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A strategy to establish Food Safety Model Repositories

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ABSTRACT

Transferring the knowledge of predictive microbiology into real world food manufacturing applications is still a major challenge for the whole food safety modelling community. To facilitate this process, a strategy for creating open, community driven and web-based predictive microbial model repositories is proposed. These collaborative model resources could significantly improve the transfer of knowledge from research into commercial and governmental applications and also increase efficiency, transparency and usability of predictive models. To demonstrate the feasibility, predictive models of *Salmonella* in beef previously published in the scientific literature were re-implemented using an open source software tool called *PMM-Lab*. The models were made publicly available in a Food Safety Model Repository within the *OpenML for Predictive Modelling in Food* community project. Three different approaches were used to create new models in the model repositories: (1) all information relevant for model re-implementation is available in a scientific publication, (2) model parameters can be imported from tabular parameter collections and (3) models have to be generated from experimental data or primary model parameters. All three approaches were demonstrated in the paper. The sample Food Safety Model Repository is available via: http://sourceforge.net/projects/microbialmodelingexchange/files/models and the *PMM-Lab* software can be downloaded from http://sourceforge.net/projects/pmmlab/. This work also illustrates that a standardized information exchange format for predictive microbial models, as the key component of this strategy, could be established by adoption of resources from the Systems Biology domain.

1. Introduction

International efforts to improve the quality and safety of food products have led to an increased interest in predictive microbial modelling among food manufacturers (Buchanan, 1993b; McMeekin et al., 2002) and regulatory agencies (Manfreda and De Cesare, 2014). As predictive microbiology can be used to predict the behaviour of microorganisms in various stages of processing, storage and distribution (McMeekin et al., 2002; Nauta, 2002), Regulation (EC), 2073/2005 (and all amendments) contemplates the use of predictive microbial models in the food industry for demonstrating compliance with established microbiological criteria. In that sense, the quantitative estimates generated by predictive microbial models can provide additional information useful in decision making during HACCP planning, process design and product reformulation (Halder et al., 2010; McMeekin et al., 2006; Nauta, 2002).

For example predictive models on growth and inactivation of *Salmonella* in beef products have a high practical relevance and a large amount of them have been generated (Hwang et al., 2009; Juneja et al., 2003, 2009). This development has been driven by the fact that *Salmonella* is considered as a major causative agent of gastrointestinal diseases (CDC, 2013; EFSA, 2010, 2012; Guillier et al., 2013; Juneja et al., 2003, 2009) and meat is highly favourable for growth of *Salmonella* (de Oliveira et al., 2013). Although the number of salmonellosis cases attributed to beef products is considered to be lower than those attributed to products derived from poultry, pork or eggs (David, 2009), some studies identified *Salmonella* as one of the most significant hazards linked to beef consumption (Fosse et al., 2008; Greig and Ravel, 2009). Additionally, in the U.S. many disease outbreaks could be directly linked to *Salmonella* contaminations in beef (CDC, 2011, 2012, 2013; McLaughlin et al., 2006; Robinson, 2013).

However, despite the fact that existing predictive models could potentially help the meat sector to reliably predict and estimate potential growth, inactivation or survival of *Salmonella* during processing and storage, the application of models into the day-to-day operations of the food industry is limited. Potential reasons for this are:

1. Models are frequently only published in scientific journals or implemented in stand-alone software solutions.

Abbreviations: DOI, Digital Object Identifier; EC, European Commission; FSMR, Food Safety Model Repository; HACCP, Hazard Analysis and Critical Control Points; ICPMF, International Conference on Predictive Modelling in Food; ICRA, Interactive Catalogue on Risk Assessment; MIRIAM, Minimal Information Required In the Annotation of Models; RMSE, Root-Mean-Square Error; SBML, Systems Biology Markup Language; PMF-ML, Predictive Modelling in Food-Markup Language

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2. Free and open databases containing predictive microbial models are not widely accepted or utilized.
3. No standardized data format for description of predictive models exists.

In order to facilitate the discussions on harmonized data formats an open community forum called *OpenML for Predictive Modelling in Food* (http://sourceforge.net/projects/microbialmodelingexchange/) has been launched recently. Such harmonized data formats would facilitate the exchange of modelling information between different software tools and also allow the creation of model repositories. A publicly available model repository hosting predictive microbial models in a standardized format would support easy access and wider application of predictive models within the research community as well as the food industry.

During the past few years, numerous software solutions in the domain of predictive microbiology have been developed (Baranyi and Tamplin, 2004; Buchanan, 1993a; ComBase, 2013; Huang, 2014; Koseki, 2009; Leporq et al., 2005) for which Table 1 provides an overview. Many of these software tools were built around models for specific microorganisms in specific food matrices (*FISHMAP, Prediction of Microbial safety in Meat Products, FSSP, Dairy product Safety Predictor, Sym'Previus, GroPIN, Listeria Meat Model*). Other tools are designed to accomplish specific tasks such as risk prioritization (*FDA-iRISK*), evaluation of microbial growth/no growth boundaries (*Microbial Responses Viewer*) or model generation (*GInaFiT, FILTREX, PMM-Lab*).

Regarding those software tools which contain a type of database for predictive models, the stand-alone software *Pathogen Modeling Program (PMP)* and the on-line software *ComBase Predictor* can be considered as the pioneering software solutions. They make unpublished and published models available by incorporating them into their web based software solution (Perez-Rodriguez and Valero, 2013). However, end users cannot implement new models in these systems themselves, as only the software owners can accomplish this task. Moreover, predictive microbial models themselves cannot be exported, only the predictions made by the web-based software tools.

New web-based prediction tools for microbial growth and inactivation have been launched recently. *MicroHibro* and *Baseline* (Manfreda and De Cesare, 2014; Posada-Izquierdo et al., 2012) allow incorporation of user defined models for any microorganisms and food of interest, enabling the user to obtain predictions for growth and inactivation. However, the type of model equation that can be used within these systems is currently restricted, especially due to the restriction to a predefined set of primary models. As in the case of *ComBase Predictor* and *PMP*, there is no functionality allowing users to export models implemented in *MicroHibro* or *Baseline* to be used for prediction by other predictive modelling tools.

Another new solution developed recently is *GroPIN*, which already contains a predictive microbial model database with more than 400 published models, including spoilage and mycotoxigenic fungi, bacteria and yeasts in several food matrices. However, *GroPIN* is not open sourced, and it does not provide the user with a feature to exchange model information with other software tools, either. Moreover, it is also focused on the model application and does not provide any functionality to integrate real experimental data or to carry out a model generation process.

Finally there is *PMM-Lab* which can be used to create new models based on microbial data and which includes a database capable of storing experimental data, predictive microbial models as well as model generation workflows. It is primarily intended to support domain experts in their efforts to create, document and share predictive microbial models in a transparent fashion (Filter et al., 2013). This tool is freely available as open source software and provides many valuable features for model generation, model import and export as well as for re-implementation of models published in scientific literature. As *PMM-Lab* also provides a prototype implementation of a module that allows exporting models into the proposed standardized data exchange format, it has been selected as the tool to create sample models for the new Food Safety Model Repository (FSMR). Additionally, the workflow-based approach creates transparency on data processing and facilitates collaboration and quality control among different researchers.

The aim of this study was to propose and illustrate a strategy for creation of FSMR for predictive microbial models of growth, inactivation and survival of microorganisms (Fig. 1). The strategy was demonstrated using models for *Salmonella* in beef re-implemented or generated within *PMM-Lab*. Three possible approaches related to the implementation process and the available data are presented.

Table 1
Software solutions available in the domain of predictive microbiology and quantitative microbial risk assessment.

Software	Link (accessed 11/27/2014)
A swift Quantitative Microbiological Risk Assessment (sQMRA) tool	http://foodrisk.org/exclusives/sqmra/
Baseline	www.baselineapp.com
ComBase	http://www.combase.cc
Dairy Product Safety Predictor	www.aqr.maisondulait.fr
DMFit	http://www.ifr.ac.uk/safety/dmfit/
FDA-iRISK	https://irisk.foodrisk.org
FILTREX	http://w3.jouy.inra.fr/unites/miaj/public/logiciels/filtrex/
FISHMAP	http://www.azti.es/fishmap
Food Spoilage and Safety Predictor (*FSSP*)	http://fssp.food.dtu.dk
FoodProcess-Lab	http://sourceforge.net/projects/foodprocesslab/
FRISBEE	http://frisbee-wp2.chemeng.ntua.gr/coldchaindb/
GInaFiT	http://cit.kuleuven.be/biotec/downloads.php
GroPIN	www.aua.gr/psomas/gropin
Interactive online Catalogue on Risk Assessment (ICRA)	http://icra.foodrisk.org/
IPMP	http://www.ars.usda.gov/Services/Docs.htm?docid=23355
Listeria Meat Model	http://www.cpmf2.be/software.php
MicroHibro	www.microhibro.com
MRV, Microbial Responses Viewer	http://mrviewer.info/
OptiPa	https://perswww.kuleuven.be/~u0040603/optipa/optipamain.htm
PMM-Lab	https://sourceforge.net/projects/pmmlab/
Prediction of Microbial Safety in Meat Products	http://dmripredict.dk
PredOxyPack	http://predoxypack.be/
Shelf Stability Predictor	http://www.meathaccp.wisc.edu/ST_calc.html
Sym'Previus	www.symprevius.org
Therm 2.0	http://www.meathaccp.wisc.edu/pathogen_modeling/therm.html

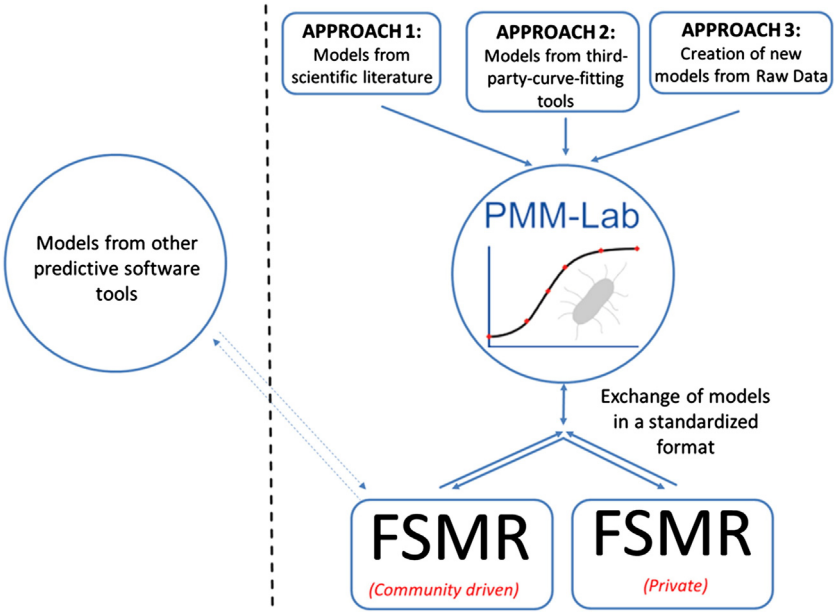

Fig. 1. Overview: Graphical overview of the aim of this paper. (FSMR: Food Safety Model Repository.)

2. Material and methods

2.1. Software solution and re-implemented models

PMM-Lab v1.06 (http://sourceforge.net/projects/pmmlab/files/) was selected as the software tool to create a *Salmonella* model repository. *PMM-Lab* is an open source community resource software that provides features to create, visualize, analyze, save, import and export predictive microbial models (Filter et al., 2013). Due to its flexibility, this tool gives the possibility of incorporating new models into a model repository through adaptable model generation workflows, depending on the type of data available (Table 2).

The following publications containing growth and inactivation models for *Salmonella* in beef were selected as sample models for the FSMR: Juneja et al. (2003, 2009). Additionally, these models were available within an independent reference software implementation (*PMP*), which allows validation of the model reimplementation and direct comparison of our model outcome with the outcome of the references.

2.2. Model generation approaches

Depending on the available data and end user requirements, different approaches might be necessary to create models for the FSMR. Here three practically relevant approaches are illustrated:

Approach 1 is designed for implementing predictive microbial models only available in scientific literature. It can be applied when all necessary information for model re-implementation, i.e. the formulas and all the estimated model parameters, are given (Filter et al., 2013). Here two sample models were selected in order to illustrate the application of approach 1: the combined logistic/Ratkowsky growth model of Juneja et al. (2009) for *Salmonella* in beef and the specific model for predicting a 6.5 $\log_{10}$ reduction of Juneja et al. (2003) for *Salmonella* in ground beef matrices containing different concentrations of salt, sodium pyrophosphate and sodium lactate (Supplements 1 and 2).

Approach 2 applies when parameter values for several primary or secondary models are already available in a tabular format, e.g. generated by a curve-fitting software tool, and the formulas of the original models are given at least implicitly. This scenario is illustrated by applying the *DMFit* Excel model fitting plugin, Version 2.1 (Baranyi and Le Marc, 2006) to experimental data reported by Juneja et al. (2009). The workflow used to import the *DMFit-generated* table with parameter estimates is provided as Supplement 3.

Approach 3 demonstrates how models for FSMR can be generated directly from experimental data inside *PMM-Lab*. For this the logistic and Ratkowsky formulas used by Juneja et al. (2009) were fitted to raw data used in approach 2. Here a one-step fitting approach, as proposed by Jewell (2012), was performed using parameter estimates from an intermediate two-step fit as starting values. The whole model generation workflow is available as Supplement 4.

All supplementary files are available online at http://sourceforge.net/projects/microbialmodelingexchange/files/Models/Plaza-Rodriguez%20et%20al./Workflows_SupplementaryFiles/.

Table 2
Main features of the approaches 1, 2 and 3.

	Approach 1	Approach 2	Approach 3
Source	All information relevant for model re-implementation is available, e.g. as unstructured information in a scientific paper.	Results from model generation or curve-fitting software tools (e.g. *DMFit*).	Models are generated from experimental data (primary models) or primary model parameters (secondary models).
Formulas	Formulas used for primary and secondary model generation should be provided explicitly in the scientific publication.	Formulas for primary and secondary models are available at least implicitly, e.g. in the documentation or source code of the applied software tool.	Formulas for primary and secondary models can be freely selected by the users.
Parameter values	Estimated parameter values for models are available in the scientific publication.	Parameter values for primary and secondary models are available in electronic format and can be imported directly.	Parameter values of models are estimated by the software.
Experimental data	Original experimental data are not required. However, for quality assurance these data would be highly beneficial.	Original experimental data are not required. However, for quality assurance these data would be highly beneficial.	Experimental data required.

2.3. Experimental data

For approaches 2 and 3, experimental data from Juneja et al. (2009) were downloaded from *ComBase* (ComBase, 2013) — *ComBase-ID:* Juneja_09c. Data points obtained at 37 °C (Juneja_09c: Beef-37C-1; Beef-37C-2) were not considered in any of the approaches as these were also excluded by Juneja et al. when they created their models. In approach 2 these data were imported into the stand-alone *DMFit* Excel model fitting plugin, Version 2.1 (Baranyi and Le Marc, 2006) in order to create a tabular listing of primary models as required for approach 2.

2.4. Quality control

Within the approaches 1 and 2 growth and inactivation curves as well as the prediction values obtained in *PMM-Lab* were compared to the curves and predictions given by *PMP* (approach 1) and *DMFit* (approach 2) in order to verify that the re-implementation of models was accurate. For approach 3, RMSE values were used to evaluate the model performance in comparison with the combined logistic/Ratkowsky model re-implemented from the literature in approach 1.

2.5. Model metadata

One challenge associated with the idea of FSMR is the need for model description using metadata, e.g. the name of the model, model creator, references, etc. Moreover, this information has to be provided in a standardized data format. This is a prerequisite for search and filter functionalities necessary in a FSMR. Therefore, an in-depth study of available metadata description systems was performed, and finally information concepts most relevant for characterizing predictive microbial models were selected (Table 3).

3. Results

3.1. FSMR establishment strategy

The central objective of this research is to present an easy to follow strategy for Food Safety Model Repository (FSMR) development. This strategy is based on the idea of establishing a standardized information exchange format for the domain of predictive microbial modelling. In its simplest form, a FMSR can be set up as a shared file directory, hosted

Table 3
Overview of information concepts covered by different metadata description schemes. Information concepts most relevant for FSMR as well as the MIRIAM compliance requirements are highlighted.

Information concepts	Description	Dublin Core www.dublincore.org	DOI www.doi.org	MIRIAM www.ebi.ac.uk/miriam
Title/name	A name given to the model within the software solution. Typically, a title will be a name by which the model is formally known.	X	X	X
Creator	Who contributed to the encoding of the model in its present form by implementing the model in the software solution.	X	X	X
Creation	Temporal information about the model creation. The creation is the date and the time upon which the model or model part was coded into the software solution.	X	X	X
Rights	Information about rights held in and over the model. Typically, rights information includes a statement about various property rights associated with the resource, including intellectual property rights.	X	X	X
Version	The version number of the model.	X	X	X
Annotations	All additional information that does not fit in any other category may be used for technical information, including references from the scientific publication from which the model has been taken.	X	X	X
Identifier	An unambiguous reference to the model within a given context.	X	X	
Type	The nature or genre of the model.	X		
Subject	The issue of the model. Typically, the subject will be represented using keywords, key phrases, or classification codes.	X	X	
Model uncertainties/ validation	Estimated parameters to determine the discrepancy between the real conditions and the mathematical model./Conditions in which the model has been validated.			
Source/ Relation	A related resource from which the described resource is derived. The described resource may be derived from the related resource in whole or in part.	X	X	
Location	Spatial region or named place where the data was gathered or about which the data is focused.	X	X	
Software Solution	Description of the software application that generated the model.			
Format	The file format, physical medium, or dimensions of the model.	X	X	
Language	The primary language of the model.	X	X	

e.g. on a web portal as demonstrated at http://sourceforge.net/projects/microbialmodelingexchange/files/models. More sophisticated FSMR solutions will combine such file repositories with a graphical user interface, allowing users to browse through model metadata and search for specific model properties. Additionally, these sophisticated solutions should also integrate a process for repository curation in order to ensure a high data quality. Even existing web-based software tools like *MicroHibro*, *PMP*, *ComBase Predictor*, *ICRA* or *FDA-iRISK* could serve as FSMR if functionalities for model import and export would be provided. Such a standardized information exchange format would also facilitate the incorporation of models generated by different software tools into the very same FSMR (Fig. 1 dashed line). Further it would enable the direct exchange of information between existing software tools.

In this research we therefore explored whether an existing exchange format from the domain of Systems Biology could be applied for predictive microbial models. The Systems Biology Markup Language (SBML) (Hucka et al., 2003) has been selected as it is an internationally accepted and highly flexible language designed for the software-independent description of mathematical models on biological processes. It is also the foundation of model repositories, like e.g. the BioModels Database (http://www.biomodels.org/www.biomodels.org).

As a technical proof-of-principle, a prototypic SBML export function was implemented into the *PMM-Lab* software which was capable of exporting many models discussed in this paper as valid SBML files. This has been verified via the SBML online validator tool (http://sbml.org/Facilities/Validator/section-print-result.jsp) and the successful model import into the SBML network simulation software CopasiWeb (http://www.comp-sys-bio.org/CopasiWeb/CopasiWebUI) (data not shown). All generated SBML-formatted model files from this research are available at the sample FSMR.

Another advantage of SBML is the fact that it also defines how to specify and exchange metadata on models. This is a prerequisite for proper interpretation of model-based prediction results. So we also investigated which metadata (information concepts) would be useful to annotate models from the domain of predictive microbiology. Table 3 provides a listing of the most relevant information concepts. This table also illustrates which of them are covered by the two independent metadata description schemes (Dublin Core, DOI) and which are required by the "Minimal Information Required in the Annotation of Models" (MIRIAM) guideline which is widely accepted in the Systems Biology community. Based on this comparison and practical experiences with model annotation illustrated in Table 4, it is recommended that modellers provide at least metadata on those concepts highlighted in Table 3 together with their mathematical equations.

3.2. Model generation approaches

A FSMR usually encompasses models originating from different sources. Here we describe three practically relevant approaches to create models which then can be integrated into a FSMR. For all approaches the open source software *PMM-Lab* has been applied. Table 5 provides an overview of the *Salmonella* in beef models re-implemented or generated.

3.2.1. Approach 1

Fig. 2 illustrates the growth curves for the combined logistic/Ratkowsky model reported in Juneja et al. (2009) for *Salmonella* in beef at 25 °C with an initial concentration of 3.0 (log_{10} cfu/g). Fig. 2A shows the growth curve obtained from *PMP* (http://pmp.errc.ars.usda.gov/PMPOnline.aspx?ModelID=25), while Fig. 2B shows the growth curve obtained after the re-implementation of the same model in *PMM-Lab*. As demonstrated in Fig. 2, both growth curves show exactly the same pattern, and the results are identical.

Fig. 3 shows the thermal inactivation curves for the model reported in Juneja et al. (2003) for *Salmonella* in ground beef containing 0.15% sodium pyrophosphate, 3% salt and 0–4.5% sodium lactate. Fig. 3A shows the curve obtained from *PMP* (http://pmp.errc.ars.usda.gov/PMPOnline.aspx?ModelID=30), and Fig. 3B shows the curve obtained from *PMM-Lab* illustrating that the results of both model implementations are identical.

3.2.2. Approach 2

Experimental data from *ComBase* (Juneja_09c) were fitted to the DModel_3 by *DMFit*. The DModel_3 corresponds to the Baranyi model (Baranyi and Roberts, 1994) with the parameters nCurv and mCurv. With the default settings, *DMFit* did not fit the full model for several data sets. No fitted values for lag and y_{end} were obtained for Beef-10C-1, Beef-10C-2, Beef-15C-1 and Beef-35C-1 where *DMFit* set nCurv and mCurv=0. No fitted values for y_{end} were obtained for Beef-15C-2, Beef-20C-1, Beef-20C-2, Beef-25C-1, Beef-25C-2, Beef-28C-1, Beef-28C-2, Beef-32C-2, Beef-35C-2 where *DMFit* set mCurv=0. In all these cases *PMM-Lab* was not able to import the models using the full Baranyi model equation. Instead we had to apply the corresponding reduced version of the DModel_3 formula, as illustrated Table 5.

Table 4
Application of the recommended annotation scheme to a sample predictive microbial model.

	Sample model 1
Title/name	salmonella_spp_Beef_in_ground_beef Logistic_Model
Creator	Carolina Plaza-Rodríguez
Creation	created: 30.10.2014 modified: 18.12.2014
Rights	CC BY-NC-SA 4.0 (http://creativecommons.Org/licenses/by-nc-sa/4.0/)
Version	1.0
Annotations	Juneja, V.K., Melendres, M.V., Huang, L., Subbiah, J., Thippareddi, H., 2009. Mathematical modeling of growth of *Salmonella* in raw ground beef under isothermal conditions from 10 to 45 degrees C. International Journal of Food Microbiology 131,106–11.; ValidRange-temperature: 10–45°C; ValidRange-time: 0–168 h; ValidRange-concentration: 2.9–4.35 Log10(cfu/g)
Identifier	salmonella_spp_Beef_in_ground_beef _Logistic_Model_vl395910217410
Type	Growth model; Combined primary/secondary model: primary model = logistic, secondary model = Ratkowsky;
Subject	Matrix: ground beef; Organism: -*Salmonella* spp
Model uncertainties/validation	–Primary models were generated on data from experiments under isothermal conditions –Primary model pseudo-R square reported in the range from 0.948 to 1.0 –Secondary model psedudo-R square reported: 0.990 –RMSE on experimental raw data from *ComBase*: 0.72
Source/relation	http://browser.combase.cc/ Juneja_09c
Software solution	Generated by *PMM-Lab* v. 1.06
Format	SBML
Language	en

Table 5
Models implemented in *PMM-Lab* and presented in this paper to illustrate approaches 1 to 3.

	References	Type of model	Primary model formula	Secondary model formula
Approach 1.1	Juneja et al., 2009	Growth model –Primary model: Logistic –Secondary model: Ratkowsky	$Log_{10}N = log_{10}N_0 + ((log10N_{max} - log_{10}N_0) / ((1 + exp(4 * log_{10mumax} * ((0.970 / log_{10mumax}) - t) / (log_{10}N_{max} - log_{10}N_0) + 2))))$	$Log_{10mumax} = a * (T - T_{min})^2 * (1 - exp(b * (T - T_{max})))$
Approach 1.2	Juneja et al., 2003	Inactivation model –Secondary model: Polynomial		$t = exp(a + b_1 * ln(T) + b_2 * NaCl + b_3 * ln(T) * NaCl + b_4 * SPP^2)$
Approach 2		Growth model –Primary model: Baranyi and Roberts, 1994.	DModel_3 with nCurv & mCurv <> 0 (full Baranyi model) $Log_{10}N = y_0 + rate * (t - lag + lag * ln(1 - exp(-nCurv * abs(t / lag)) + exp(-nCurv * abs(t / lag) + nCurv)) / nCurv) - ((y_{end} - y_0) / mCurv) * ln(1 - exp(-mCurv) + exp(-mCurv + (mCurv * rate / (y_{end} - y_0)) * (t - lag + lag * ln(1 - exp(-nCurv * abs(t / lag)) + exp(-nCurv * abs(t / lag) + nCurv)) / nCurv)))$ DModel_3 with nCurv <> 0 & mCurv = 0 $Log_{10}N = y_0 + rate * (t - lag + lag * ln(1 - exp(-nCurv * abs(t / lag)) + exp(-nCurv * abs(t / lag) + nCurv)) / nCurv)$ DModel_3 with mCurv & nCurv = 0 $Log_{10}N = y_0 + rate * t$	
Approach 3	Raw data from *ComBase*: Juneja_09c	Growth model Combined Primary (logistic)/secondary (Ratkowsky) model:	$Log_{10}N = log_{10}N_0 + ((log_{10}N_{max} - log_{10}N_0) / ((1 + exp(4 * [a * (T - T_{min})^2 * (1 - exp(b * (T - T_{max})))] * ((0.970 / [a * (T - T_{min})^2 * (1 - exp(b * (T - T_{max})))]) - t) / (log_{10}N_{max} - log_{10}N_0) + 2))))$	

Approach 1.1, 2 and 3: $Log_{10}N$: population density at time t - log_{10}( ) scaled; $log_{10}N_0$: initial population density - log_{10}( ) scaled; $log_{10}N_{max}$: maximum population density - log_{10}( ) scaled; t: elapsed time (h); T: temperature (°C); T_{max}: maximum growth temperature (°C); T_{min}: minimum growth temperature (°C); a: regression coefficient; b: regression coefficient.
Approach 1.2: t: time(min) needed to obtain a 6.5 log relative reduction of *Salmonella*; NaCl: salt concentration (%); SPP: sodium pyrophosphate concentration (%); T: temperature (°C); a: regression coefficient; b_1: regression coefficient; b_2: regression coefficient; b_3: regression coefficient; b_4: regression coefficient.
Approach 2: $Log_{10}N$: population density at time t - log_{10}( ) scaled; y_{end}: final population density - log_{10}( ) scaled; y_0: initial population density - log_{10}( ) scaled; lag: latency time phase duration (h); mCurv: curvature parameter used in DMFit: mCurv=m * abs($y_{end}-y_0$); rate: growth rate; nCurv: curvature parameter for the pre-exponential transition phase; time: elapsed time (h).

Fig. 4 presents exemplarily the growth curves for the data sets Beef-15C-1, Beef-25C-1 and Beef-42C-1 obtained from *DMFit* and *PMM-Lab* after successful model import. Again it is evident that there are no differences between the predictions values made by these models in *DMFit* and in *PMM-Lab*.

3.2.3. Approach 3

As an example for the third approach, *PMM-Lab* was used to create a combined logistic/Ratkowsky model for the Juneja_09c data set by application of a so-called one-step fitting approach. A graphical representation of the generated models in comparison to the published model of Juneja (already implemented in approach 1) is given in Fig. 5. The raw data from *ComBase* are displayed together with the curves. Fig. 5A illustrates the model predictions for 10 °C, whereas Fig. 5B shows the curves for 45 °C. As Fig. 5A illustrates the predictions of the two models generated from the very same dataset differ greatly for 10 °C, and neither of the models fit the raw data perfectly. In contrast, at 45 °C the raw data are fitted more accurately by both models.

Table 6 compares the goodness of fit of the two different models by means of statistical criteria: the RMSE values of the one-step fit model are lower compared to the model re-implemented from the literature (approach 1). These results support the visual impression that the model generated in the one-step fit approach should be preferred over the original model published in the scientific literature.

3.2.4. Supplementary data

The *PMM-Lab* workflows used to generate the models described in the three approaches are freely available at the sample FSMR. Each *PMM-Lab* workflow is annotated such, that each step of the model generation process is explained in detail. Also relevant background information is given. The workflows further include all associated data and can be imported into any local *PMM-Lab* v1.06 software installation

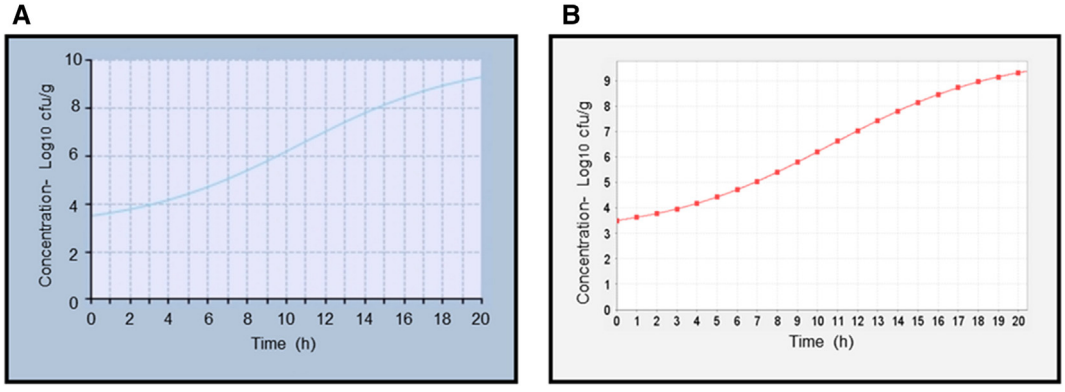

Fig. 2. Approach 1.1: Graphic comparison between the growth curves for *Salmonella* in beef obtained from *PMP* (Fig. 2A) and *PMM-Lab* (Fig. 2B). (Data from Juneja et al., 2009. Combined logistic/Ratkowsky model at 25 °C.)

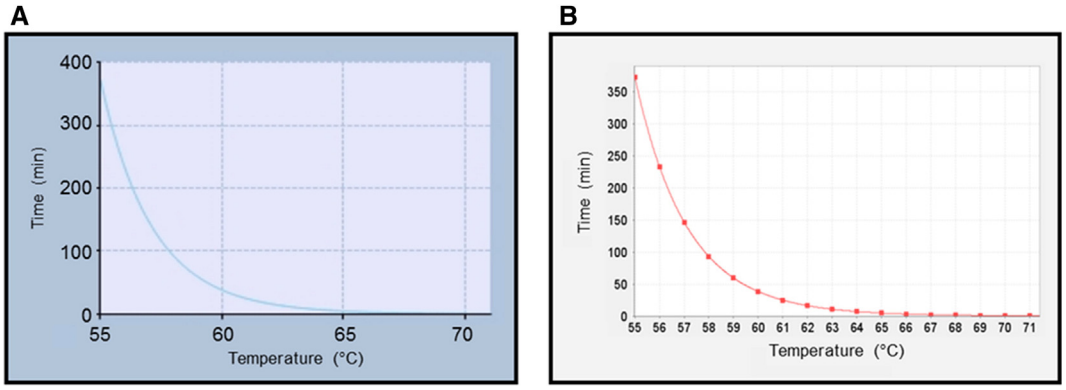

Fig. 3. Approach 1.2: Graphic comparison between the thermal inactivation curves (times needed to reach the 6.5 lethality at different temperatures (°C)) obtained from *PMP* (Fig. 3A) and *PMM-Lab* (Fig. 3B). (Data from Juneja et al., 2003. Secondary model. *Salmonella* in beef: sodium pyrophosphate: 0.15%; salt: 3%; sodium lactate: between 0 and 4.5%.)

via: "File -> Import KNIME workflow -> Source: Select archive file -> Browse".

4. Discussion

Predictive microbiology has demonstrated a broad utility within the food industry, as it can be used to reduce the number of scheduled challenge tests, predict shelf life, identify critical control points, etc. (Buche et al., 2006; Fakruddin et al., 2011). However, there are at least two issues that hamper the wider application of published predictive microbial models in food industry: 1.: Based on our experience with re-implementation of models from scientific literature a significant number of publications do not include all required model specifications or sometimes even contain errors. 2.: Currently there is no public community model repository available promoting the application of models generated by the scientific community. This is true despite the fact, that there are web-based software tools available which provide features for creating and sharing model libraries (e.g. *MicroHibro*, *ICRA*, *FDA-iRISK*). In our opinion the limited adoption of these solutions is to a great extend caused by the lack of harmonized import and export formats and functions. The establishment of a common description language for predictive microbial models would facilitate the development of such software features and would also support the direct information exchange between other software tools from the domain of predictive

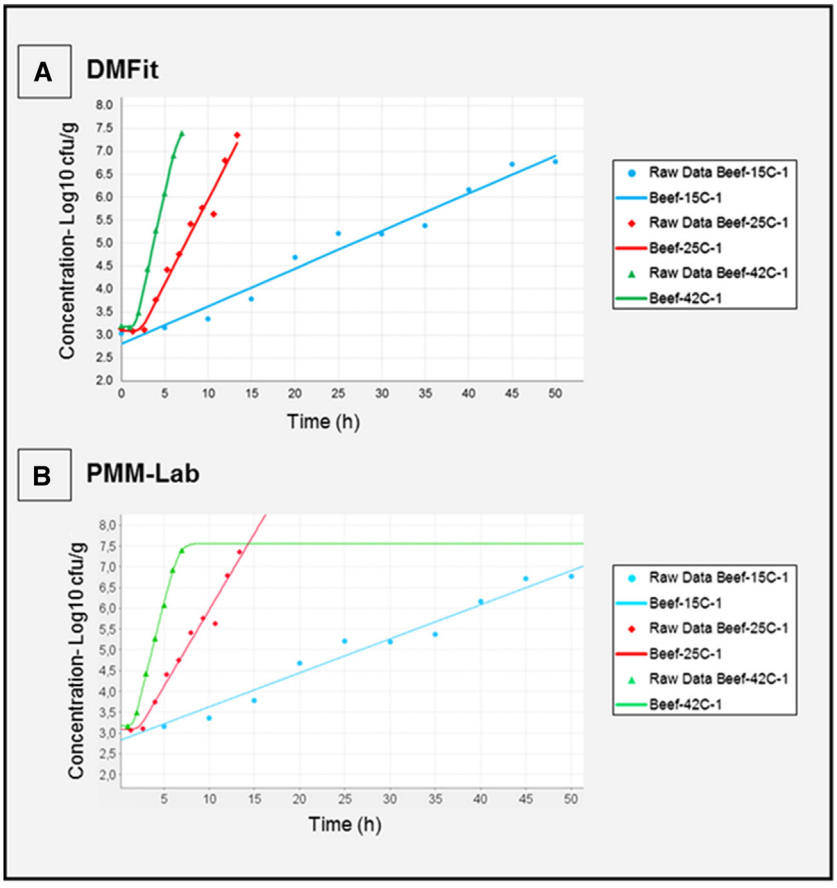

Fig. 4. Approach 2: Graphic comparison between the growth curves obtained from *DMFit* (Fig. 4A) and *PMM-Lab* (Fig. 4B). (Models fitted by *DMFit* to the formula from Baranyi and Roberts (1994). Raw data from *ComBase*: Juneja_09c. *Salmonella* in beef.)

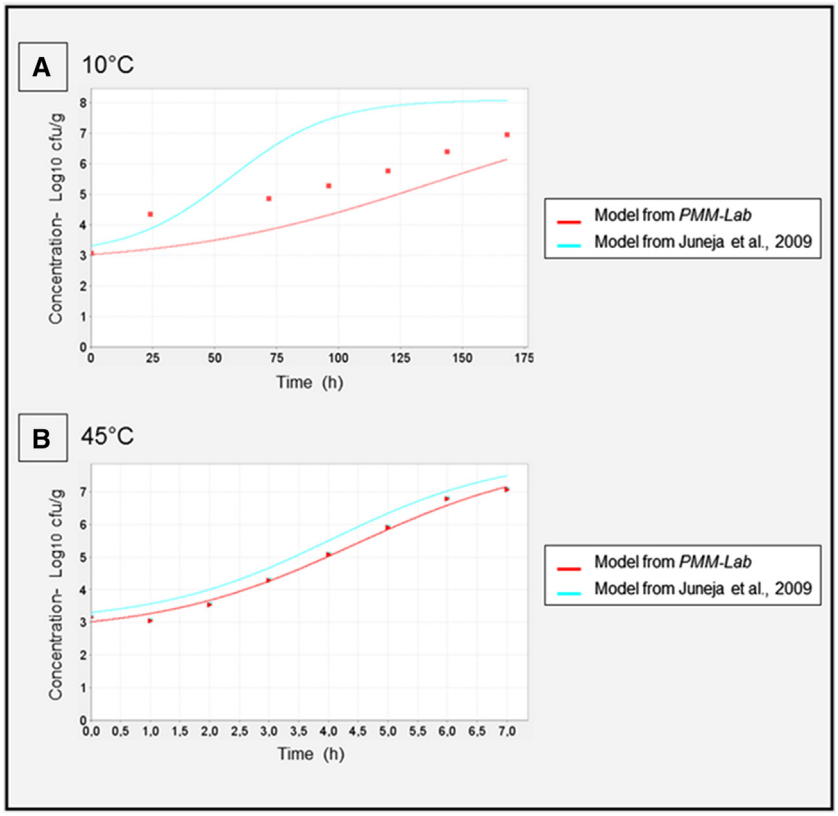

Fig. 5. Approach 3: Graphical comparison of the combined logistic/Ratkowsky model generated with *PMM-Lab* (with the one-step fitting approach) and the combined logistic/Ratkowsky model from the literature (incorporated in *PMM-Lab* within the approach 1). Dots represent raw data from *ComBase*. (Fig. 5A: predictions at 10 °C; Fig. 5B: predictions at 45 °C). (Raw data from *ComBase*: Juneja_09c. *Salmonella* in beef.)

microbiology. Finally this would increase the motivation of modellers to contribute their models into public repositories as they would not have to re-implement their models into a tool-specific syntax (as is currently the case).

Table 6
Performance (RMSE) of two combined logistic/Ratkowsky models generated by different model fitting strategies on the same experimental data (*ComBase*: Juneja_09c. *Salmonella* in beef). The one-step fitting strategy was applied in approach 3 (see text for details) using the software *PMM-Lab* whereas the "Juneja et al., 2009 model" is a pure re-implementation of the model published in the paper — as described in approach 1.

Data ID	Temp. [°C]	RMSE values	
		PMM-Lab one-step fitting model	Juneja et al., 2009 model
Beef-10C-1	10	1.48	4.01
Beef-10C-2	10	0.38	4.66
Beef-15C-1	15	0.50	1.30
Beef-15C-2	15	0.61	1.56
Beef-20C-1	20	0.45	0.39
Beef-20C-2	20	0.25	0.66
Beef-25C-1	25	0.41	0.50
Beef-25C-2	25	0.26	0.40
Beef-28C-1	28	0.36	0.45
Beef-28C-2	28	0.38	0.48
Beef-32C-1	32	0.55	0.49
Beef-32C-2	32	0.62	0.44
Beef-35C-1	35	0.71	0.55
Beef-35C-2	35	0.28	1.07
Beef-42C-1	42	0.31	1.62
Beef-42C-2	42	0.36	1.61
Beef-45C-1	45	0.17	0.82
Beef-45C-2	45	0.25	0.79
Global value		**0.28**	**0.72**

With this paper we demonstrated that it is in principle possible to adopt the Systems Biology Markup Language (SBML) as an information exchange format for the domain of predictive microbiology. We showed that software solutions like *PMM-Lab* can be extended to support the generation of SBML-formatted microbial model files which has been facilitated by the fact that the SBML community provides a plethora of free resources for software developers (e.g. at http://sbml.org/Software). However it also became evident, that certain specifications and conventions have to be stipulated by the predictive microbiology community when adopting the existing SBML standard. We propose to name this set of specifications "Predictive Modelling in Food Markup Language" (PMF-ML) and provide a first PMF-ML software developer guidance document at the community portal "*OpenML for Predictive Modelling in Food*" (http://sourceforge.net/projects/microbialmodelingexchange/files/). In future work these specifications will be extended to other model categories relevant for quantitative microbial risk assessments.

Experiences from the Systems Biology domain also tell, that standardized information exchange formats help to describe models effectively as they usually also encompass rules for model annotation (Hedley et al., 2001; Hucka et al., 2003; Juty et al., 2012; Le Novere et al., 2005; Lloyd et al., 2008). As part of this research we provide a collection of information concepts relevant for annotation of predictive microbial models. Based on a comparison with the MIRIAM guidelines (Le Novere et al., 2005) we propose that the following information should be provided for any predictive microbial model: model name, identifier, creator(s), creation date(s), rights, version, type and subject. Furthermore an additional annotation section should contain information on model reference(s), food matrix and microorganism(s) in the model's experimental raw data and the range of validity (environmental parameters, time, prediction values). These mandatory metadata may be

complemented by other non-compulsory information such as "goodness of fit", parameter and model uncertainties, references to files containing data used for model generation or validation, range of application (e.g. other microorganisms/matrices) or references to related publications. Even though the latter metadata are not termed mandatory, in many cases, this is highly important information, e.g. when it comes to the interpretation of model-based predictions. Compliance to this annotation proposal would also facilitate the practical application of predictive microbial models by increasing the interoperability between different software tools.

With respect to the actual FSMR generation process, we applied the software *PMM-Lab* to illustrate three different starting points which were considered relevant:

Approach 1 can be applied when models have to be re-implemented from scientific literature. The example given here resulted in identical predictions compared to the reference implementations, thus demonstrating that *PMM-Lab* is a suitable tool for model re-implementation. Approach 2 is relevant when information on several models is already available in tabular format, e.g. as a result of model fitting tools like *DMFit*. Finally approach 3 illustrated that *PMM-Lab* itself can be used to create models from experimental data. In the given example it was even possible to derive improved model parameter estimates compared to the model published in scientific literature. In all three examples *PMM-Lab* additionally created a transparent documentation of the applied model generation workflow. In this feature *PMM-Lab* resembles to statistical software packages, like R, Matlab or SAS. However, these tools are usually only applied by modelling experts.

5. Conclusions

The results of this study demonstrated that tools like *PMM-Lab* in combination with a standard information exchange format for the description of predictive microbial models could pave the way for FSMR. Depending on the intention of the FSMR creators, such repositories can be established as local private or web-based public resources. The latter option would contribute to transparent communication within the scientific community as well as to the application of predictive microbiology in food industry. However, these goals will only be achieved if the proposed strategy is supported by additional efforts in related fields, like improved usability of software solutions (e.g. tools should be as simple as possible), improved tools for data management and the improvement of procedures for quality control. The creation of a curated public FSMR would be highly beneficial in this respect. Again, a common information exchange format as proposed here, would support this, as features for quality control could be implemented into software tools and even scientific journals could easily provide (and demand) predictive microbial models as supplementary material.

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