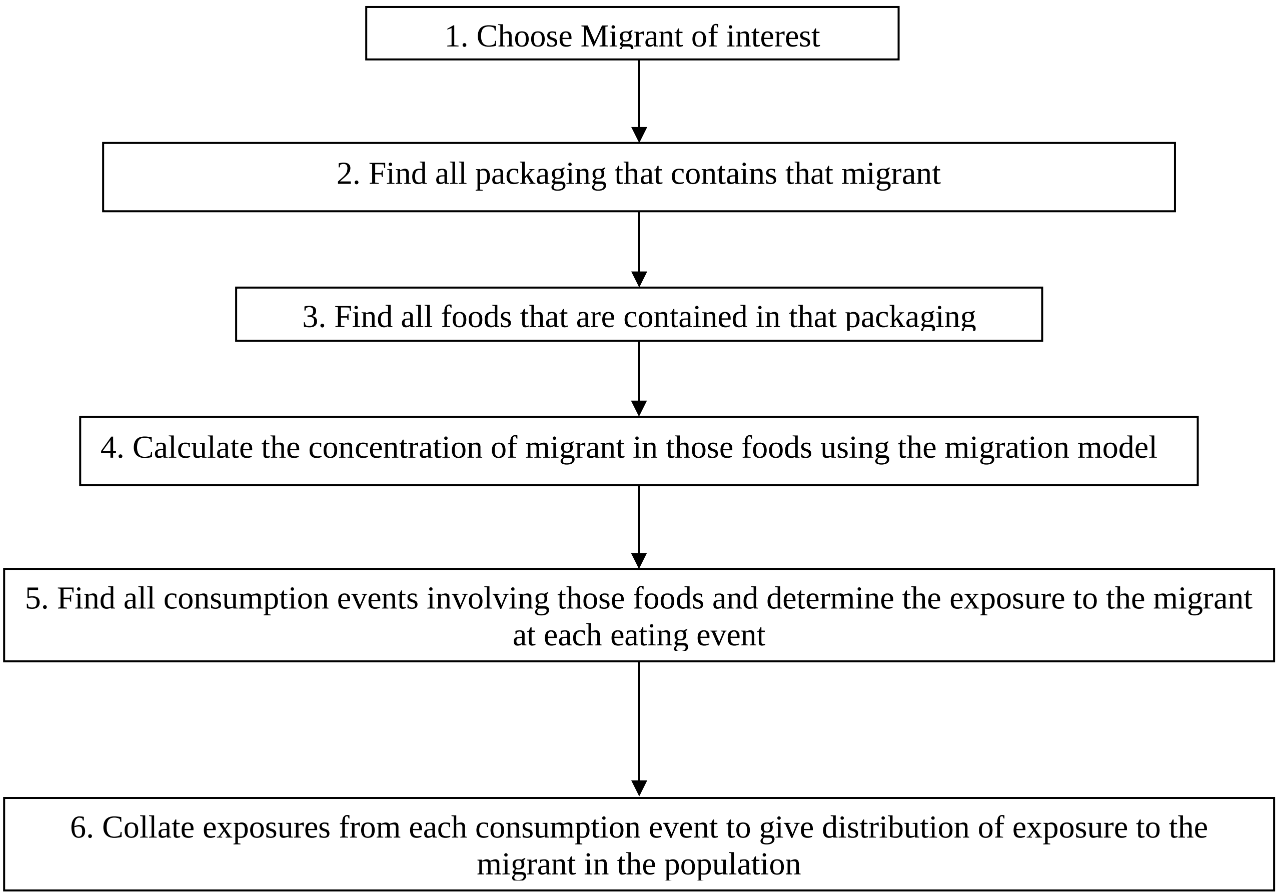

Figure 6: The basic packaging migrant exposure model in FACET

We focused primarily on steps three and four as outlined in Figure 6. A number of inputs are required at Step 4 in order to run the Migration Model, and these are gathered at Steps 2 and 3. Thus, we begin by highlighting the inputs required in order to perform Step 4, and show how these can be determined in Step 3 when linking foods to packaging.

Calculating the concentration of a migrant in foods using the Migration Model (Step 4)

The migration model is a one-dimensional partial differential equation that outputs the concentration of a migrant in food (i.e. the migration level) as a function of time, based on solutions to Fick's second law of diffusion. The migration model requires the following inputs in order to run:

- The number of layers of materials in the packaging (up to nine layers can be used)
- The thickness of each layer
- The area of contact between each layer and the food
- The number of time and temperature regimes the packaging undergoes (e.g. filling, storage, processing etc), including the time and temperature of each regime (up to five regimes can be used)
- The density of each layer
- The initial concentration of migrant in each layer
- The diffusion coefficients (D) of each layer during each temperature regime
- The partition coefficients (K) between each layer during each regime of temperature

Two important physiochemical parameters are required for the modelling of migration of substances between packaging materials and foods. These are a Diffusion Coefficient, D, and a Partition Coefficient, K, both of which are temperature dependent. The temperature and substance dependence of the Diffusion Coefficient can be parameterized using an approximate formula called Piringer's Formula, requiring two material specific parameters A_p' and τ. This has the form:

$$D_p = D_0 \exp(Ap - 0.1351 M_w^{2/3} + 0.003\, M_w - 10454/T),$$

where

$$A_p = A'_p - \tau/T,$$

M_w is the molecular weight of the molecule, T is the temperature and D_0 is a constant. So, for a given molecule in a given material at a given temperature, we can estimate its diffusion coefficient in that material.

In principle, the Diffusion Coefficient parameters (A_p' and τ) would be known for all materials and food categories in the FACET project. Equally, the Partition Coefficient should be known for all material-material and all material-food category boundaries, at a suitable range of temperatures, for every migrant. This is a mammoth task beyond the scope of the project. So, for the purpose of the migration modelling in FACET, materials are being aggregated into broad material groups, and food categories being aggregated into a small number of food simulants.

The Link from a Food to a Migrant (Steps 2 and 3)

The number of links from a food to a migrant is a complicated one, owing to the complexity of packaging structures themselves and the nature of the packaging industry. Each of the links are explained in detail below, and what information is provided at each step. For ease of understanding, we describe the link from food to a migrant (although in practice the exposure algorithm works the other way round, as shown in Figure 1).

PASTA Table

One of the most important structures in the FACET project is the Pack Size, Type and Association (or PASTA) table. This connects a food type to its packaging components and is based on commercial market research performed by Euromonitor, taking inputs from the Matrix project where appropriate. The PASTA table provides the following information:

- The market share distribution of pack types for a given food
- The amount of food contained in that pack
- The pack components for those pack types (i.e. main, closure, outer and insert)
- The contact ratio for each of those components
- The industry association responsible for the construction of those particular components

An outline of the structure of the PASTA table can be seen in Figure 2 (note that the figures are fictitious and the actual table provides more detail than this).

Table 19: The PASTA table

			Pack Components												
Country	Food Tier 3	Size g/ml	Main	Closure	Outer	Insert	Million Packs	Main Contact Ratio	Closure Contact Ratio	Outer Contact Ratio	Insert Contact Ratio	Main Source	Closure Source	Outer Source	Insert Source
UK	P.16.2.2 Crisps	100	Flexible				26.2	80.54				FPE			
UK	P.14.3.2 Dry tea	40	Carton				3.8	16.62				CITPA			
Italy	P.15.1.1 Beer	330	Glass Bottle	Crown Closure			679.4	9.61	0.21			-	EMPAC		
Italy	P.08.1.1 Fresh Meat	200	Plastic Tray	Sealed Lidding		Drip Pad	62	12.23	4.08		6.52	EUPC	FPE		CITPA
Spain	P.08.1.1 Fresh Meat	400	Plastic Tray		Flexible		6.5	9.7		3.23		EUPC		FPE	

The last piece of information provided by the table (the industry source) is crucially important; this forms the next link in the chain. For a given food in a given pack type we look to the information provided by the appropriate industry sector for the structure of that particular component.

Component Structure Tables

For a given food, in a given pack type, produced by a given packaging association, we look to the data provided by that association for the next link in the chain. Component Structure Tables provided by each industry sector give the following information:

- FACET Food Code for packaging
- Component Type (e.g. Sealed Lidding, Flexible bag etc.)
- A description of the layers of the component structure, providing
    - FACET Material Code
    - The Thickness of each layer
- The Conditions of use, i.e. time and temperature information for that component
- The Volume (i.e. distribution) for each food/structure combination

Note that the FACET Food Code is still required at this stage. This connection to food is crucially important and cannot be ignored. For example, a particular closure construction for a container may be used across many different foods, but for each of the foods and each pack structure the market share may be different – we cannot simply have a market share across all foods for that closure construction.

From a data gathering point of view, this link in the chain is the greatest possible source of data gaps. Different industry sectors may be responsible for the collection of component structure information for the same component, requiring a “breakdown-by-sector” factor to account for this.

Table 20 shows how to link from the PASTA Table to the appropriate Component Structure Table, using a simplified FPE (Flexible Plastics Europe) table as an example.

Table 20: Linking the PASTA Table to a Component Structure Table

Country	Food Tier 3	Size g/ml	Pack Components				Million Packs	Main Contact Ratio	Closure Contact Ratio	Outer Contact Ratio	Insert Contact Ratio	S
			Main	Closure	Outer	Insert						
UK	P.16.2.2 Crisps	100	Flexible				26.2	80.54				F
UK	P.14.3.2 Dry tea	40	Carton				3.8	16.62				C
Italy	P.15.1.1 Beer	330	Glass Bottle	Crown Closure			679.4	9.61	0.21			-
Italy	P.08.1.1 Fresh Meat	200	Plastic Tray	Sealed Lidding		Drip Pad	62	12.23	4.08		6.52	E
Spain	P.08.1.1 Fresh Meat	400	Plastic Tray		Flexible		6.5	9.7		3.23		E

I	
Food Tier 3	Componen
P.08.1.1 Fresh Meat	Sealed Lidd
P.08.1.1 Fresh Meat	Flexible

In slightly more detail, a Component Structure Table would look like something shown in Table 21, again taking fictitious FPE data as an example.

Table 21: Layer information from FPE for component type for particular foods

Food	Component Type	Layer 1	Layer 2	Regime 1	Regime 2
P.3.4.2	Flexible	Material – OPET Thickness – 10 µm	Material – G. Ink Thickness - 1 µm	Temp – 5 C Time – 1 day	Temp – 23 C Time – 1 hr
P.3.4.3	Plastic Tray	Material – OPA Thickness – 7.5 µm	Material - OPP Thickness - 3 µm	Temp – 0 C Time – 5 day	Temp – 80 C Time – 5 min
P.3.4.5	Plastic Tray	Material – PET Thickness – 12 µm	Material - OPP Thickness - 5 µm	Temp – 2 C Time – 2 day	Temp –180 C Time –20 min

Migrant Concentration Tables

The final step in linking a food consumption event to a migrant is to find the concentration of the migrant in each layer of material in the packaging. In order to do this we look up the appropriate Migrant Concentration Table, which contains the concentrations of all the migrants contained in each of the materials used in FACET.

As with all concentration data in FACET, migrant concentration data can be presented in a variety of forms:

- Typical concentration
- Typical min/max concentrations
- Extreme min/max concentrations
- A statistical distribution of concentrations
- A histogram of concentrations
- Measured raw data points

All of these provide varying levels of detail but are acceptable forms of input. For example, polymer data provided by Plastics Europe represents the “European distribution” of concentrations of additives in each polymer, based on the combined tonnages provided by each participating member. Taking Plain OPET which has material code 13.1, this has the form (again with fictitious data) (Table 22):

Table 22: Plain OPET: Sample concentration data from Plastics Europe for the material “Plain OPET”, which has the material code 13.1

Bisphenol A			Acrylic Acid		
Concentration (ppm)	Weight fraction	Volume (T)	Concentration(ppm)	Weight fraction	Volume (T)
50	0.015	1957	50	0.007	12354
100	0.230	30015	110	0.004	6875
120	0.100	13050	120	0.408	651869
125	0.274	35757	125	0.006	9957
200	0.132	17226	220	0.041	65432
225	0.098	12789	225	0.041	65165
250	0.151	19705.5	300	0.491	783511

In this example, the weight fraction allows the software algorithm to probabilistically choose a concentration; so in the case of Bisphenol A the software would choose a concentration of 50 parts-per-million with a probability of 1.5%, a concentration of 100 parts-per-million with a probability of 23%, and so on.

Partition Coefficient Table

For each material/material and material/food interaction, we require the appropriate partition coefficient. As was mentioned previously, materials and foods have been aggregated into groups based on their solubility properties. Thus each material is a member of a *solubility group*, where the partition coefficient between each solubility group is known. These can be found in the Partition Coefficient table, whose i - j*th* entry provides the partition coefficient between solubility groups i and j.

Diffusion Parameter Table

The diffusion coefficient can be parameterized using the Piringer formula, which uses the temperature information gathered in the Component Structure Tables, the molecular weight of the migrant and the material dependant parameters A_p' and τ. Again, materials and foods were aggregated into groups, and the diffusion parameters of these groups were known. Thus, if a migrant of a given molecular weight is in a particular material which is a member of a particular *diffusion group,* its diffusion coefficient can be ascertained using the Diffusion Parameter Table.

Once all of this information is gathered when linking a migrant to a food, we have all the inputs needed to run the migration model. This then provided an estimate of the concentration of the migrant in foods, which can be used to calculate exposure at each consumption event.

Diary

Subject	Food	Amount	Flags
1001	P.3.4.2	100 g	…
1002	P.3.4.3	150 g	…

PASTA Table

Food	Size	Component Sources	Component Type	Contact Ratios
P.3.4.2	500 g	Main – FPE Closure – CITPA	Main – Flexible Closure – Crown	Main – 80.5 Closure – 5.6
P.3.4.3	100 g	Main - FPE Outer - EUPC	Main – Plastic Tray Outer – Flexible	Main – 16.3 Outer – 6.6

Component Structure Table, e.g. FPE

Food	Pack Type	Layer 1	Layer 2	Regime 1	Regime 2
P.3.4.2	Flexible	Material – OPET Thickness – 10 µm	Material – G. Ink Thickness - 1 µm	Temp – 5 C Time – 1 day	Temp – 23 C Time – 1 hr
P.3.4.3	Plastic Tray	Material – OPA Thickness – 7.5 µm	Material - OPP Thickness - 3 µm	Temp – 0 C Time – 5 day	Temp – 80 C Time – 5 min

Migrant Concentration Data

Material	Migrant	Concentration	Occurrence
OPET	Bisphenol A	0.03	12%
OPA	Bisphenol A	0.05	73%

Determine the partition coefficients, diffusion parameters and diffusion coefficient for all materials and foods

Calculate concentration of Bisphenol A in P.3.4.2 using migration model

Exposure = Concentration x Amount

Figure 7: The link from an eating event to a migrant and calculating the exposure

Packaging Flags

In the food consumption diaries, flags 1-5 have been allocated a value where possible. When set, the flag settings were used to further inform the exposure algorithm. The precise interpretation by the exposure algorithm of each packaging flag is yet to be defined. All possible flag values are listed below.

Flag 1: "Place of Purchase"

Possible values:

1. Retail including over the counter.
2. Take away/vending/fast food.
3. Restaurant/canteen.
4. Home-grown/Homemade.

-1. Unknown.

Flag 2: "How Prepared"

Possible values:

1. Industrially prepared.
2. Homemade.
3. Artisanal (local bakers, markets)

-1. Unknown

Flag 3: "Processing at time of purchase"

Possible values:

1. Not processed (unprocessed, raw, unprepared, …)
2. Processed (prepared, cured, treated, …)

-1. Unknown

-2. Not applicable

Flag 4: "State of product at time of purchase"

Possible values:

1. Frozen
2. Refrigerated/Chilled
3. Ambient (room temperature)
4. Hot
5. Dried/Dehydrated

-1. Unknown

-2. Not applicable

Flag 5: “Type of Packaging”

Possible values:

1. Not Packaged
2. Canned/tinned
3. Not canned
4. Bottle: unknown pack material type
5. Jar: Unknown pack material type
6. Bottle: glass
7. Bottle: plastic
8. Jar: glass
9. Jar: plastic
10. Aluminium tray/foil
11. Plastic rigid container (e.g. tray) without plastic film overwrap
12. Plastic rigid container (e.g. tray) with plastic film overwrap
13. Plastic Film, Bag, Pouch
14. Beverage Carton (E.G. Tetra-Pak)
15. Paper/Board rigid box
16. Paper flexible wrap
17. Aerosol can
18. Cardboard box with separate inner lining (e.g. breakfast cereal bag-in-box)
19. Tube: composite (e.g. Pringles tube)
20. Tube: metal (e.g. tomato puree)
21. Packet/sachet for dried powder (e.g. dry soup mix)
22. Mixed packaging

-1. Unknown

Matching Information at Different Food Levels

An issue arises when it has only been possible to describe a food at a higher level in the FACET food categorisation hierarchy. In this discussion, “higher” means fewer dots in the food category code, “lower” means more dots, e.g. P14.2 is a “higher” level than P14.2.3, which is at a “lower” level. In principle, this issue can arise at any stage in the packaging data chain linking migrants to foods. There are four possible scenarios (Table 23)

Table 23: Scenarios

Scenario	Food Level in Diary	Food Level in Packaging Data
1	Low	Low
2	High	High
3	Low	High
4	High	Low

The first two scenarios pose no difficulty, as there is a direct match in both cases. The difficulty arises in scenarios three and four.

Scenario 3: Low level in Diary, High level in Packaging Data

This is the more straightforward of the two scenarios. If we have no concentration information at the low level, but we do have packaging information at the high level, we simply use the high level information.

Scenario 4: High level in Diary, Low level in Packaging Data

In this scenario, we need to specify packaging information for the higher level food, but we only have packaging information for foods at a lower level. In order to do this we need to know the distribution of foods in the next level lower in the hierarchy. This information may or may not be available.

In the case of the PASTA Table, the distribution of pack types can be ascertained from the market share distribution of pack types, which can be selected probabilistically. This information may or may not be available at the next link in the chain, in the Component Structure Tables, and at the next link etc. Provided market share information is available at each link, the software can select packaging data with the appropriate probability at each link. When this data is lacking, an alternative approach has to be found.

Exposure Calculations

The following are the principal values calculated and outputted by the software:

- Substance exposure per kilogram of bodyweight per day
- Absolute substance exposure per day
- Food intake per kilogram of bodyweight per day
- Absolute food intake per day

The above values are presented by the FACET Food Categories. Statistics on these values are presented along with estimates of the error on the statistic in each case, as described in the next section.

Monte Carlo Sampling and Statistics

In order to accurately determine exposure to a substance in a population, Monte Carlo sampling is used. Re-simulation of consumption events in the food consumption diaries is used to build up a profile of exposure in the population, which captures the variability and uncertainty in the various inputs, for example chemical concentration and packaging data.

Once the desired number of iterations is achieved, statistics can be calculated over the simulated events (mean, standard deviation, percentiles, min, max etc). Statistics (for example the mean exposure per kilogram bodyweight per day) are calculated over the period of the consumption diary only. Bootstrapping is then used to estimate the standard error and confidence intervals on these statistics, whereby subsets of the simulated population are sampled with replacement a large number of times.

Statistics are calculated for two population types; “Food Consumers” and “Total Population”. The “Total Population” statistics are statistics calculated over all the subjects of interest in the assessment. The “Food Consumers” statistics are statistics over the subset of the subjects of interest in the diary that consumed the particular food in question.

Consumer Loyalty

For packaging, concentration data is calculated using a mathematical model of the migration of substances from packaging into foods. The data for the distribution of pack types for a particular food comes from industry, based on the market share of different pack types. Each pack type can have a distribution of configurations of materials, and the concentration of migrants in each material is in turn a distribution. Further physiochemical parameters are required to calculate the concentration of a migrant in food, which are also distributions.

In the case of consumer loyalty, a food in a subject’s consumption diary has to be a calculated concentration of migrant based on a random sample of all of the required parameters (pack type, packaging structures, parameters etc). This random sample is from a particular pack type. Then, all subsequent consumption events for the same food and same subject will have a concentration sampled from the within distribution of pack types they were initially allocated.

Advanced User

It is a requirement of the FACET software that the advanced user be able to investigate the impact of introducing a new packaging structure to the European market. In order to estimate the exposure to a packaging migrant in a population of consumers, it is necessary to know the concentration of the migrant in all foods consumed by the population. The user can specify or calculate the concentration of a migrant in foods in any one of three ways:

- Determine the concentration in foods using the migration model for multi-layer structures as developed for FACET
- Specify the migration or extraction rate per unit of contact area between the food and packaging structure (applies mainly to can coatings)
- Specify the raw concentration of migrant in selected food categories

Each approach is described in detail below.

Using the Migration Model

The concentration of a migrant in foods can be estimated by a mathematical model of the migration of substances from packaging into foods, as developed by Work Package 4.2 (note that this model does not apply to metals or glass). In order to use this model with a new packaging structure, the advancer user has to specify the following:

1. What foods the packaging is intended for, according to their FACET categorisation
2. The materials used for each layer in the packaging (up to nine layers can be used)
3. The thickness of each layer
4. The area of contact between each layer and the food
5. The number of time and temperature regimes the packaging undergoes (e.g. filling, storage, processing etc), including the time and temperature of each regime (up to five regimes can be used)
6. The initial concentration of migrant in each layer
7. Parameters to specify diffusion coefficients (D) of each layer during each temperature regime
8. Parameters to specify partition coefficients (K) between each layer during each regime of temperature
9. The presence probability or market share the structure has in each food category

The details of each step are described below.

1. Foods

The exposure model in FACET is diary driven; i.e. it is based on consumption patterns recorded in national dietary surveys. These dietary surveys have been recoded into food categories that target the different pack types that foods are packaged in. These food categories are well defined and in a hierarchical system, and the user is able to select relevant food categories from a pre-defined list.

2. Materials for each layer

Packaging structures are typically composed of one or more layers of materials. All food packaging materials in FACET have been recoded into a hierarchical system, and the user is able to select what material is used for the construction of each layer.

3. Layer thicknesses

The user has to specify the thickness of each layer in microns. This can be done in a number of ways. The user can specify a point value or the user can specify the layer thickness as a parameterised distribution, e.g. Lognormal(a,b).

4. Contact Area

The size of the contact area between the food and the packaging is a major determinant of migration. This is specified as a single value and is assumed to be constant between all layers and the food.

5. Time and temperature regimes

The time and temperature regimes that the packaging undergoes while in contact with the food are required, and up to five regimes can be specified. Times and temperatures can be specified as either a point value, or a range, e.g. 90° - 100° C for 7 – 10 minutes.

6. Initial migrant concentrations

The user has the option of assessing exposure as a result of a new use of a migrant that already exists in the built-in FACET databases, or assessing exposure to novel migrant not included in the databases. In both cases, the concentration of the migrant of interest in each layer must be specified by the user. This can be specified as a point value, or as a parameterised distribution.

7. Diffusion coefficients

The diffusion coefficient is the kinetic factor that determines the rate of diffusion within a medium, and depends on both the migrant and the material. In cases where the migrant of interest already exists in the FACET databases, the diffusion is known for each combination of material and migrant. If a new migrant is being assessed, additional information is required from the user. The diffusion coefficient is calculated using the following equation:

$$D_p = D_0 \exp(Ap - 0.1351 M_w^{2/3} + 0.003\, M_w - 10454/T)$$

where

$$A_p = A'_p - \tau/T.$$

M_w is the molecular weight of the molecule, T is the temperature, D_0 is a known constant, while A'_p and τ are two material dependent parameters. The temperature, T, is specified at step 5, and the distribution of A'_p and τ is known for the materials selected. Thus, in the case of new migrant, all the user has to specify is its molecular weight.

8. Partition coefficients

To calculate the partitioning at each material/material and material/food interface, materials and foods have been aggregated into groups based on their solubility properties. This aggregation is known for all materials and migrants in FACET. In the cases of a new migrant, all that is required of the user is an estimate of the polarity of the migrant, i.e. is it non-polar, medium polar, or polar (this can obtained from the log $k_{o/w}$ of the migrant).

9. Presence probability or market share

The user has the option of specifying the presence probability for the structure for each food category. For example, specifying a probability of 60% for a specific food category would mean that for a particular consumption event involving that food category, there is a 60% chance that that particular packaging structure is used.

If the migrant selected is listed in the FACET databases, then the exposure estimates were combined with the packaging structures already in FACET. Thus, in the above example, there is a 40% chance that the usual distribution of pack types containing the migrant (for the relevant food categories) is used.

If the migrant of interest is not listed in the FACET databases, then the exposure estimates were not combined with the built in FACET databases. Thus in the above example there is a 40% chance that there is no exposure at each consumption event involving the selected food categories.

Note that a default figure of 100% can be used, meaning that the structure is always used for that food category (i.e. 100% market share).

Calculating the concentration

Once all the required information is input, the software calculated the distribution of concentration of the migrant for the selected food categories, and save the concentration distributions to a database. The user is then able to use this custom data in future exposure assessments, as required. The advantage of this approach is that the migration calculation only needs to be done once, and the user can invoke the data as required, and can run various scenarios using the calculated data, e.g. using different combinations of food categories. Note that the raw calculated concentration data is visible to the user.

Migration levels per unit of contact area

This approach applies mainly to metals, although in principle it can be applied to any combination of migrant and food category. The user must specify the following:

1. What foods the packaging is intended for, according to their FACET categorisation
2. The area of contact between the packaging and the food
3. The level of migration of migrant per unit of contact area
4. The presence probability or market share the structure has in each food category

This information is then used to calculate the concentration of migrant in each food category, which will be saved to a database. This database of concentrations can then be invoked for use in exposure assessments by the user, as required.

In the case of a new use of a listed migrant the software will use the user specified data in combination with the built in concentration data, while in the case of a new migrant the data will be used alone.

Specifying raw concentration data

The user will also have the option of specifying raw concentration data for a novel migrant, if they have an estimate of what this is. This can be done by selecting specific FACET food categories (as described above) and specifying what the concentration of migrant is in each category is, along with the presence probability of the concentration for each category. The concentration can be specified as a point value or a parameterised distribution. The concentration data will be saved to a database and can be used in subsequent assessments by the user, as required.

In the case of a new use of a listed migrant the software will use the user specified data in combination with the built in concentration data, while in the case of a new migrant the data will be used alone.

Appendix – Choosing the Maximum Value

The problem outlined is how to choose the largest likely concentration value, given two distinct pairs of concentrations and presence probabilities.

In order to decide which concentration to use, a conservative choice is made to use the maximum of either possible concentration. The mean concentration, i.e. the product of the concentration and the presence probability is not sufficient, and further steps are necessary to make a conservative choice as the presence probability for the added concentration must be considered.

The general problem of how to choose the "maximum" concentration is as follows. Consider two concentrations and two presence probabilities.

Probability	Concentration	Probability	Concentration
P1	C1	P2	C2

We only make the following assumption:

C2 > C1

Thus, we make no assumptions on the presence probabilities. Recall that P1 and P2 are both less than or equal to one. The exposure algorithm will work as follows.

For each consumption event, with probability P2, we use concentration C2.

With probability (1-P2), we split this again by selecting concentration C1, with probability P1, and a concentration of 0, with a probability of (1-P1). Thus, for each consumption event we select:

- A concentration of C2 with probability of P2 for each consumption event
- A concentration of C1 with probability (1-P2)P1 for each consumption event
- A concentration of 0 in (1-P2)(1-P1) of the time for time for each consumption event

This is still a conservative choice, since (1-P2)(1-P1) < (1-P1), so we are choosing a zero concentration less of the time we would than if we chose concentration C1 with presence probability P1. Note that this also allows for ingredient fractions, as these are essentially absorbed into the concentration and so do not change the presence probabilities.

Since we are making no assumptions on the presence probabilities, this works for the cases where P1 = P2, P1 > P2, P1 < P2.

Consider a numerical example.

Probability	Concentration	Probability	Concentration
0.1	10 mg/g	0.95	50 mg/g

To apply this approach to the example above, the algorithm would:

- Choose a concentration of 50 mg/g, 10% of the time
- Choose a concentration of 10 mg/g, 85.5% of the time
- Choose a concentration of 0 mg/g , 4.5% if the time

This approach includes the high percentiles that would otherwise be ignored. Alternatively we can formulate the problem using random variables as follows. Let X1 be a random variable with distribution Bernoulli(P1) x C1, and X2 be a random variable X2 with distribution Bernoulli(P2) x C2. We define a third random variable Y with distribution Max(X1, X2). Examining all possible outcomes, we have the following table:

X1	X2	Probability	Y = Max(X1, X2)
0	0	(1-P1)(1-P2)	0
C1	0	P1(1-P2)	C1
0	C2	(1-P1)P2	C2
C1	C2	(P1)(P2)	C2

Thus we see that the random variable Y = Max(X1, X2) has the correct distribution as used in the example. In particular, as we have

Pr[Y = 0] = (1-P1)(1-P2),

Pr[Y = C1] = P1(1-P2),

Pr[Y = C2] = (1-P1)P2 + (P1)(P2) = P2,

as is used above. Note that in original problem the presence probability for the natural concentration is always set to one, however the only assumption we made is that C2 > C1, so if P1 or P2 has a value of one then the method is still valid.

Revisions October 2016

- For substances with Log Pow of <=0 in non-polar materials migration results are now set to zero (whether the user creates a new substance or uses an existing one).

- Substances created in New Substance Wizard (metal) become available to prepopulate and those created in New Packaging Wizard (metal) do not because there is a subtle difference between substances created in the NSW and those created in the NPW.

  Prepopulation assigns a migration value to each food:Pack Type combination

  In NPW a substance created isn't available for prepopulation because each food:Pack Type combination is already defined (thus the resulting migration table created from NPW is available to use in an assessment, it doesn't need to be prepopulated)

  In NSW Pack Type is not considered, only migration from a material code. This substance becomes available to prepopulate because prepopulation is required on top of this to define migration at the food:Pack Type combination level

- If a user creates a combination of pack components (closure, main and outer) that is not in use in real life (in the existing data) the software creates a new combination and assigns a new pack type name to it and this name appears in the Pack Table.

- PT8 has been removed. PT8E and PT8B are now present in its place.

- The Set Off in FACET is set to 20%. Specifically, 20% of the mass of the substance in a material code beginning with M21, or M27, will, prior to simulating migration, be added to the initial concentration of that migrant in the innermost layer and effectively be distributed in the thickness of that innermost layer, thus making it available for migration to the food.

In version 3.0.2 there are no special exceptions for layers that are `Absolute` barriers. The ap' and Tau values make them effective barriers but any check boxes which ignore migration in layers on the “left” (the far side from the food layer) of the barrier have been removed

Annex 1: Migration Model Report

List of Figures

List of Tables

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Objectives

Introduction

To estimate migration a number of inputs are required. One important input is the partition coefficient. The partition coefficient is defined as a ratio of concentrations of a substance in a mixture of two immiscible phases at equilibrium.

The lack of transparency around how partition coefficients are calculated in the FACET migration model presents an issue with regards to the verification of the estimates used. It is important that complete transparency is achieved in making both the formula, and experimental data, available for scrutiny by users of the FACET tool (including regulatory bodies).

The objective of this work is to incorporate all FACET project data into the partition framework, including the 600 partition coefficients outlined in (Seiler, et al., 2014). This includes a transparent implementation, including a record of how all values were calculated and allocated to the materials and substances gathered in the project.

Outline Structure of this Report

Section 0 provides a summary of the kinetic experiments completed during the FACET project. In Section 0 a description of the approach used to estimate the partition coefficients is summarised.

Section 0 considers a set of migration modelling scenarios for a selection of foods and presents the outcomes of those tests. For those foods not considered in Section 0, a set of graphs summarising partition coefficients between a polymer and food (Kpf) data is provided in Appendix 0.

Data Inputs

Table 24 provides a summary of the kinetic experiments performed during the FACET project. Each experiment provides substance concentrations in the polymer material (i.e. LDPE) at different time points as well as partition coefficients associated to each scenario.

Table 24: Summary of Kinetic Experiments

Food	Model Migrants	Temperature
Wine	BHT, ITX, DPP, BPA, Triclosan	20/40/60
Apple sauce	Styrene, ATBC, 1-Octene, DEHA	20/40/60
Ketchup	Uvitex OB, DIPN, Chimasorb 81	20/40/60
Tomato sauce	BHT, ITX, DPP, BPA, Triclosan	20/40/60
Pork 10% fat	Styrene, ATBC, 1-Octene, DEHA	5/20
Wheat flour	BP, Uvitex OB, DPBD DINP, DINCH, Irganox 1076	20/40/60
Fish in Brine	ATBC, DEHA, Styrene, Octene	10/20/40
Noodles	Uvitex OB, DIPN, Chimasorb 81	20/40/60
Orange Juice	BP, Uvitex OB, DPBD DINP, DINCH, Irganox 1076	20/40/60
Cottage cheese	Styrene, ATBC, 1-Octene, DEHA	20/40/60
Pork 20% fat	Styrene, ATBC, 1-Octene, DEHA	5/20
Fish fingers	Uvitex OB, DIPN, Chimasorb 81	5/20
Salmon	Uvitex OB, DIPN, Chimasorb 81	5/20
Instant soup	BP, Uvitex OB, DPBD DINP, DINCH, Irganox 1076	20/40/60
Cake	BHT, ITX, DPP, BPA, Triclosan	20/40/60
Cheese sauce	Styrene, ATBC, 1-Octene, DEHA	20/40/60
Rice	BP, Uvitex OB, DPBD DINP, DINCH, Irganox 1076	20/40/60
Yoghurt	Styrene, ATBC, 1-Octene, DEHA	20/40/60
Pork 30% fat	Styrene, ATBC, 1-Octene, DEHA	5/20
Turkey	BP, Uvitex OB, DPBD	5/20/40
Butter toast	Styrene, ATBC, 1-Octene, DEHA	20/40/60
Cooked ham	BHT, ITX, DPP, BPA, Triclosan	20/40/60
Mayonnaise	Uvitex OB, DIPN, Chimasorb 81	20/40/60
UHT milk	Styrene, ATBC, 1-Octene, DEHA	20/40/60
Condensed milk	Styrene, ATBC, 1-Octene, DEHA	20/40/60
Pate	BHT, ITX, DPP, BPA, Triclosan	20/40/60
Gouda	BP, Uvitex OB, DPBD DINP, DINCH, Irganox 1076	20/40/60
Ground nuts	BP, Uvitex OB, DPBD DINP, DINCH, Irganox 1076	20/40/60

Chocolate spread	BHT, ITX, DPP, BPA, Triclosan	20/40/60
Whipping cream	Styrene, ATBC, 1-Octene, DEHA	20/40/60
Dough	BP, Uvitex OB, DPBD DINP, DINCH, Irganox 1076	20/40/60
Margarine	Styrene, ATBC, 1-Octene, DEHA	10/20/40
Salami	Styrene, ATBC, 1-Octene, DEHA	10/20/40
Olive oil	Styrene, ATBC, 1-Octene, DEHA	20/40/60
Dark chocolate	Uvitex OB, DIPN, Chimasorb 81	20/40/60

Table 25 lists the 17 models substances used in the FACET project with each substance's LogPow.

Table 25: Summary of Model Substances

Substance	LogPow
Styrene	2..95
Benzophenone	3.18
BPA	4.045
DPP	4.1
ATBC	4.29
1-Octene	4.57
Triclosan	4.76
BHT	5.1
DPBD	5.29
ITX	5.54
DIPN	6.08
Chimassorb 81	6.96
DEHA	8.12
Uvitex OB	7.58
DINP	8.8
DINCH	9.82
Irganox 1076	12.536

Methodology

Predicting the Partition Coefficient

For each unique combination of polymer, food, and temperature considered in the FACET project, attributes of the substance are required to estimate the partition coefficient between a polymer and a food (Kpf). In the approach outlined in this document the substance LogPow (i.e. octanol/water partition coefficient) is the attribute used to represent the migrant in the Kpf formula. Findings in Ozaki, *et al.,* (2008) report that the LogPow is “widely used in environmental, pharmaceutical, biochemical and toxicological to describe the lipophilic nature of various compounds” and “using linear regression lines, Kpf values could be predicted from the LogPow values of the migrants”. A similar approach is used to estimate Kpf values in the Food Migrosure project, as reported by Franz & Simoneau, (2008) where “the partition coefficient between plastic and food for a migrant based on its octanol/water partition coefficient gives a realistic estimate of the migrant’s migration from the plastic to food”.

Curve Fitting

For the approximately 600 combinations of polymer (LDPE), food, substance, and temperature, curves were fitted to the log scaled Kpf data using a iterative mathematical procedure called **non-linear least squares regression**. This technique fits a non-linear curve to a set of data points with the objective of minimising the total error. Here the total error is defined as the sum of the squares of the errors between the actual data points and the fitted values for those points. These error values are collated and form a distribution which can be simulated from at run time. Ultimately the magnitude of these errors influences the size of the variance in the migration model outputs.

Since the data being modelled is log scaled, it makes sense to use a curve which takes the shape of a log type function. For this study, a starting function of the form $f(x) = a*log(b*x + c)$ is used for unknown values *a, b,* and *c.* During the iterative process *a, b,* and *c* are refined until optimal values for the parameters are found. Note that the independent variable *x* in the above formula represents the LogPow of the substance.

Extension of FACET Scenarios

Since the number of scenarios presented in FACET is a subset of the set of all possible scenarios, it is necessary to raise a question regarding a map between the two for the estimation of partition coefficients. To answer this question requires an examination of the different components of each scenario individually, that is polymer, food, substance and temperature.

Polymer

Individual polymers are placed in one of three classes taking into consideration their polarity. The three classes are identified by non-polar, medium-polar and polar.

Food

Here the 168 lowest tier foods defined in the FACET Packaging module are represented by one of 35 model foods using a mapping agreed upon during the course of the FACET project.

Substance

At run time, a Kpf value is estimated by selecting the appropriate curve for a particular combination of polymer, food, temperature, predicting the response (i.e. Kpf) using the substance LogPow as input.

Temperature

As only a limited number of temperatures were considered in the experimental testing phase in FACET, there is a requirement to consider temperatures outside this range. In the approach outlined in this document temperatures falling outside the current range of values available are considered by interpolating between (or extrapolating outside) existing temperature values where possible.

Results

In Section 0 the following information is provided for seven model foods which range from wine (hydrophilic) to olive oil (lipophilic) for a range of substances of varying polarity:

- comparison of experimental and model Kpf values for each food
- effect of temperature on Kpf
- comparison of experimental and model migration data

Migration of Substances from LDPE

Wine

Overall, this food shows a good agreement between experimental and fitted data.

Kpf (fit versus actual)

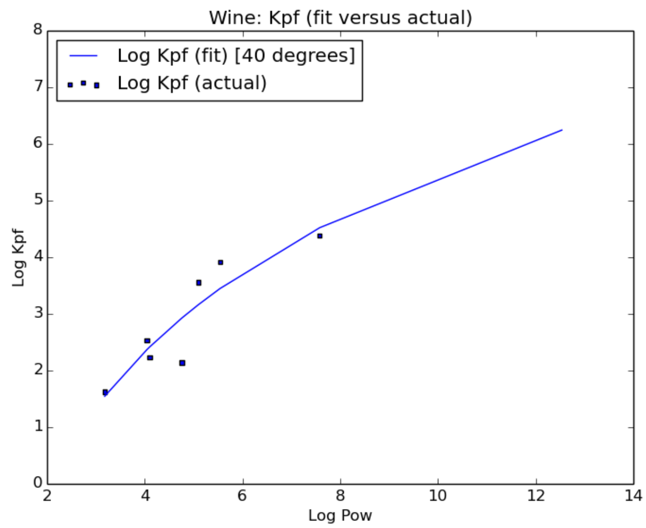


Figure 6: Kpf - Wine [40 degrees]

Kpf (Temperature variation)

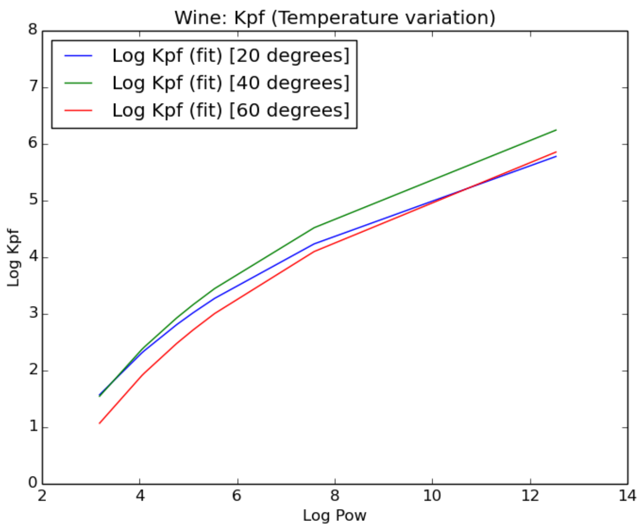


Figure 7: Kpf - Wine (Temperature variation) [40 degrees]

Migration (fit versus actual)

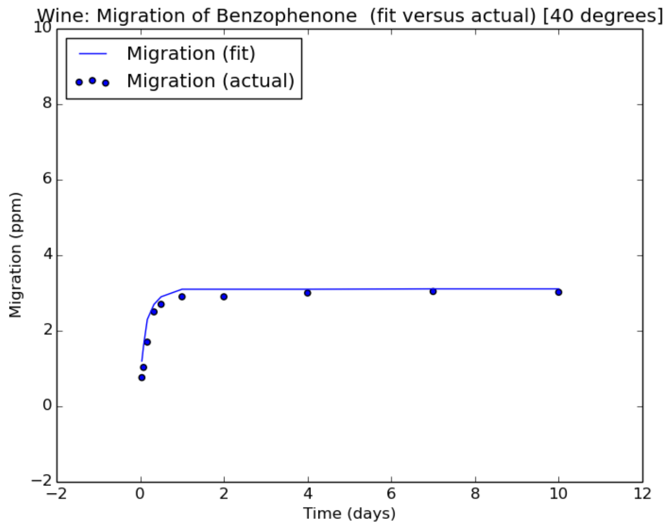


Figure 8: Migration - Wine - Benzophenone [40 degrees]

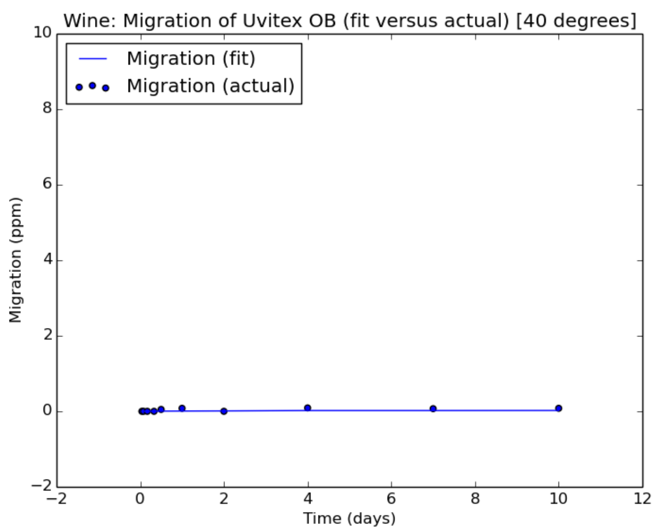


Figure 9: Migration - Wine - Uvitex OB [40 degrees]

Orange Juice

For this food, a good fit is shown for all substances except Uvitex OB. For this substance the fitted curve in **Figure 10** shows an overestimation of the Kpf if compared with the experimental Kpf value. The consequence of this is an underestimation of the migration as shown in **Figure 13**.

Kpf (fit versus actual)

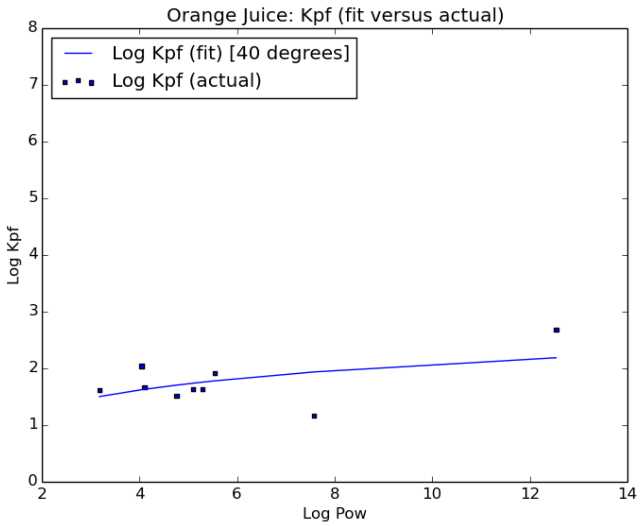


Figure 10: Kpf - Orange Juice [40 degrees]

Kpf (Temperature variation)

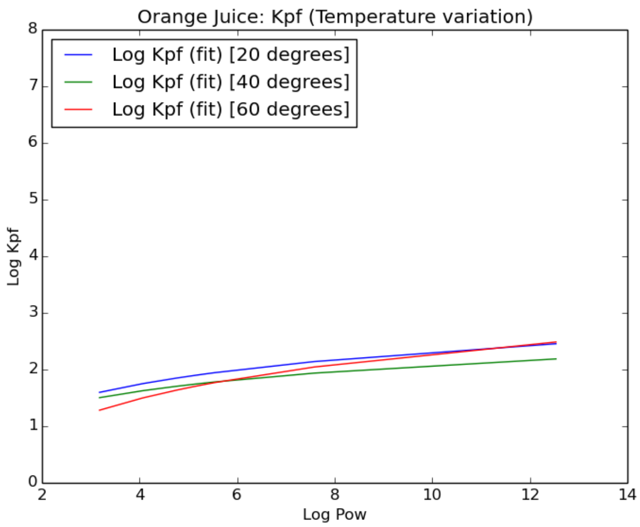


Figure 11: Kpf - Orange Juice (Temperature variation)

Migration (fit versus actual)

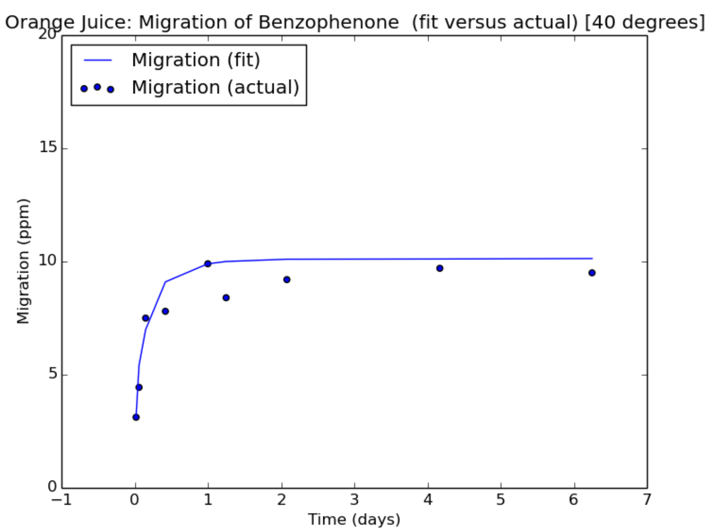


Figure 12: Migration - Orange Juice - Benzophenone [40 degrees]

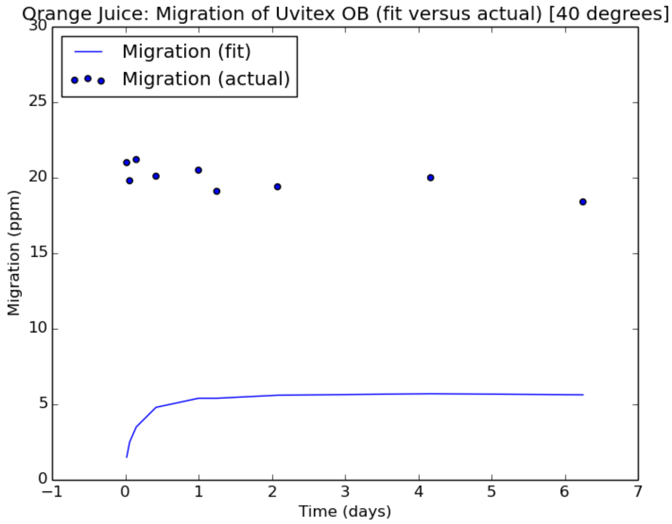


Figure 13: Migration – Orange Juice - Uvitex OB [40 degrees]

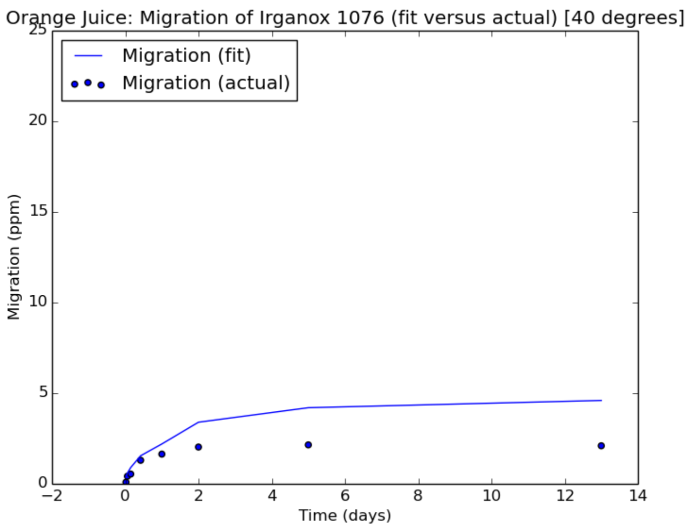


Figure 14: Migration - Orange Juice – Irganox1076 [40 degrees]

Pork (30% fat)

Overall, this food shows a good agreement between experimental and fitted data.

Kpf (fit versus actual)

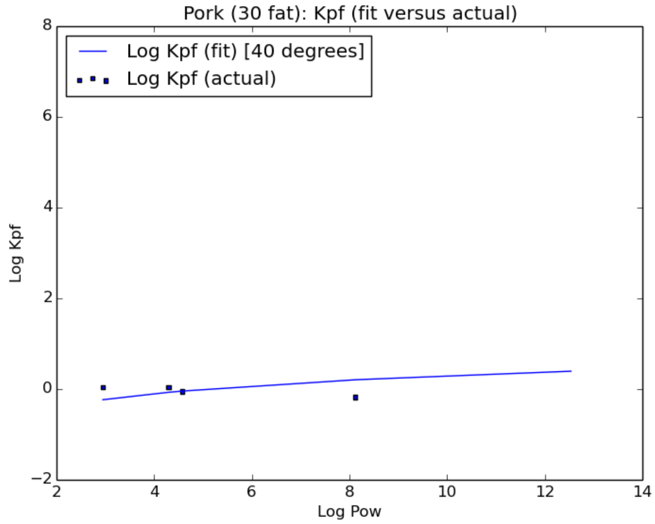


Figure 15: Kpf - Pork (30% fat) [40 degrees]

Kpf (Temperature variation)

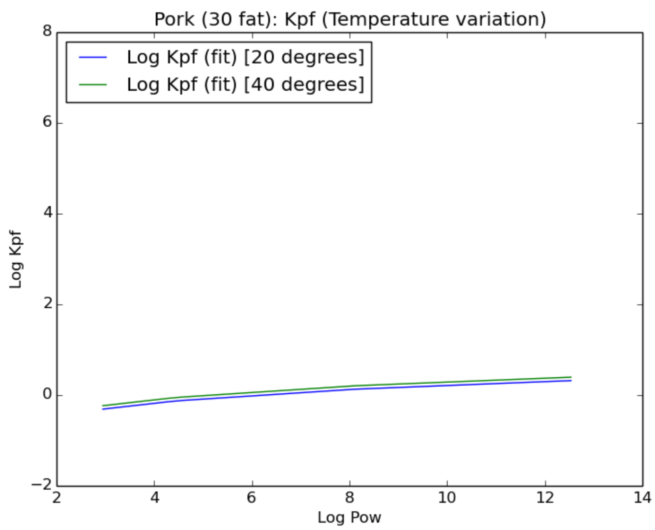


Figure 16: Kpf - Pork (30% fat) (Temperature variation)

Migration (fit versus actual)

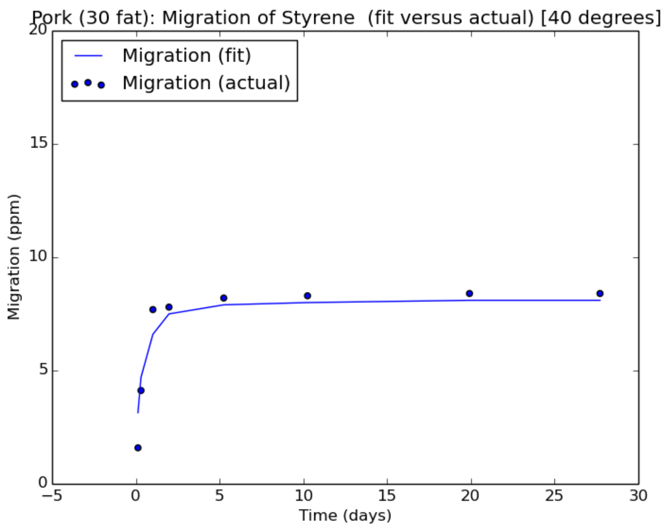


Figure 17: Migration - Pork (30% fat) - Styrene [40 degrees]

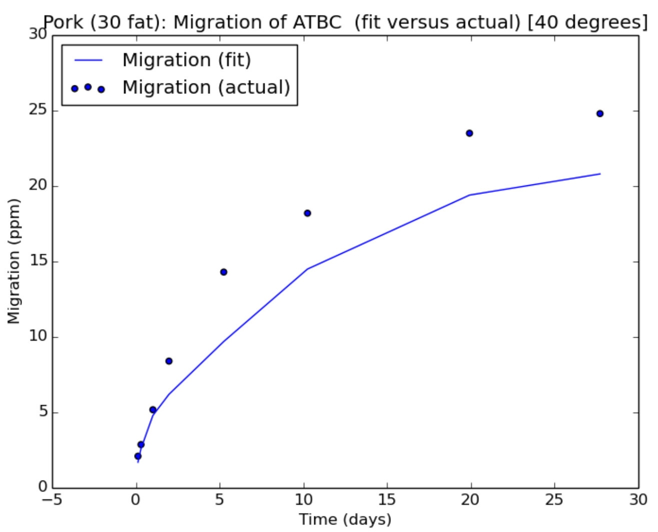


Figure 18: Migration - Pork (30% fat) - ATBC [40 degrees]

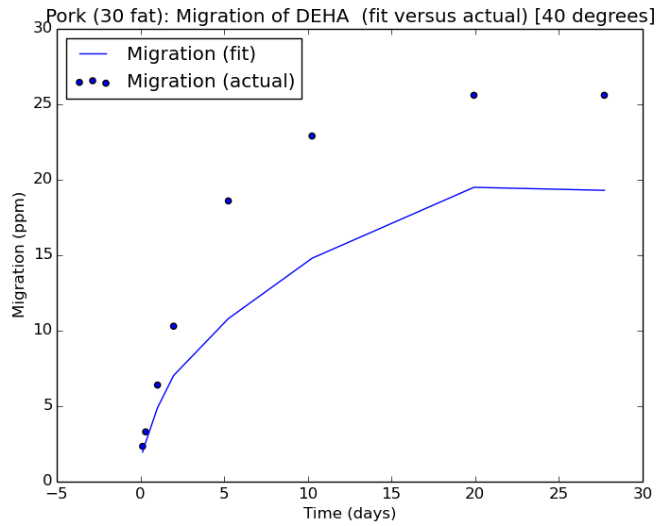


Figure 19: Migration - Pork (30% fat) - DEHA [40 degrees]

Butter Toast

Overall, this food shows a good agreement between experimental and fitted data.

Kpf (fit versus actual)

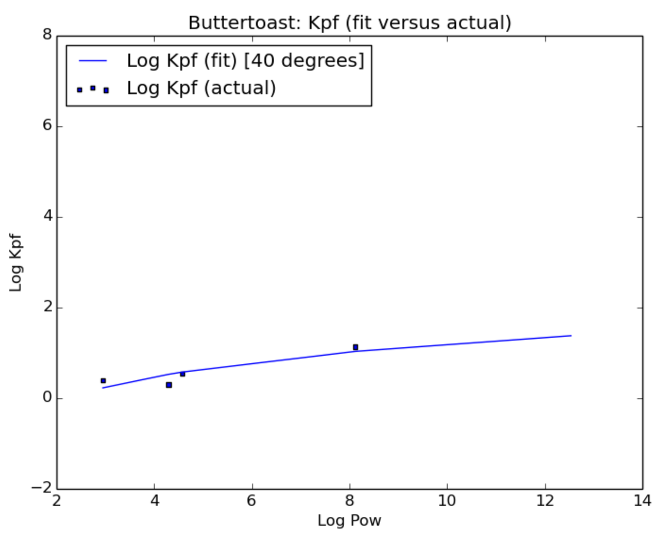


Figure 20: Kpf - Butter Toast [40 degrees]

Kpf (Temperature variation)

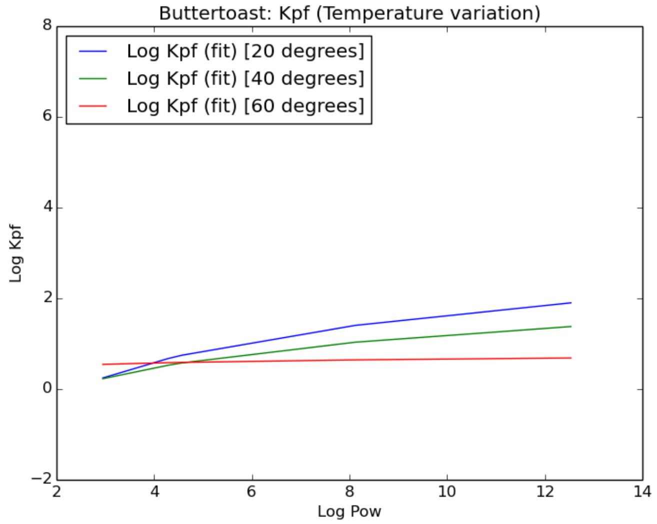


Figure 21: Kpf - Butter Toast (Temperature variation)

Migration (fit versus actual)

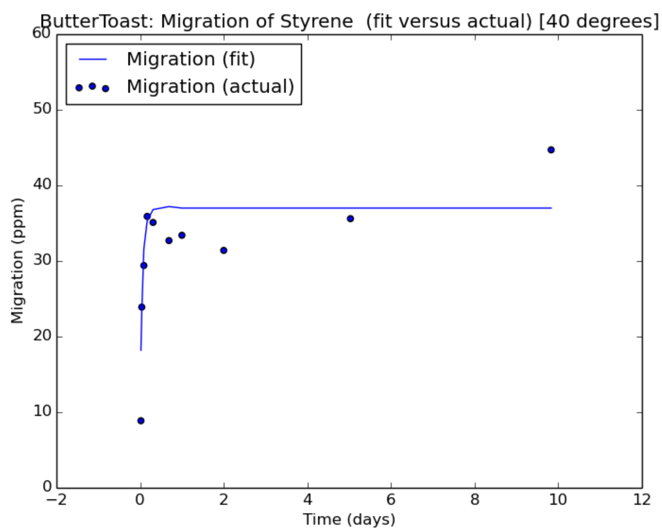


Figure 22: Migration – Butter Toast - Styrene [40 degrees]

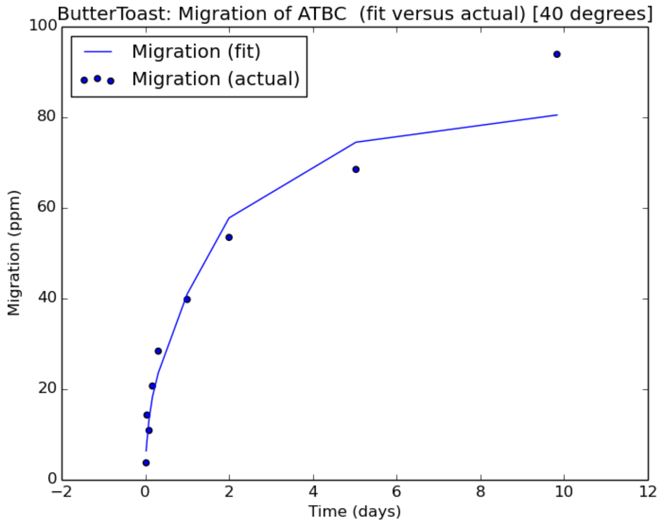


Figure 23: Migration - Butter Toast - ATBC [40 degrees]

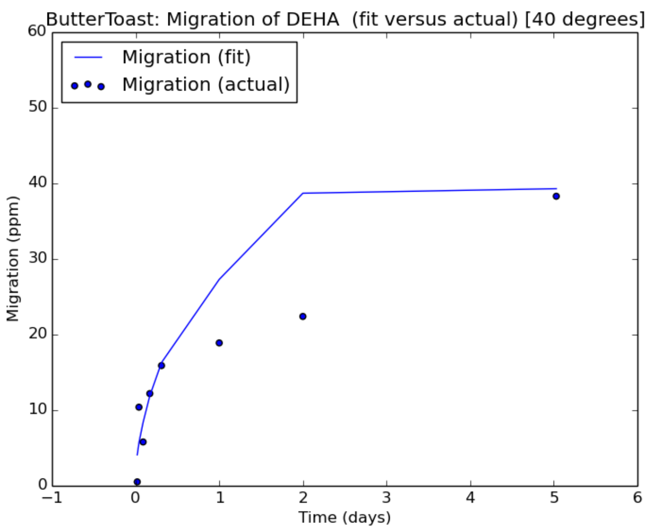


Figure 24: Migration - Butter Toast - DEHA [40 degrees]

Ground Nuts

The curve fitted to the experimental data for ground nuts shows that the Kpf for Uvitex OB is slightly underestimated. This results in an overestimation for the migration of the substance as illustrated in Figure 28.

Kpf (fit versus actual)

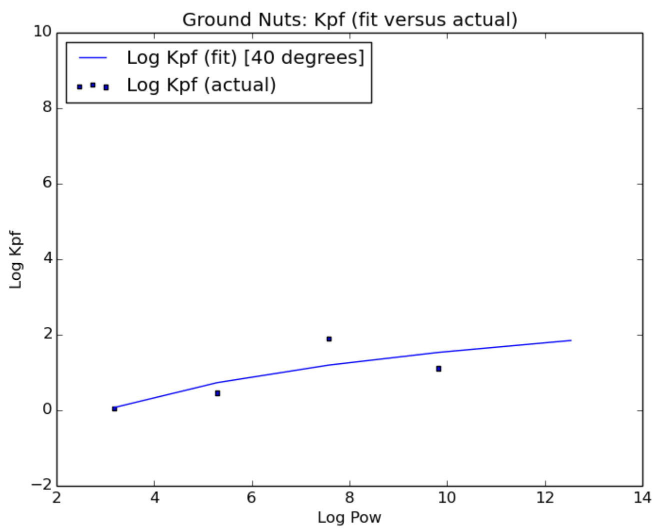


Figure 25: Kpf - Ground Nuts [40 degrees]

Kpf (Temperature variation)

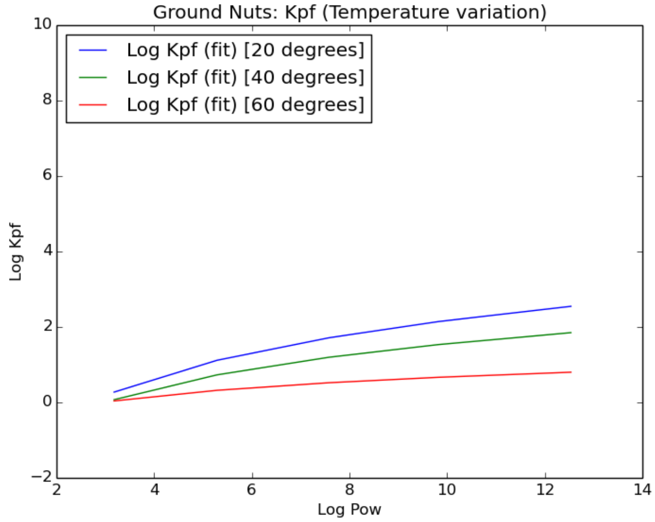


Figure 26: Kpf - Ground Nuts (Temperature variation)

Migration (fit versus actual)

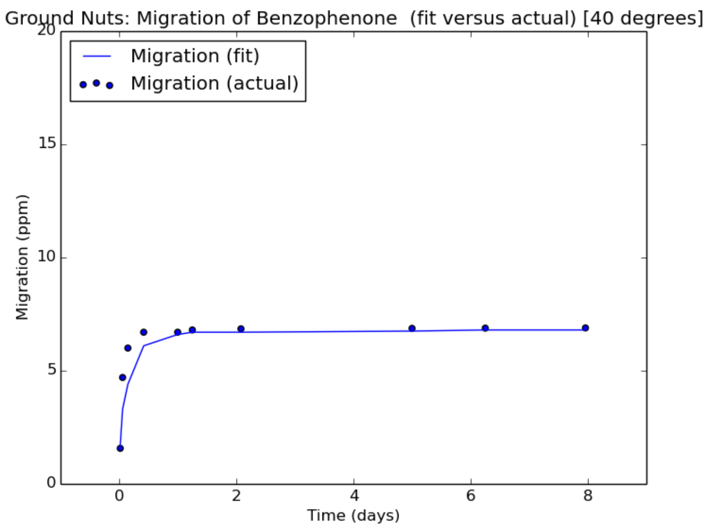


Figure 27: Migration - Ground Nuts – Benzophenone [40 degrees]

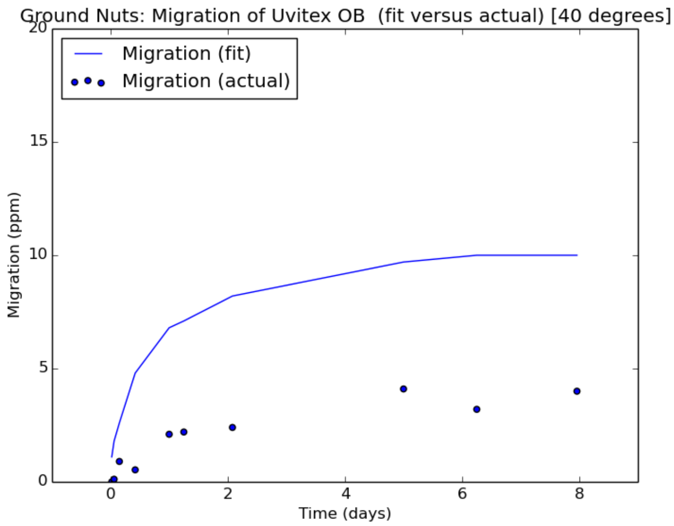


Figure 28: Migration - Ground Nuts - Uvitex OB [40 degrees]

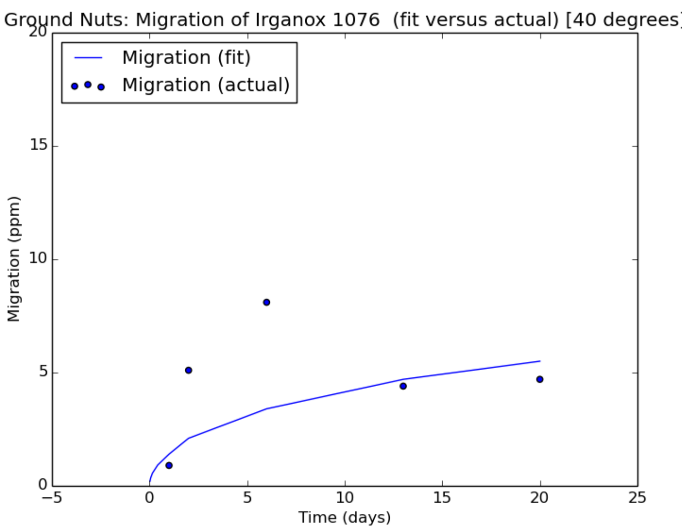


Figure 29: Migration - Ground Nuts - Irganox 1076 [40 degrees]

Margarine

Overall, this food shows a good agreement between experimental and fitted data.

Kpf (fit versus actual)

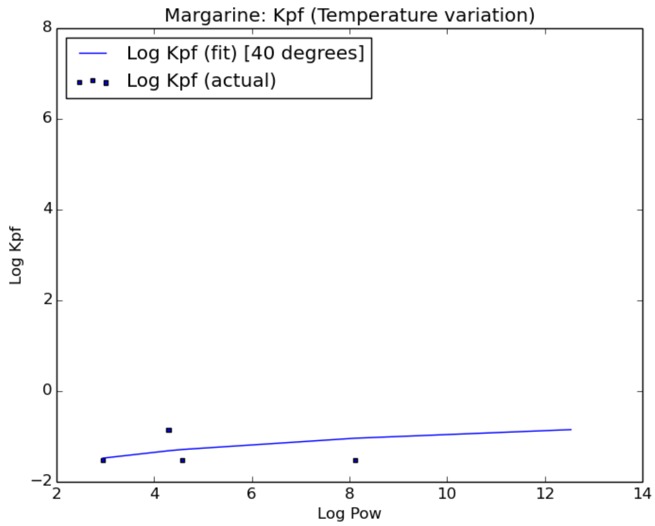


Figure 30: Kpf - Margarine [40 degrees]

Kpf (Temperature variation)

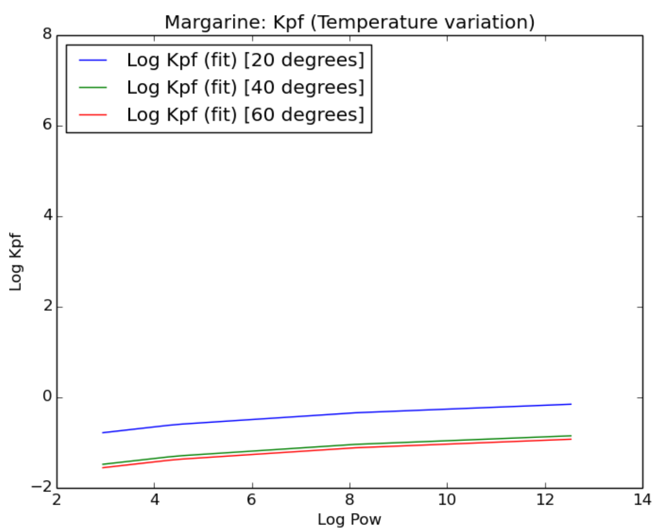


Figure 31: Kpf - Margarine (Temperature variation)

Migration (fit versus actual)

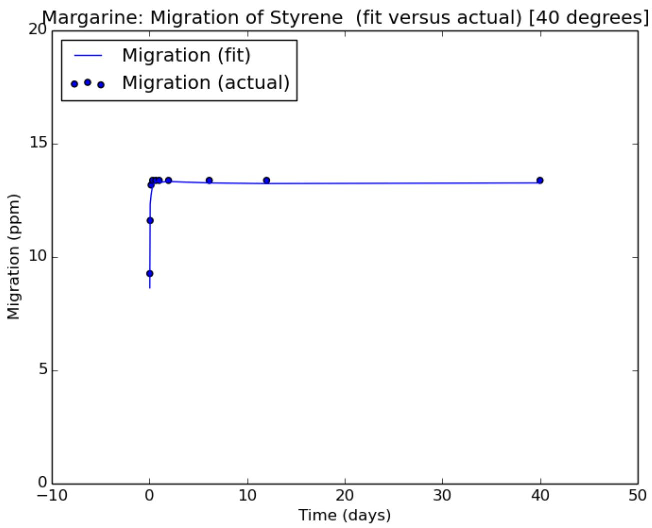


Figure 32: Migration: - Margarine – Styrene [40 degrees]

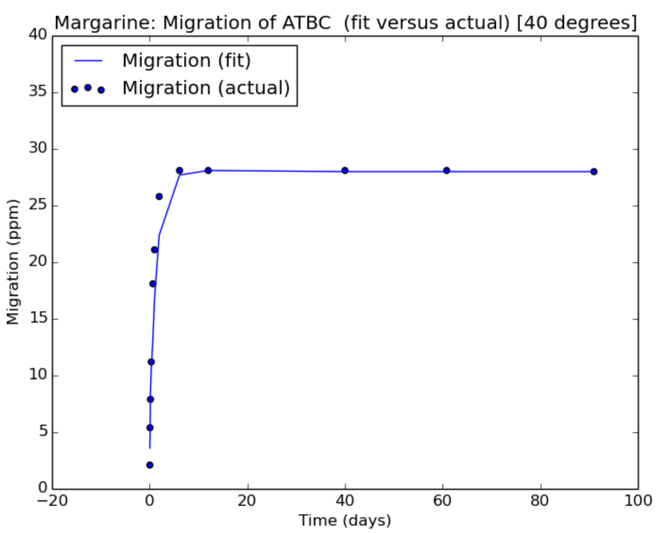


Figure 33: Migration - Margarine – DEHA [40 degrees]

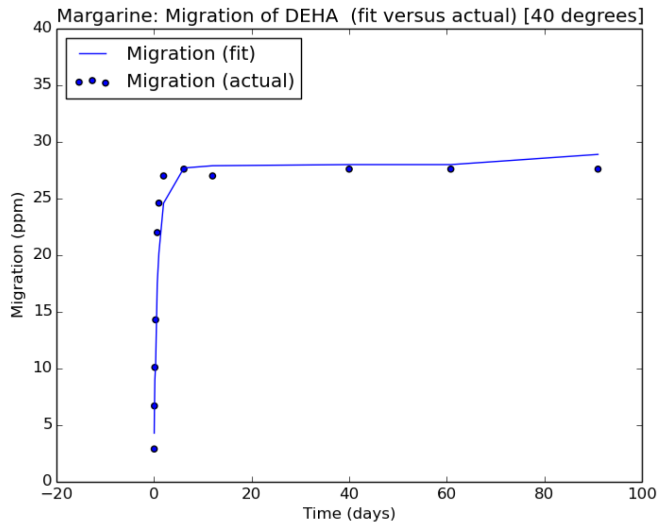


Figure 34: Migration - Margaine – DEHA [40 degrees]

Olive Oil

Overall, this food shows a good agreement between experimental and fitted data.

Kpf (fit versus actual)

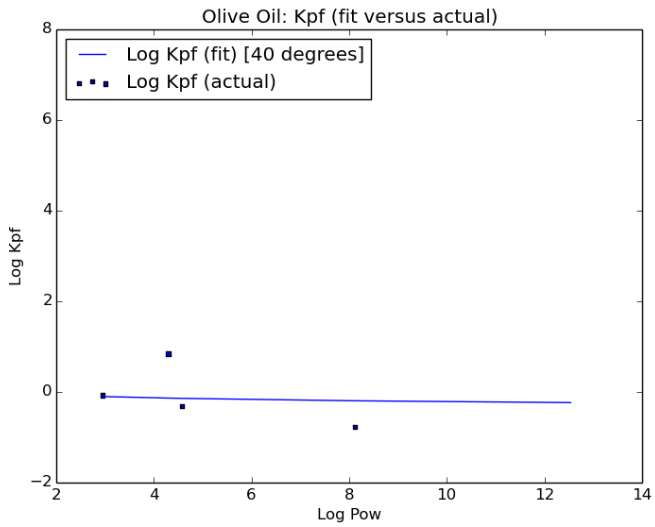


Figure 35: Kpf - Olive Oil [40 degrees]

Kpf (Temperature variation)

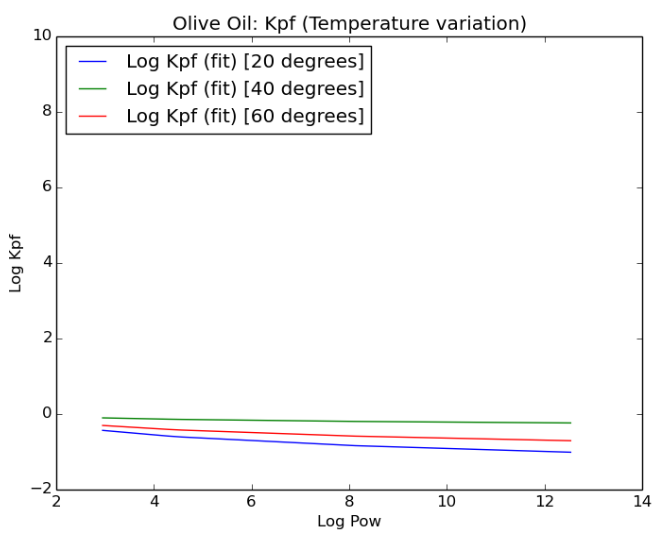


Figure 36: Kpf - Olive Oil (Temperature variation)

Migration (fit versus actual)

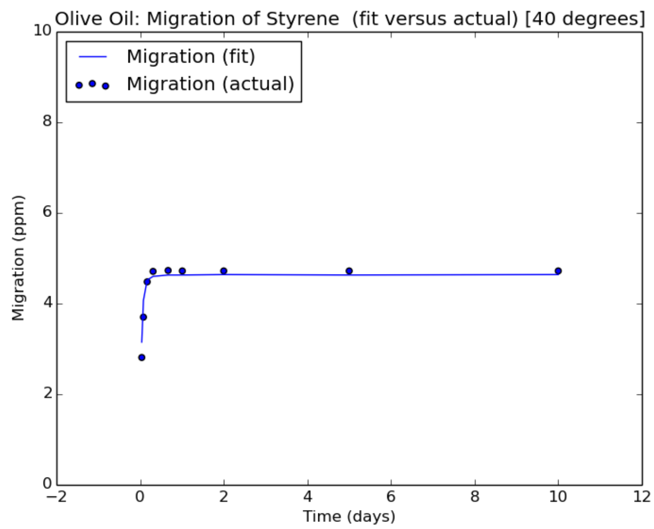


Figure 37: Migration - Olive Oil – Styrene [40 degrees]

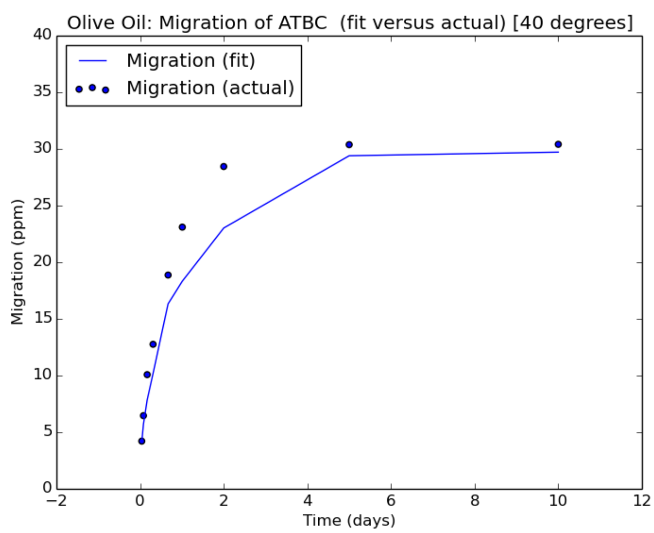


Figure 38: Migration - Olive Oil – ATBC [40 degrees]

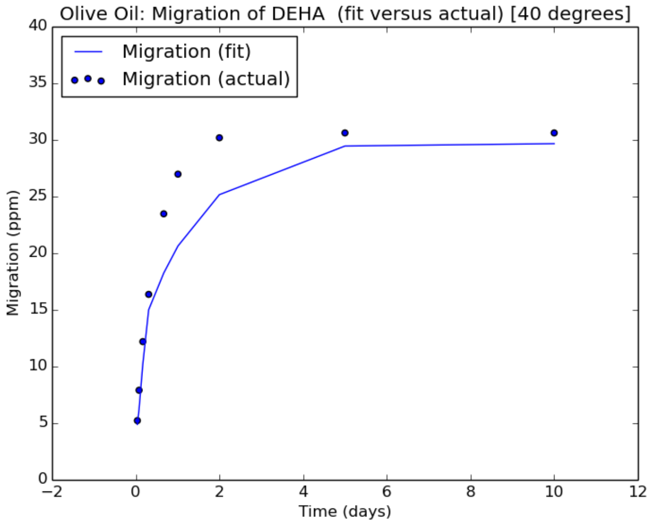


Figure 39: Migration - Olive Oil – DEHA [40 degrees]

Migration of Substances from PA

Bacon

Kpf (fit versus actual)

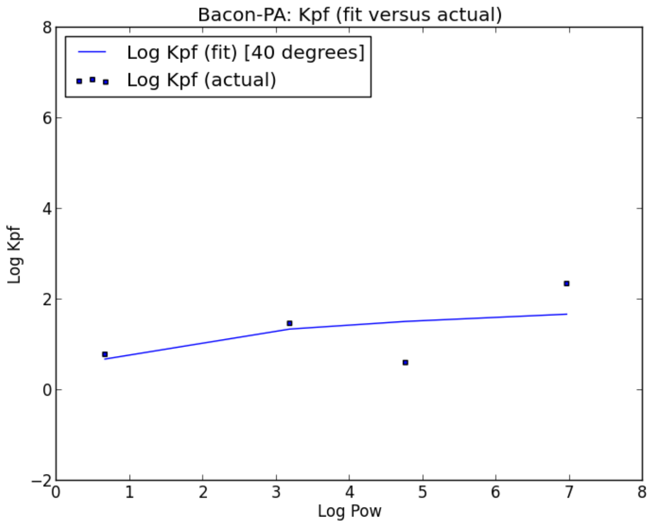


Figure 40: Kpf - Bacon [40 degrees]

Kpf (Temperature variation)

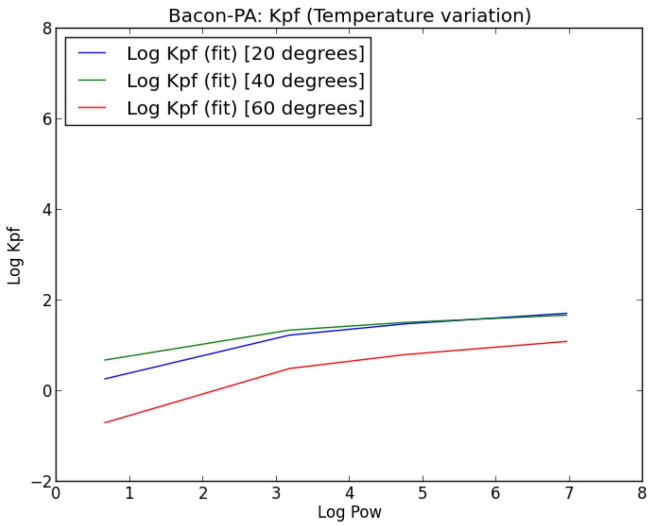


Figure 41: Kpf - Bacon (Temperature variation)

Migration (fit versus actual)

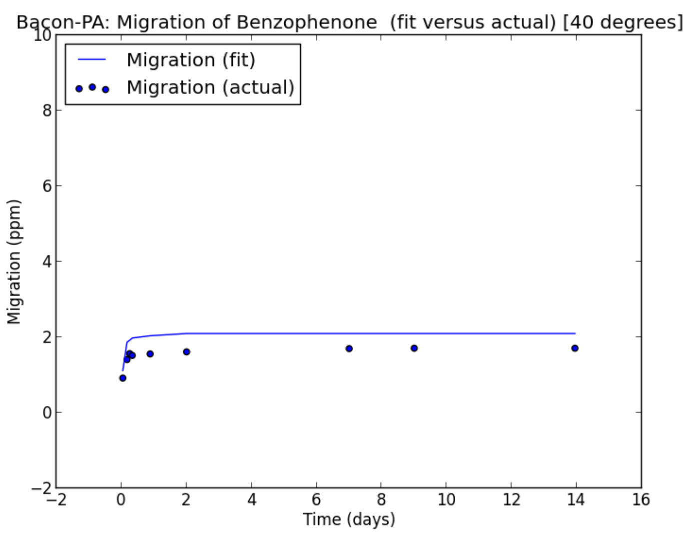


Figure 42: Migration - Bacon - Benzophenone [40 degrees]

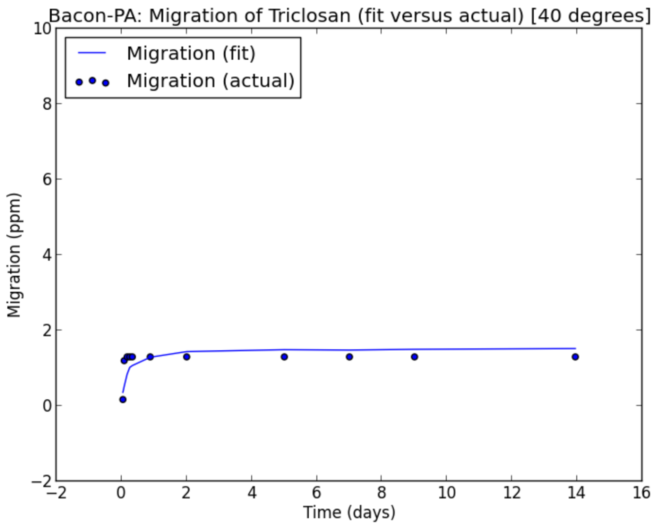


Figure 43: Migration - Bacon - Triclosan [40 degrees]

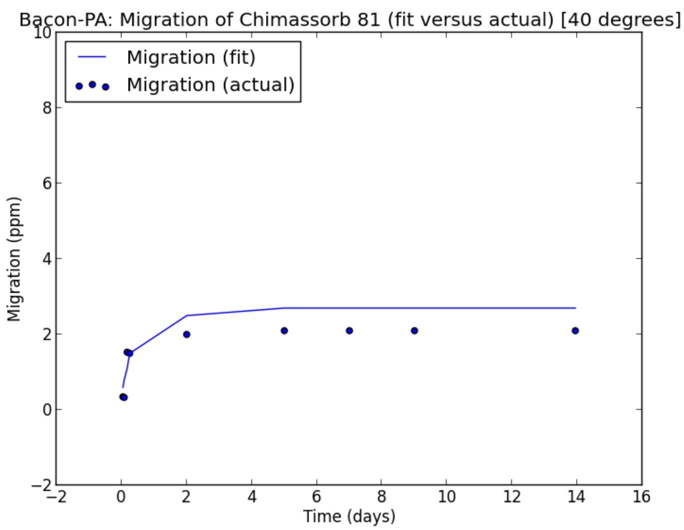


Figure 44: Migration - Bacon - Chimassorb 81 [40 degrees]

Gouda

Kpf (fit versus actual)

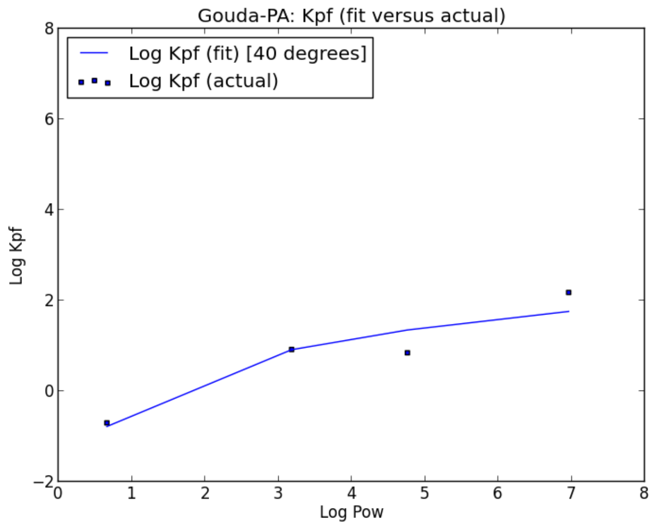


Figure 45: Kpf - Gouda [40 degrees]

Kpf (Temperature variation)

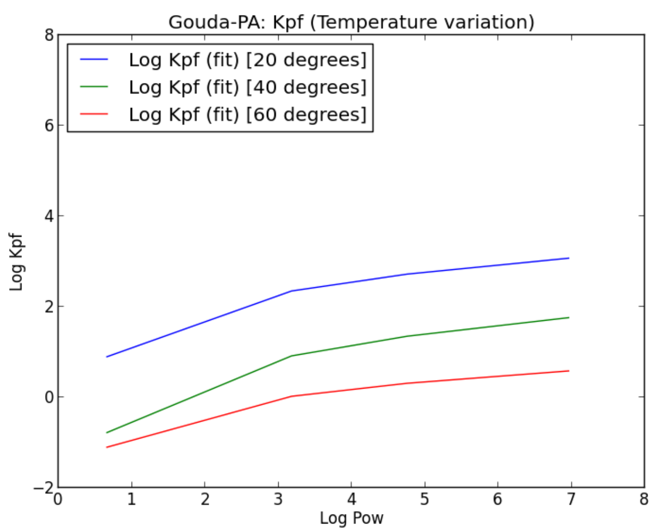


Figure 46: Kpf - Gouda (Temperature variation)

Migration (fit versus actual)

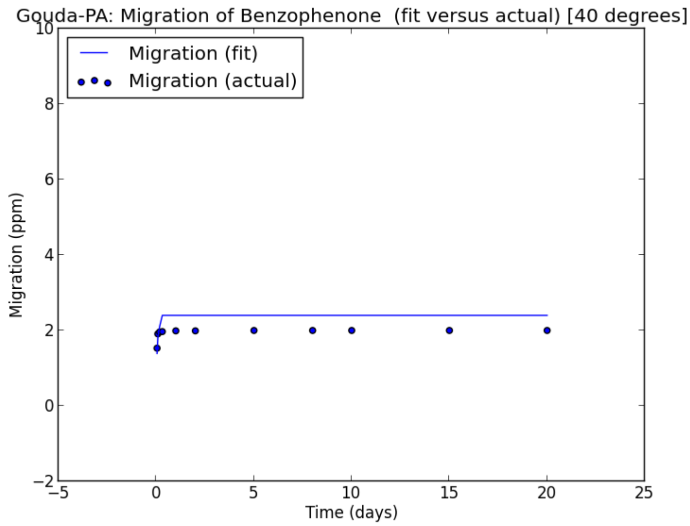


Figure 47: Migration - Gouda - Benzophenone [40 degrees]

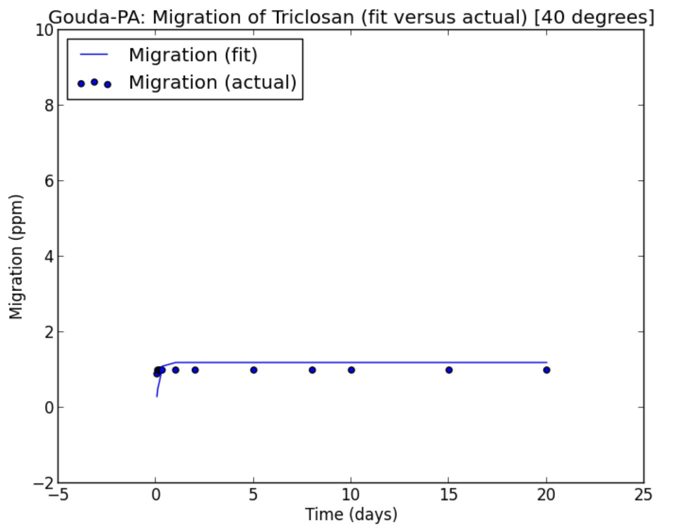


Figure 48: Migration - Gouda - Triclosan [40 degrees]

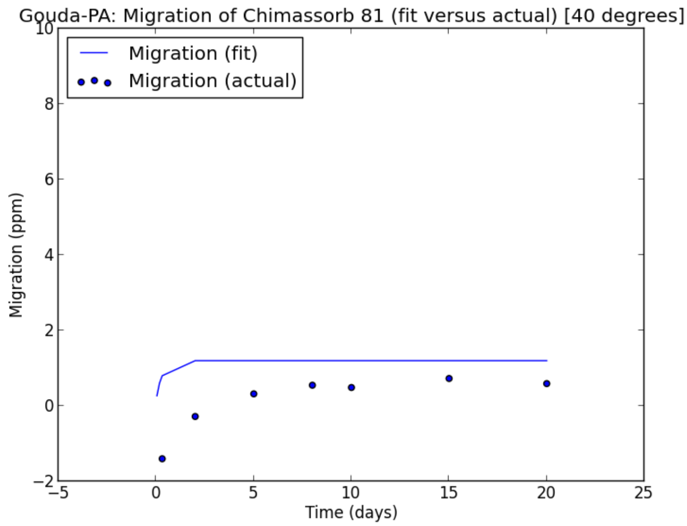


Figure 49: Migration - Gouda - Chimassorb 81 [40 degrees]

Polony

Kpf (fit versus actual)

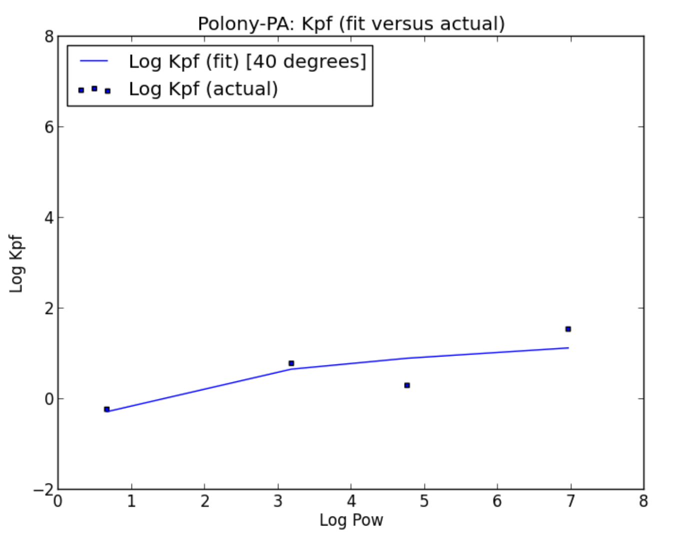


Figure 50: Kpf - Polony [40 degrees]

Kpf (Temperature variation)

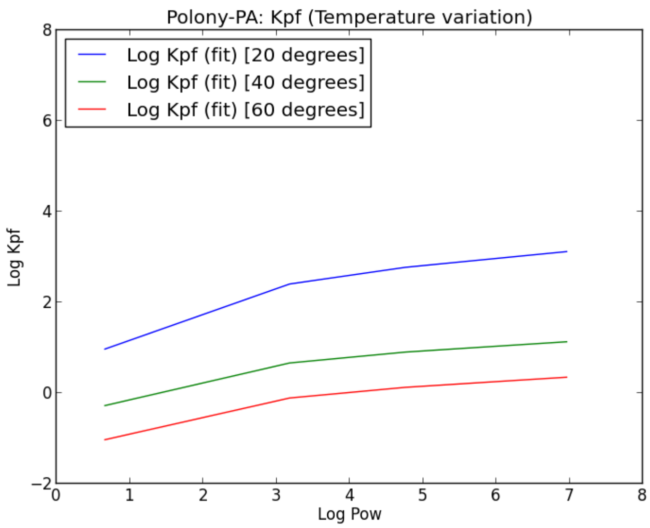


Figure 51: Kpf - Polony (Temperature variation)

Migration (fit versus actual)

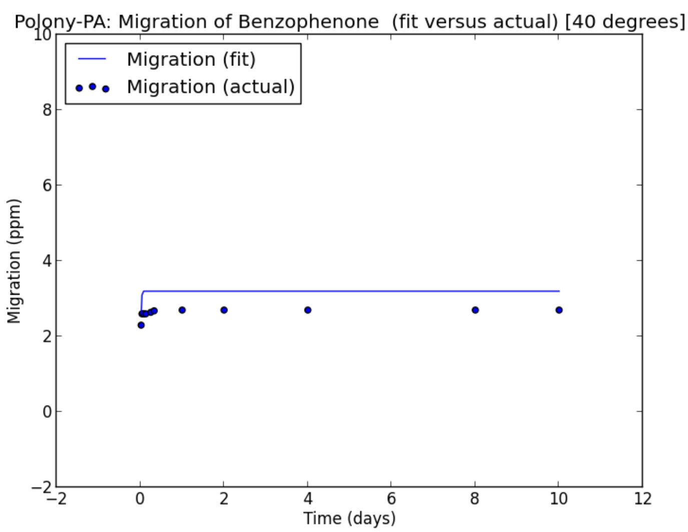


Figure 52: Migration - Polony - Benzophenone [40 degrees]

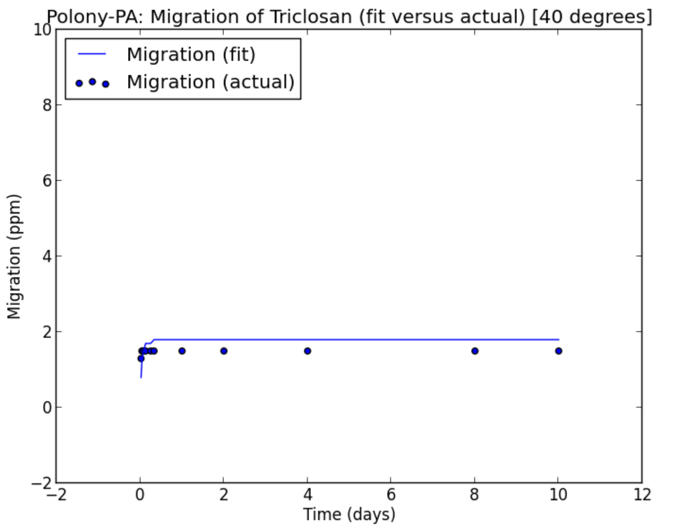


Figure 53: Migration - Polony - Triclosan [40 degrees]

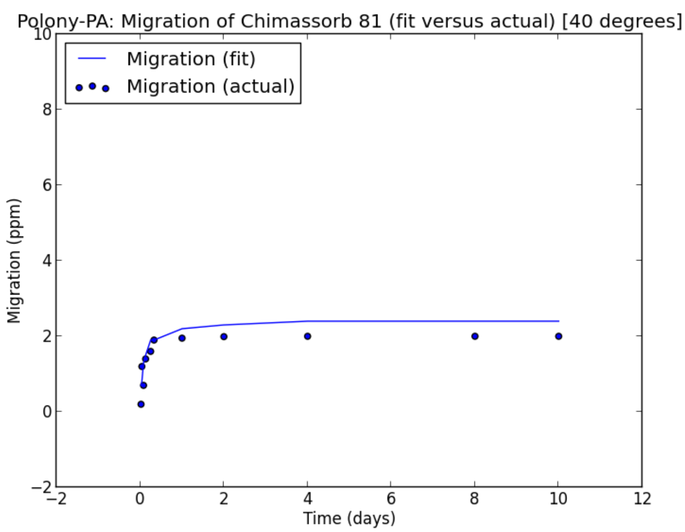


Figure 54: Migration - Polony - Chimassorb 81

Appendix

In **Appendix** , graphs comparing actual Kpf data with fitted results are provided for each of the model foods not considered in Section 0. In each case the polymer used is LDPE and the temperature is fixed at 40 degrees centigrade.

Apple sauce

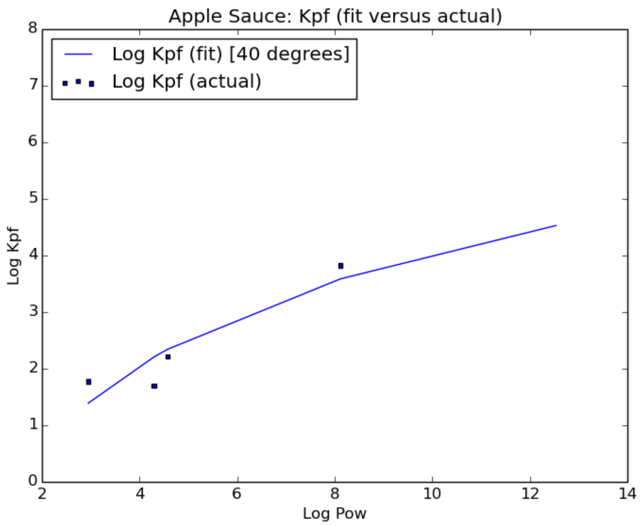


Figure 55: Kpf - Apple Sauce [40 degrees]

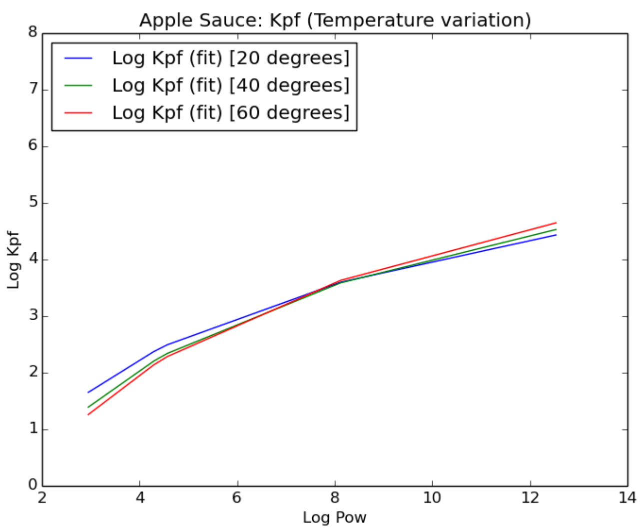


Figure 56: Kpf - Apple Sauce (Temperature variation)

Ketchup

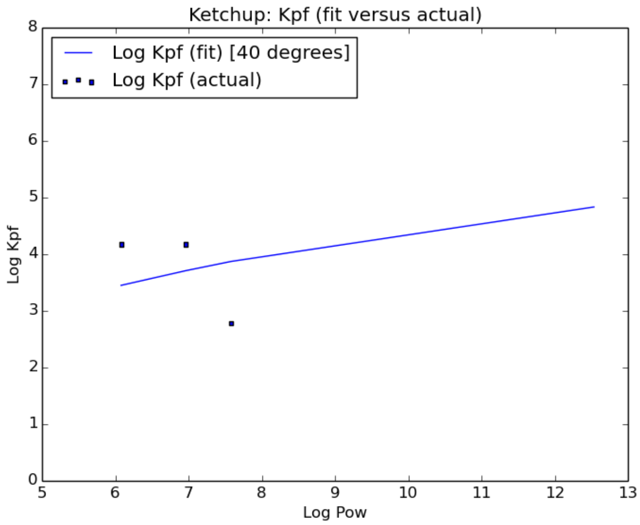


Figure 57: Kpf - Ketchup [40 degrees]

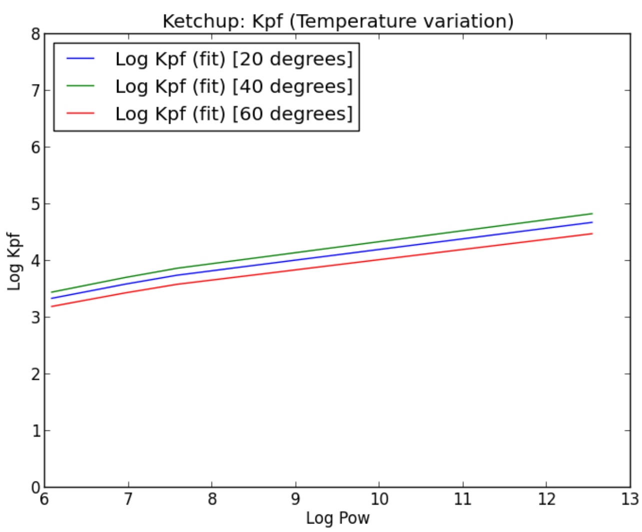


Figure 58: Kpf - Ketchup (Temperature variation)

Tomato sauce

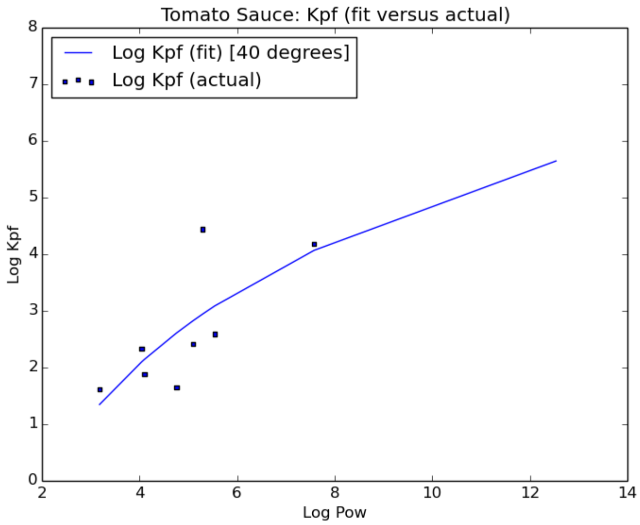


Figure 59: Kpf - Tomato Sauce [40 degrees]

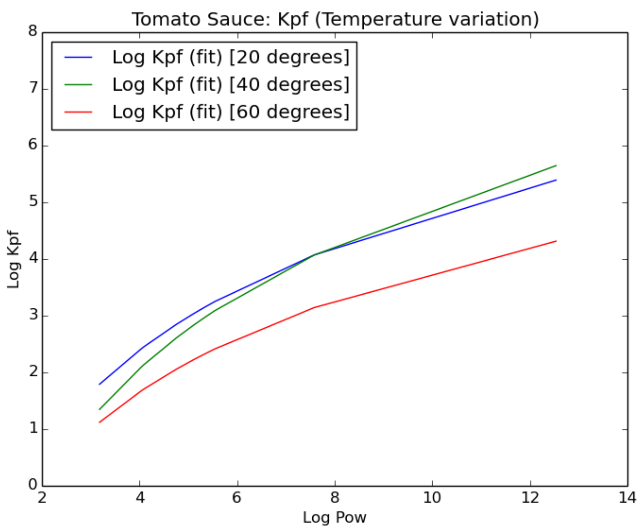


Figure 60: Kpf - Tomato sauce (Temperature variation)

Pork (10% fat)

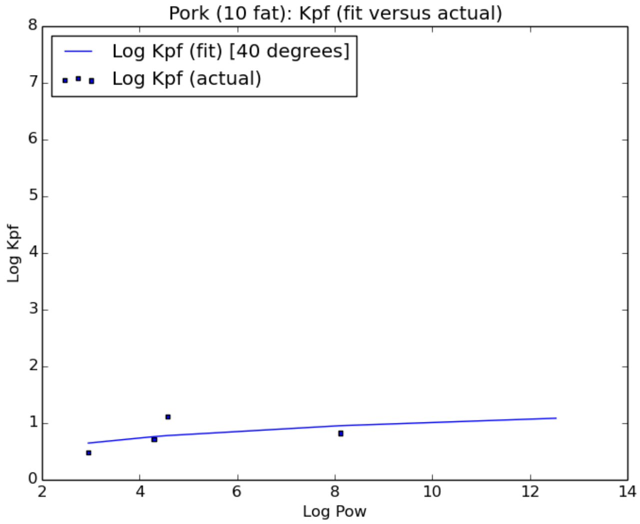


Figure 61: Kpf - Pork (10% fat) [40 degrees]

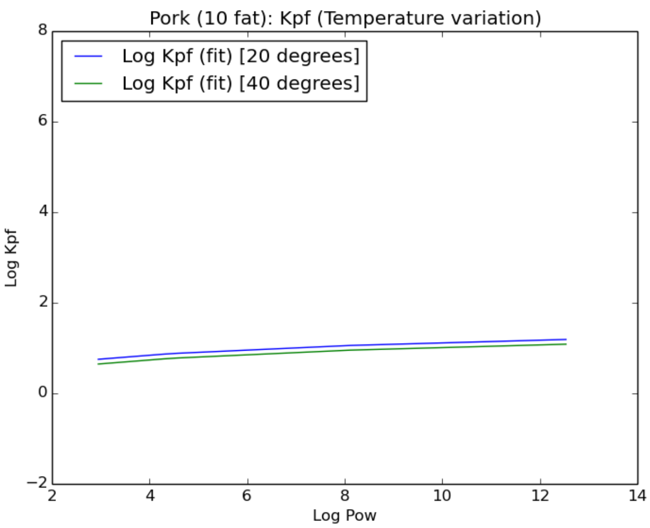


Figure 62: Kpf - Pork (20% fat) (Temperature variation)

Wheat flour

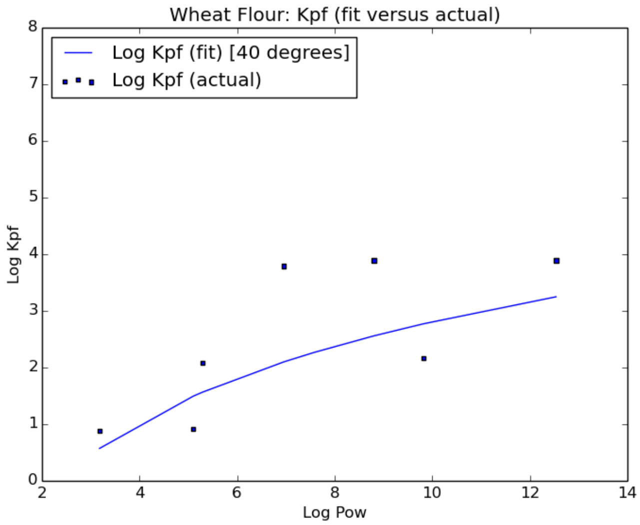


Figure 63: Kpf - Wheat Flour [40 degrees]

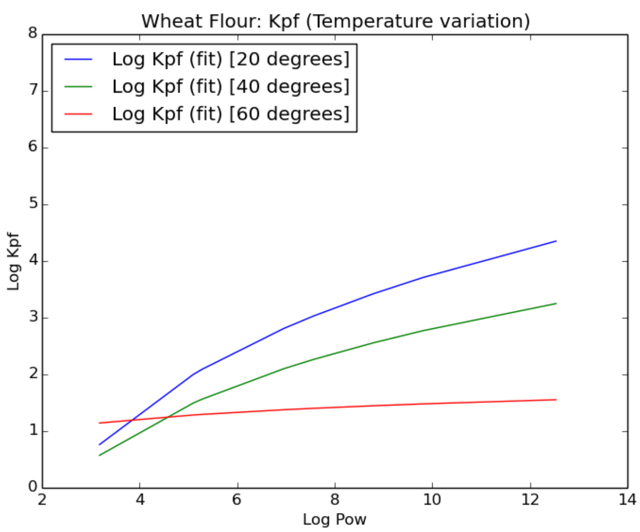


Figure 64: Kpf - Wheat Flour (Temperature variation)

Fish in Brine

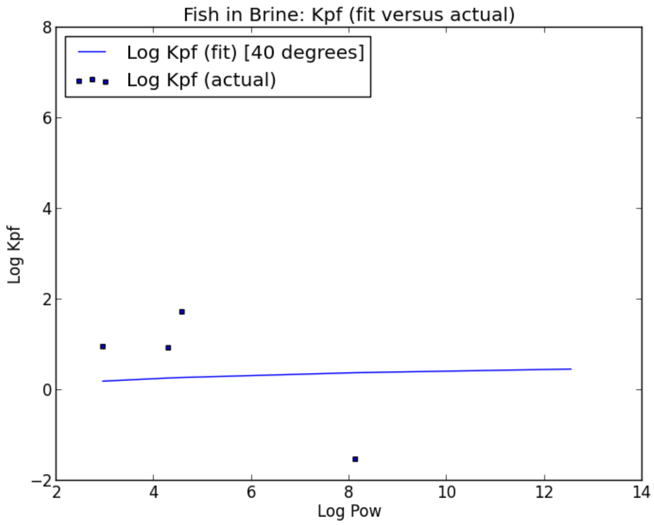


Figure 65: Fish in Brine [40 degrees]

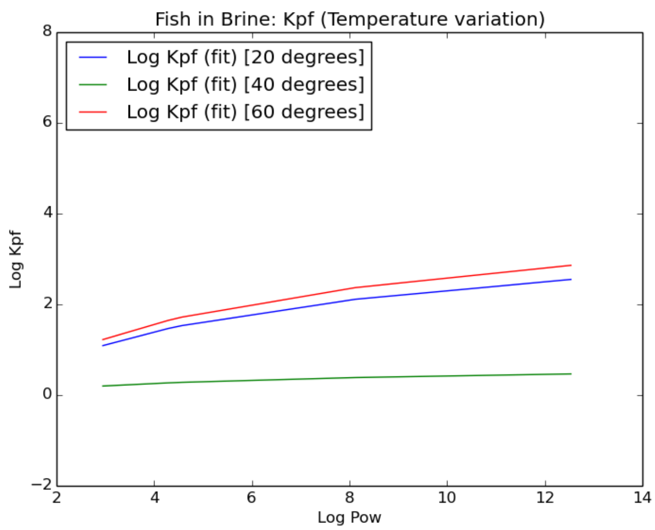


Figure 66: Kpf - Fish in Brine (Temperature variation)

Cottage cheese

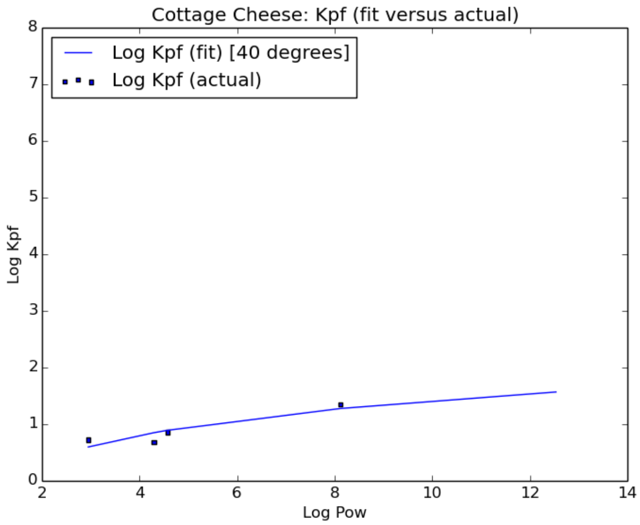


Figure 67: Kpf - Cottage Cheese [40 degrees]

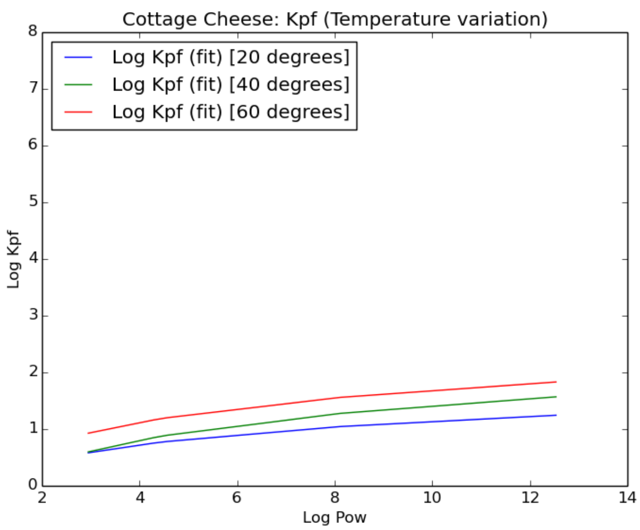


Figure 68: Kpf - Cottage Cheese (Temperature variation)

Pork (20% fat)

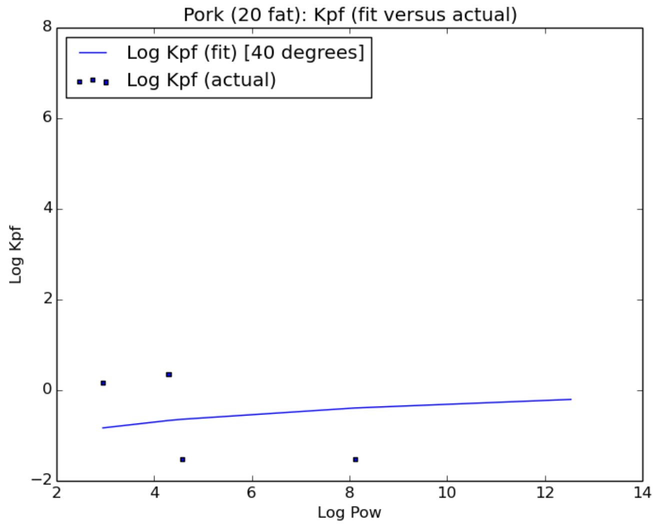


Figure 69: Kpf - Pork (20% fat) [40 degrees]

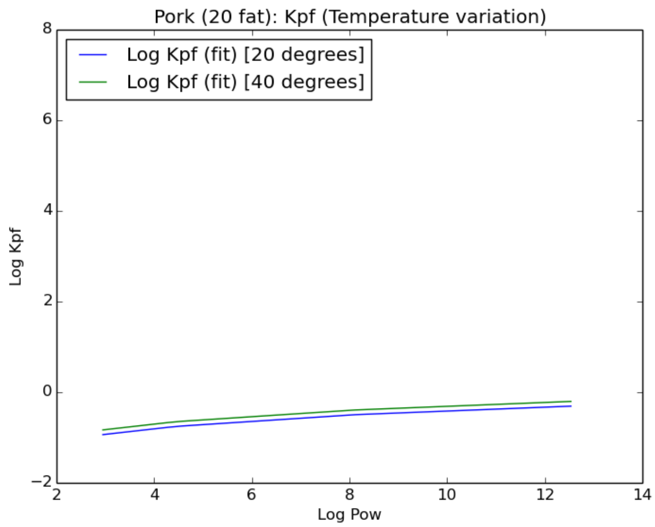


Figure 70: Pork (20% fat) (Temperature variation)

Fish Fingers

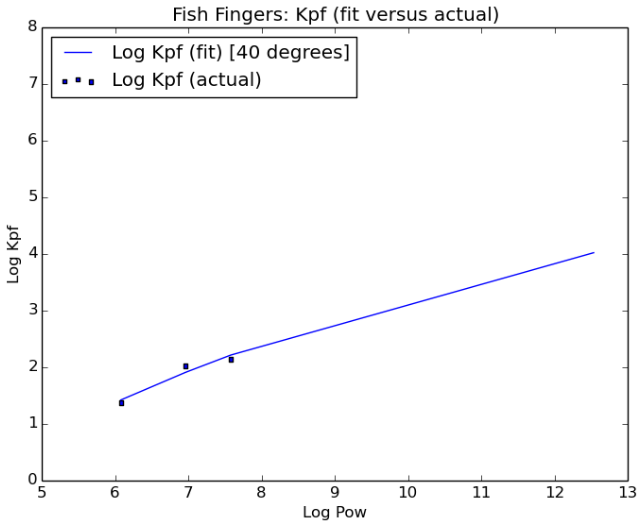


Figure 71: Kpf - Fish Fingers [40 degrees]

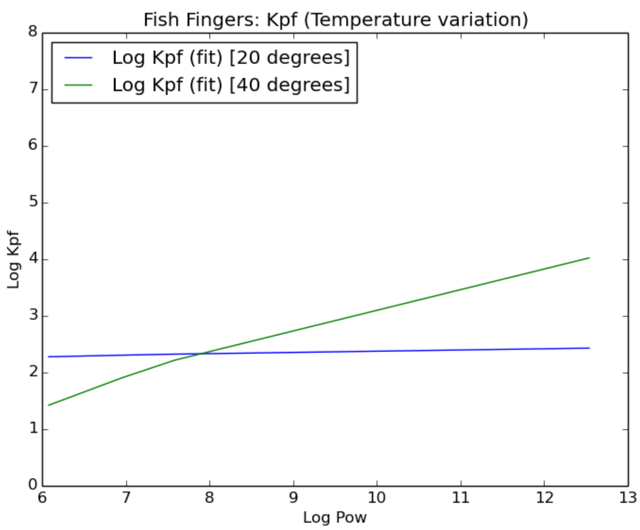


Figure 72: Kpf - Fish Fingers (Temperature variation)

Salmon

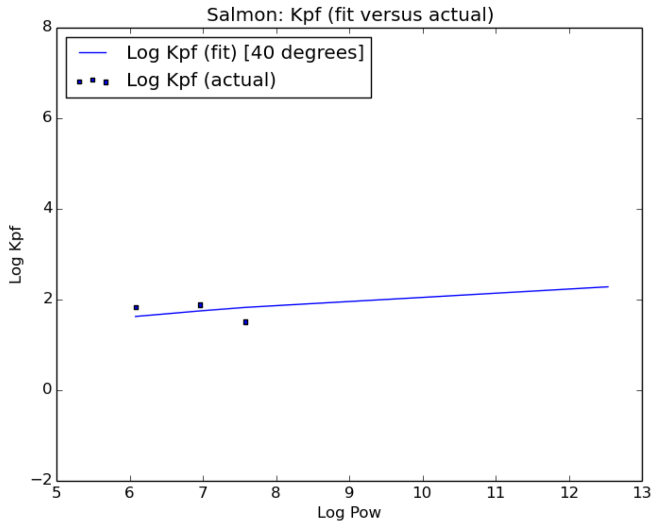


Figure 73: Kpf - Salmon [40 degrees]

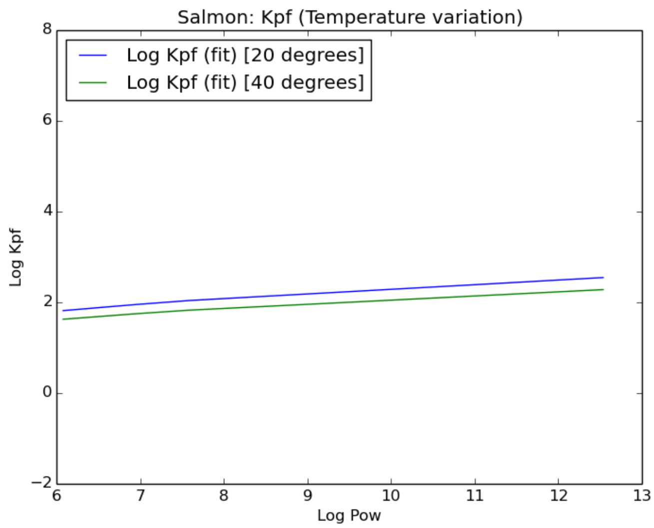


Figure 74: Kpf - Salmon (Temperature variation)

Instant soup

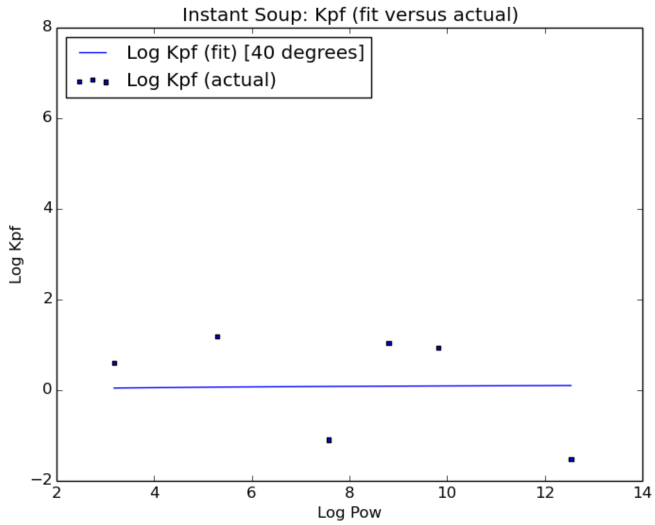


Figure 75: Instant Soup [40 degrees]

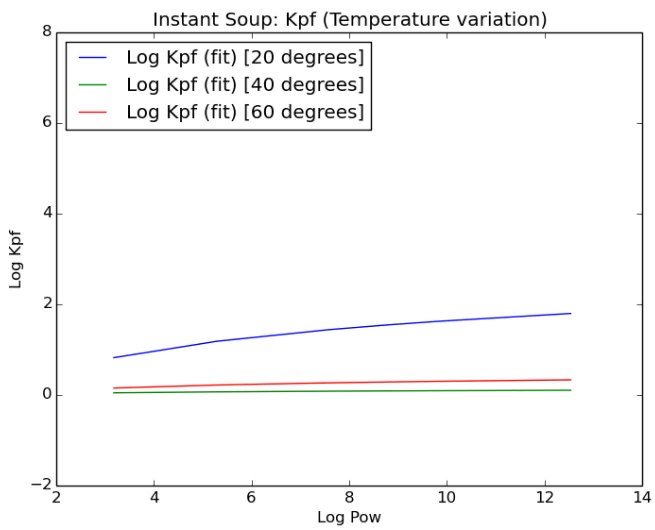


Figure 76: Kpf - Instant Soup (Temperature variation)

Cake

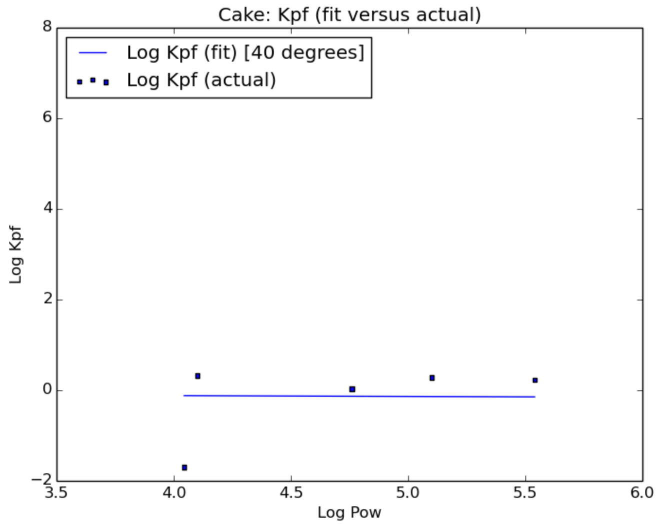


Figure 77: Cake [40 degrees]

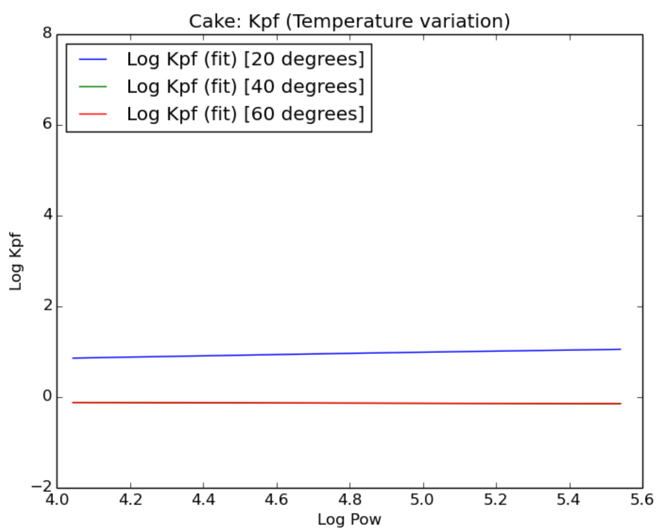


Figure 78: Kpf - Cake (Temperature variation)

Cheese sauce

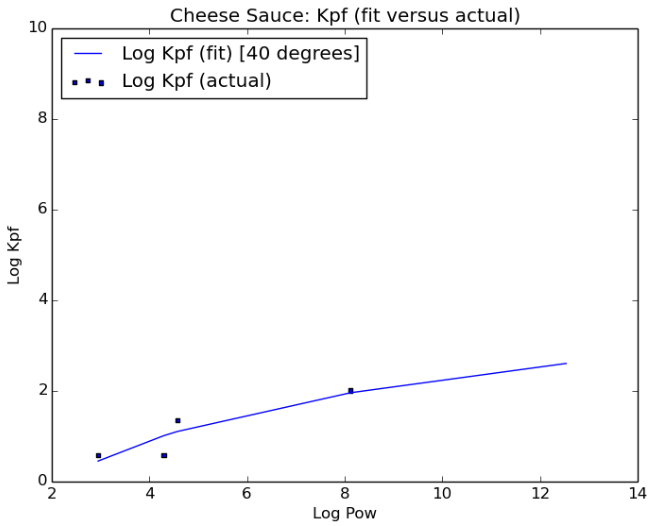


Figure 79: Kpf - Cheese Sauce [40 degrees]

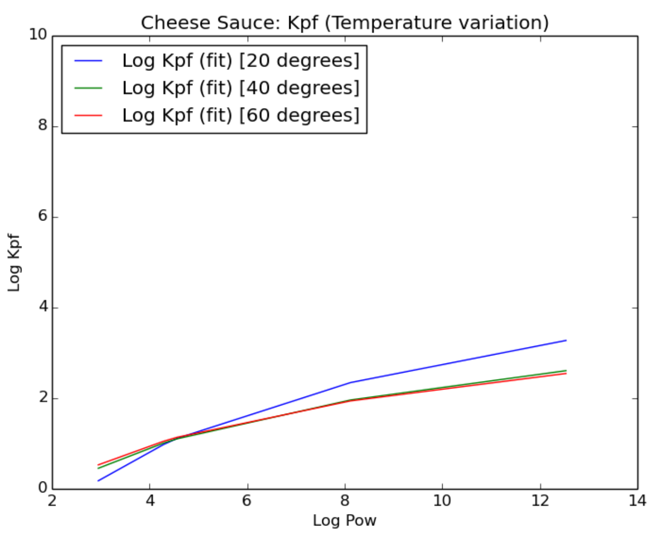


Figure 80: Kpf - Cheese Sauce (Temperature variation)

Rice

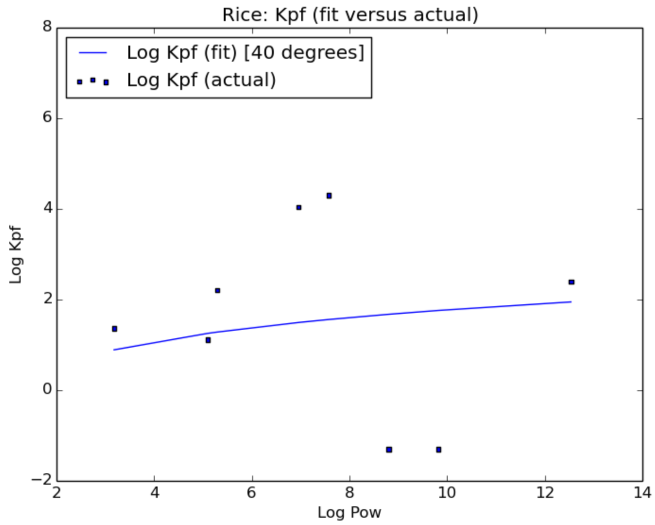


Figure 81: Kpf - Rice [40 degrees]

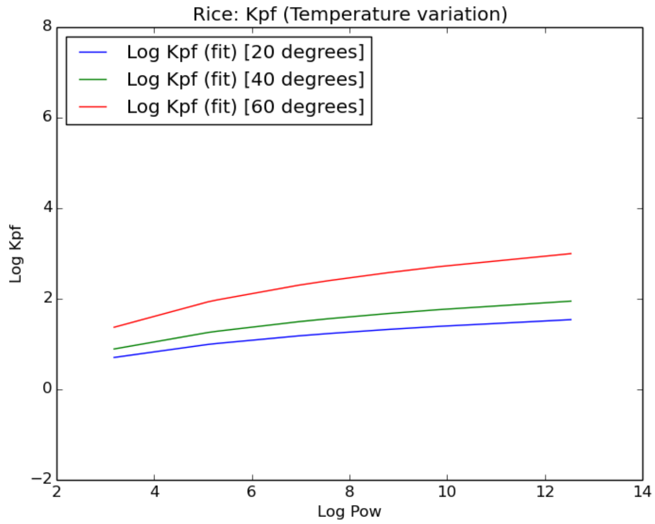


Figure 82: Kpf - Rice (Temperature variation)

Yoghurt

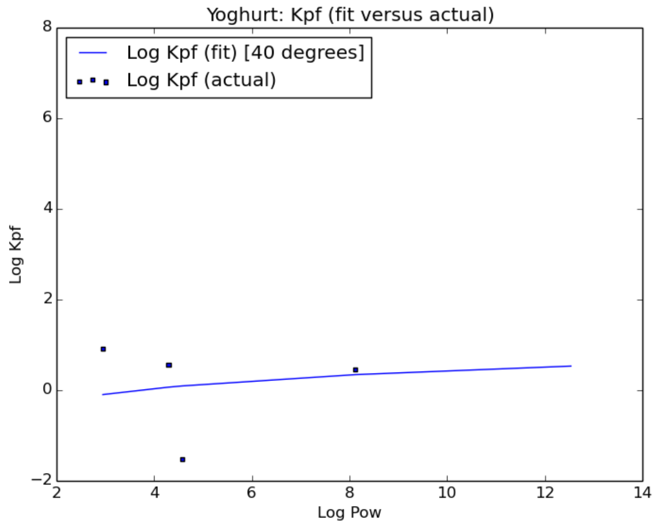


Figure 83: Yoghurt [40 degrees]

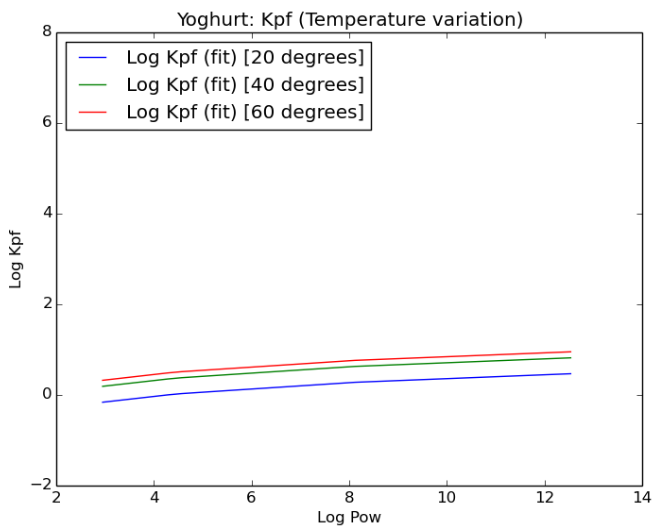


Figure 84: Kpf - Yoghurt (Temperature variation)

Pork (30% fat)

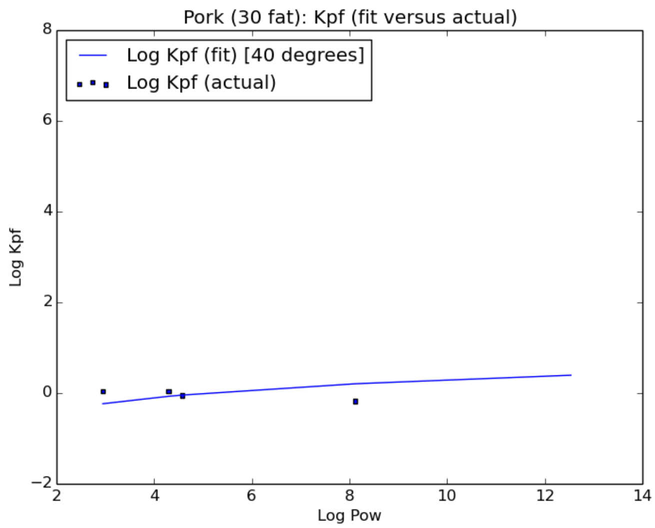


Figure 85: Kpf - Pork (30% fat) [40 degrees]

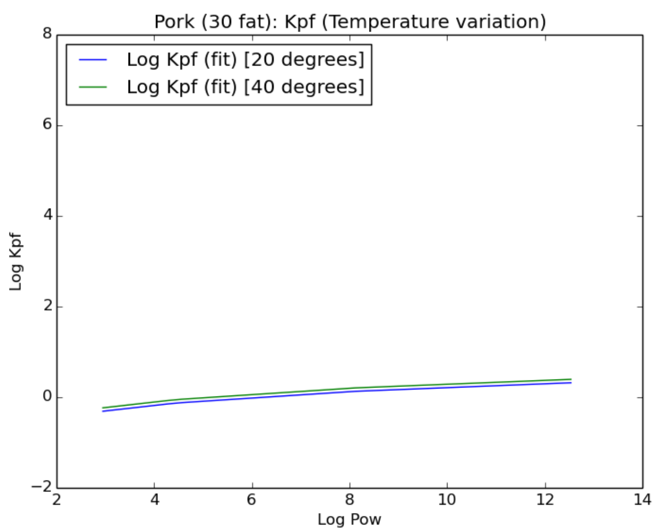


Figure 86: Kpf - Pork (30% fat) (Temperature variation)

Milk powder

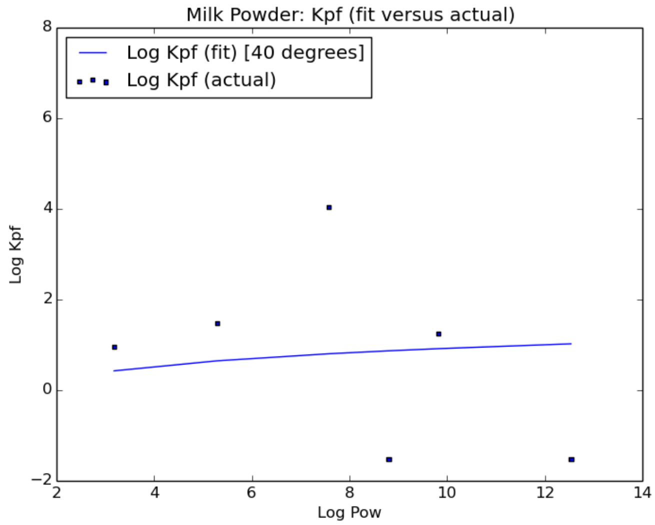


Figure 87: Kpf - Milk Powder [40 degrees]

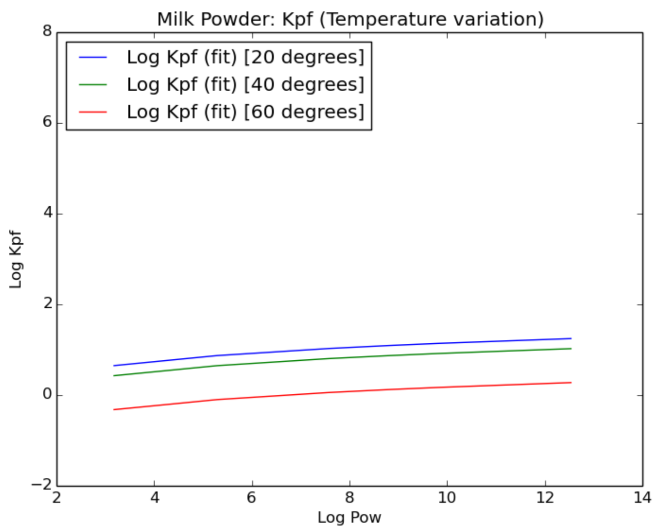


Figure 88: Kpf - Milk Powder (Temperature variation)

Soft cheese

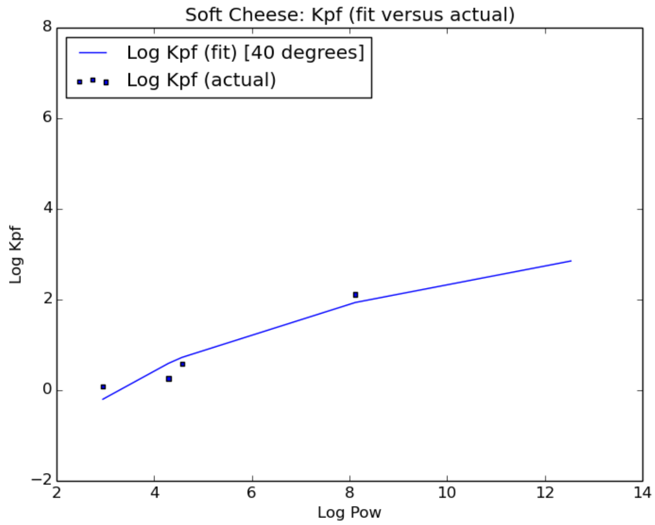


Figure 89: Kpf - Soft Cheese [40 degrees]

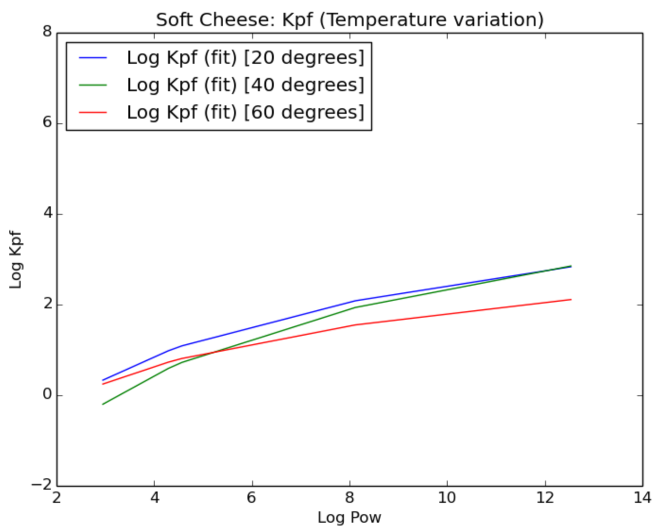


Figure 90: Kpf - Soft Cheese (Temperature variation)

Turkey

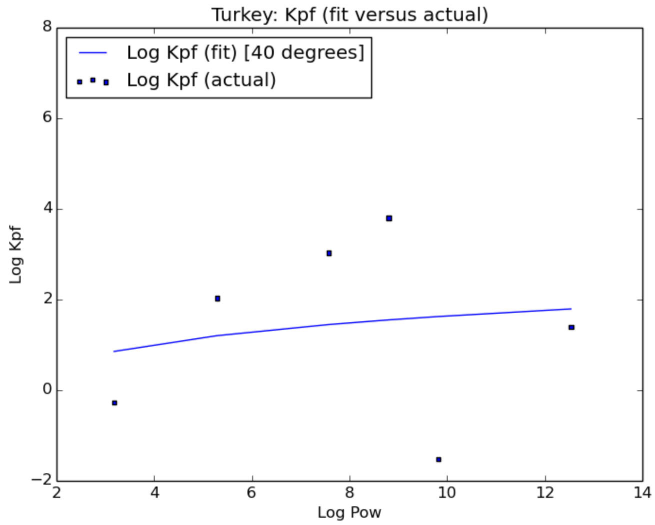


Figure 91: Kpf - Turkey [40 degrees]

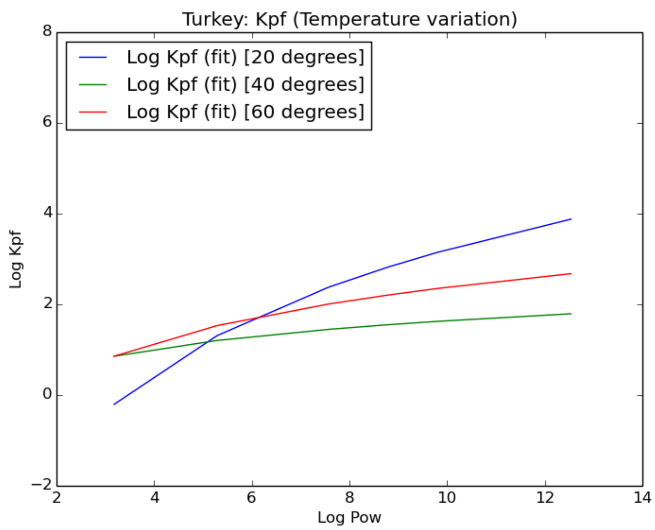


Figure 92: Kpf - Turkey (Temperature variation)

Cooked ham

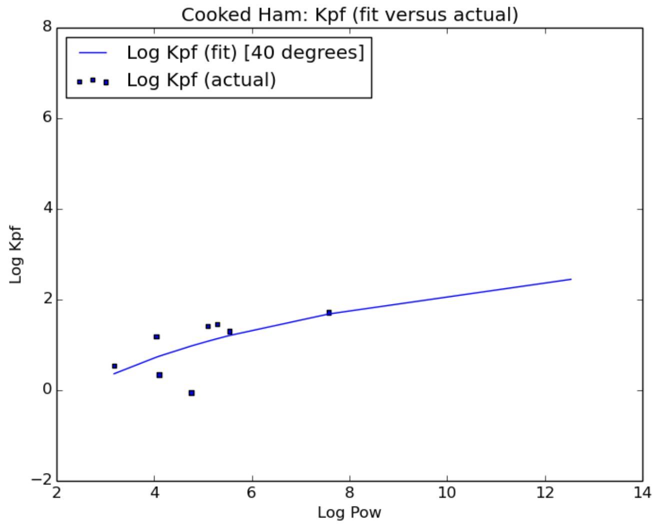


Figure 93: Kpf - Cooked Ham [40 degrees]

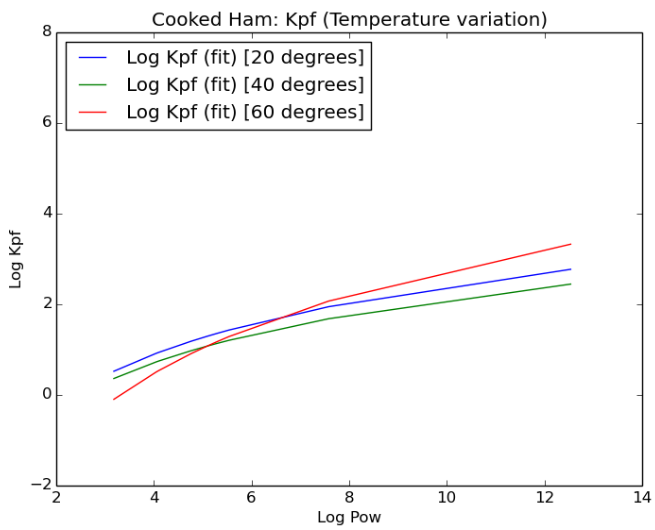


Figure 94: Kpf - Cooked Ham (Temperature variation)

Mayonnaise

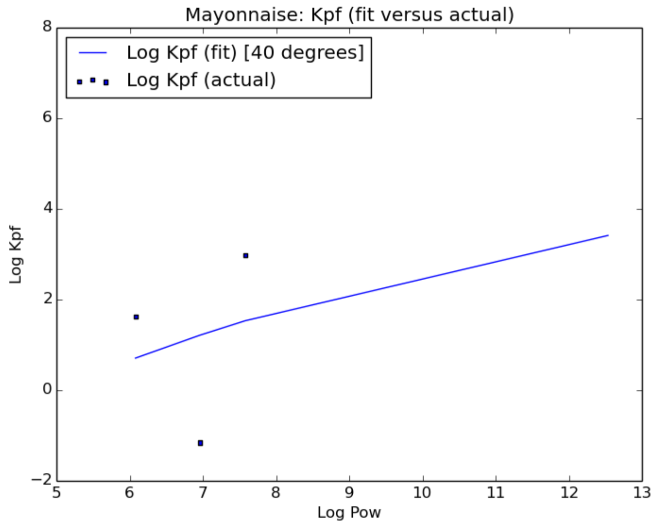
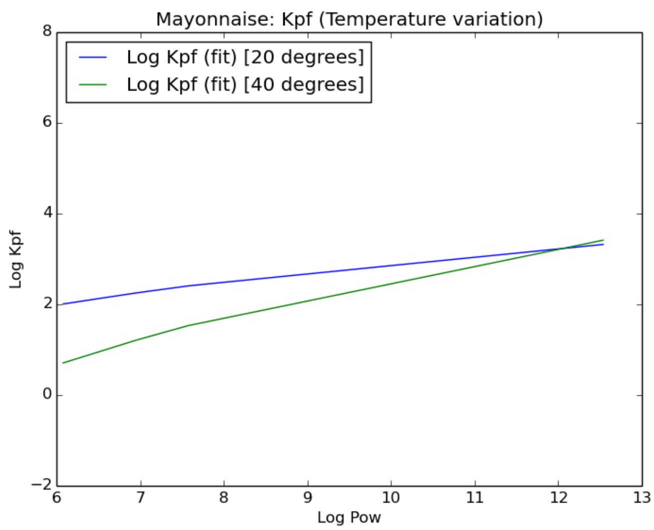


Figure 95: Kpf - Mayonnaise [40 degrees]



UHT milk

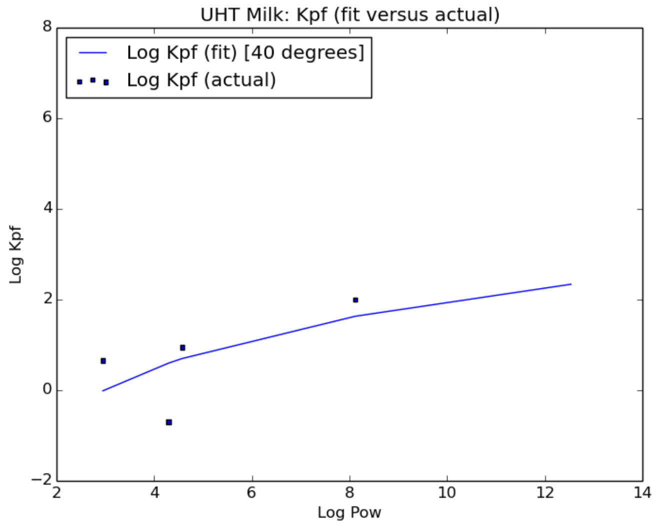


Figure 96: Kpf - UHT milk [40 degrees]

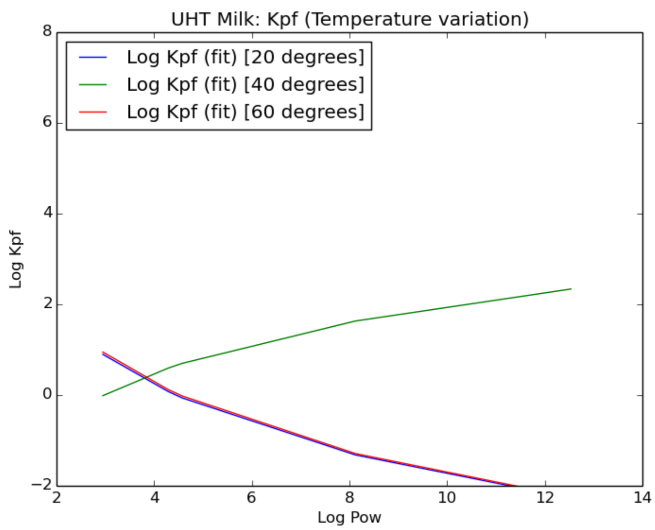


Figure 97: Kpf - UHT Milk (Temperature variation)

Condensed milk

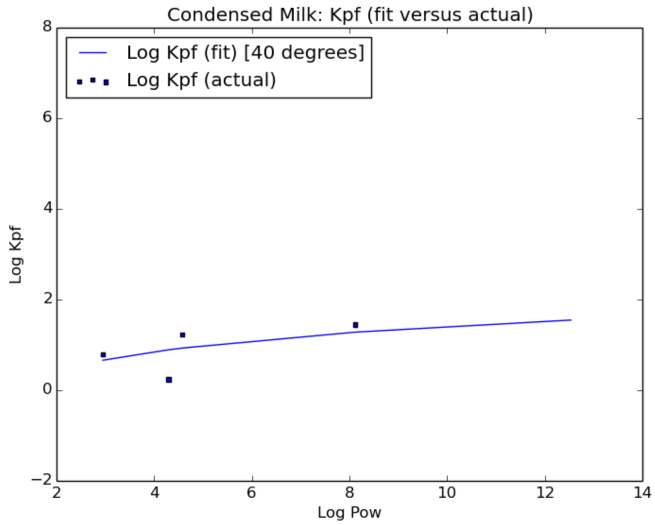


Figure 98: Kpf - Condensed Milk [40 degrees]

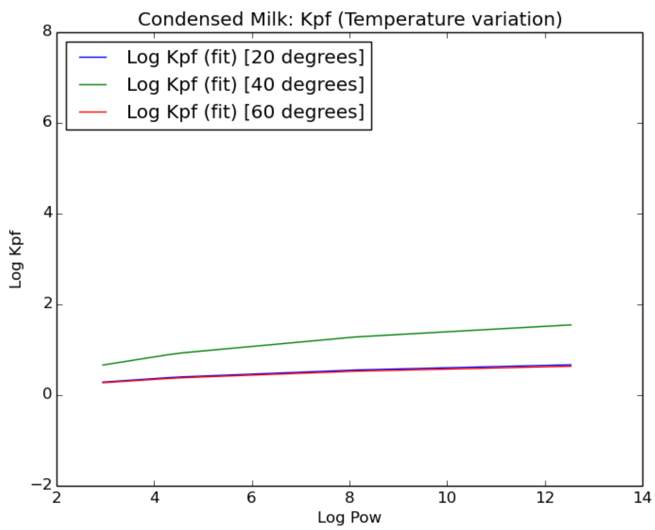


Figure 99: Condensed Milk

Pate

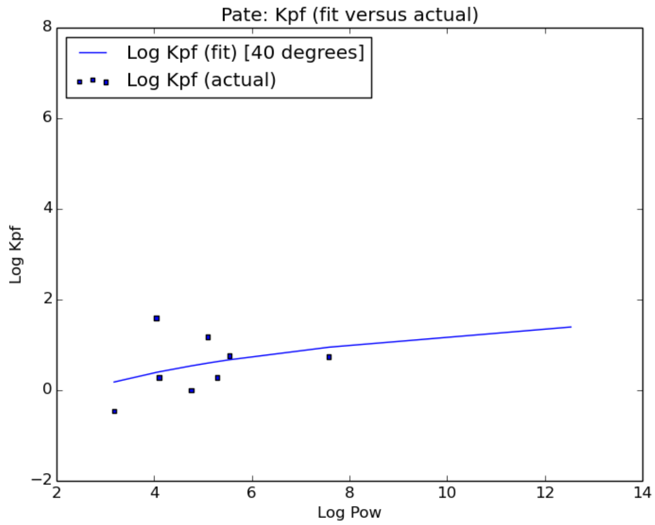


Figure 100: Kpf - Pate [40 degrees]

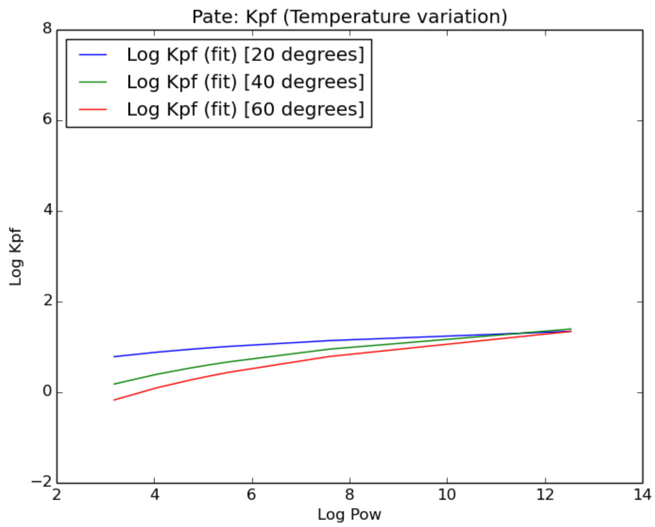


Figure 101: Kpf - Pate (Temperature variation)

Gouda

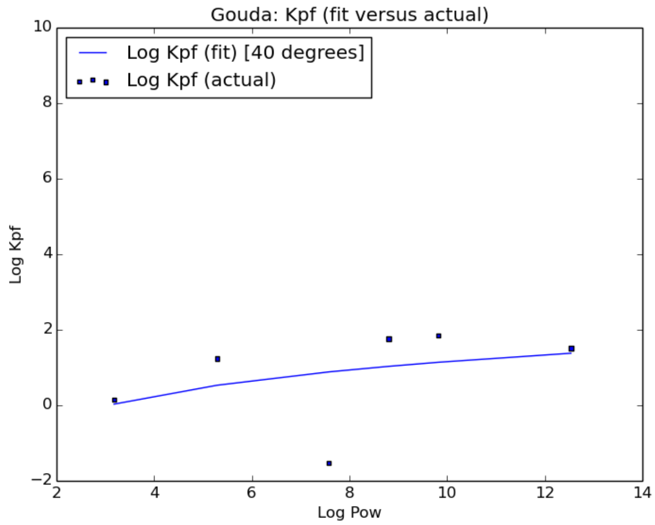


Figure 102: Kpf - Gouda [40 degrees]

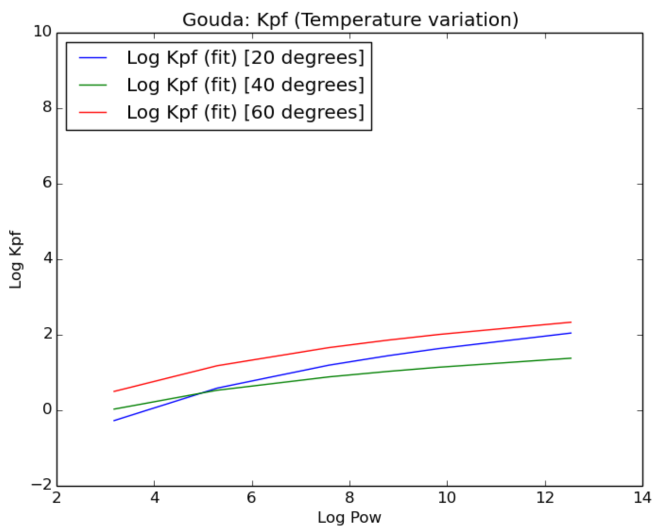


Figure 103: Kpf - Gouda (Temperature variation)

Chocolate spread

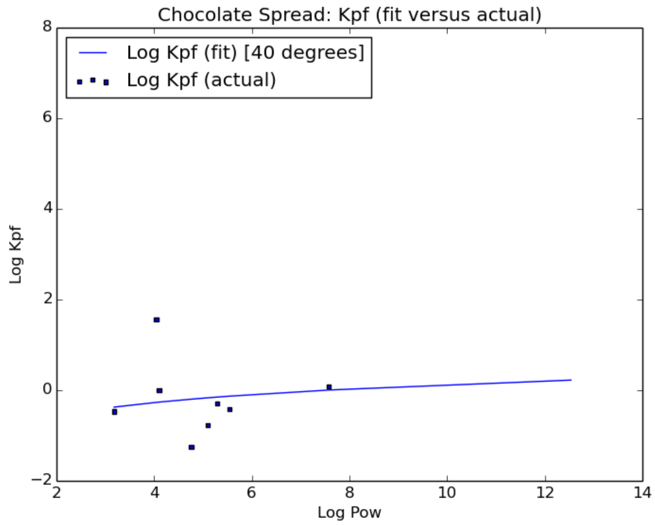


Figure 104: Kpf - Chocolate Spread [40 degrees]

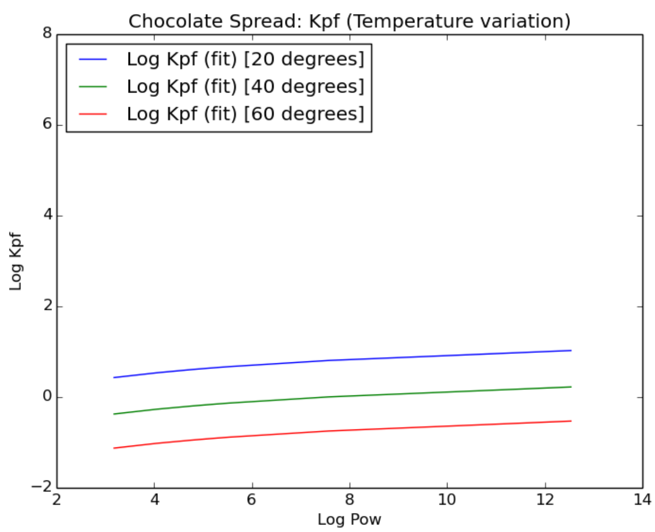


Figure 105: Kpf - Chocolate Spread (Temperature variation)

Whipping cream

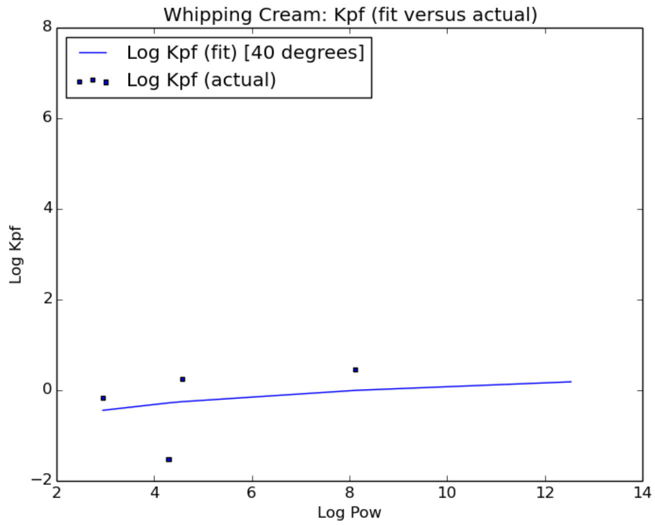


Figure 106: Kpf - Whipping Cream [40 degrees]

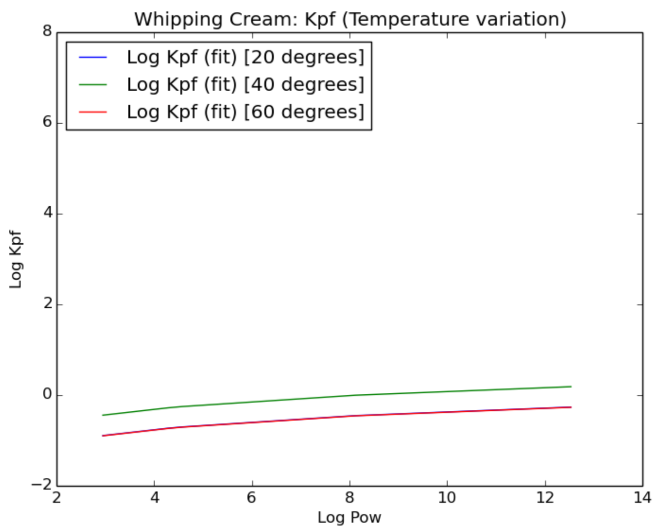


Figure 107: Kpf - Whipping Cream (Temperature variation)

Dough

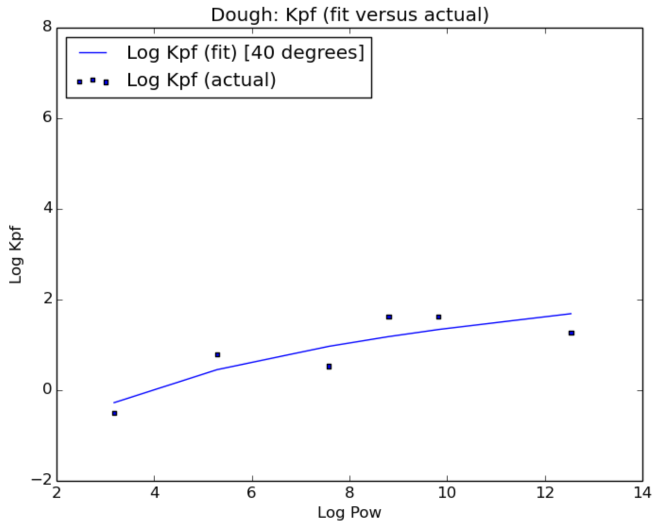


Figure 108: Kpf- Dough [40 degrees]

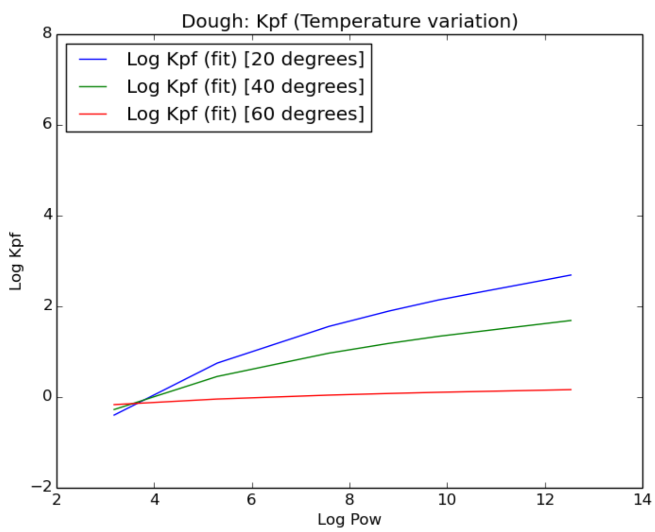


Figure 109: Kpf - Dough (Temperature variation)

Salami

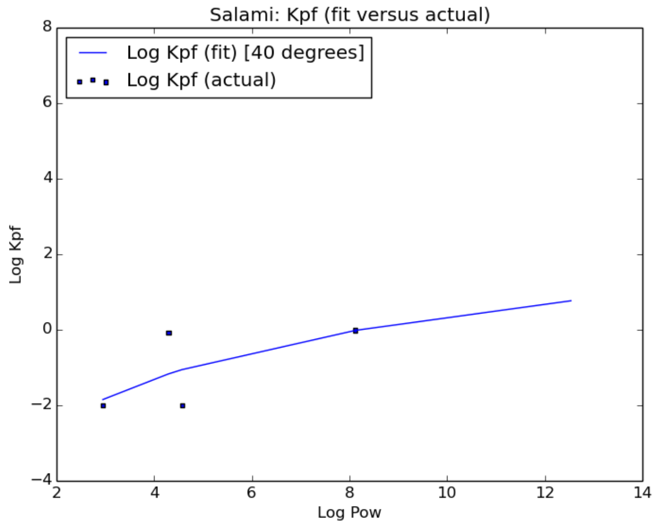


Figure 110: Kpf - Salami [40 degrees]

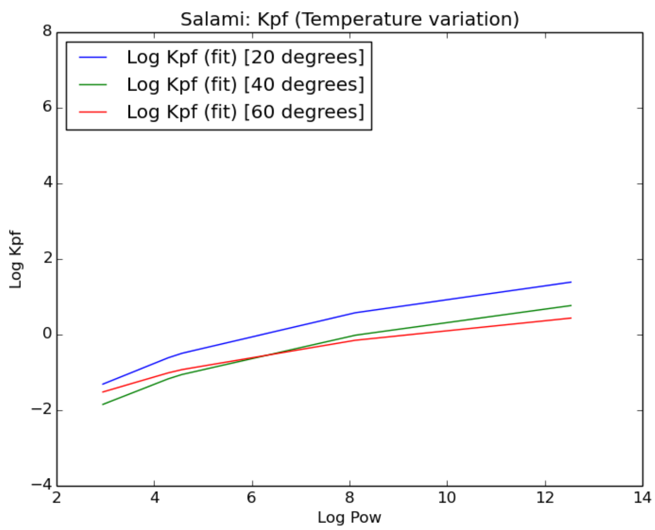


Figure 111: Kpf - Salami (Temperature variation)

Dark Chocolate

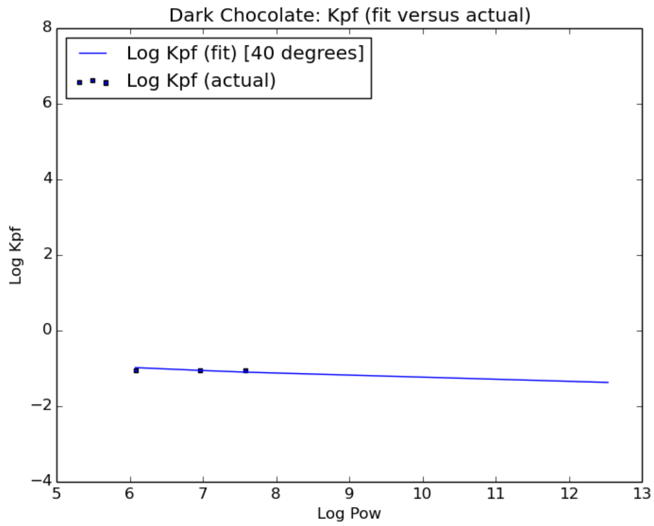


Figure 112: Dark Chocolate [40 degrees]

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