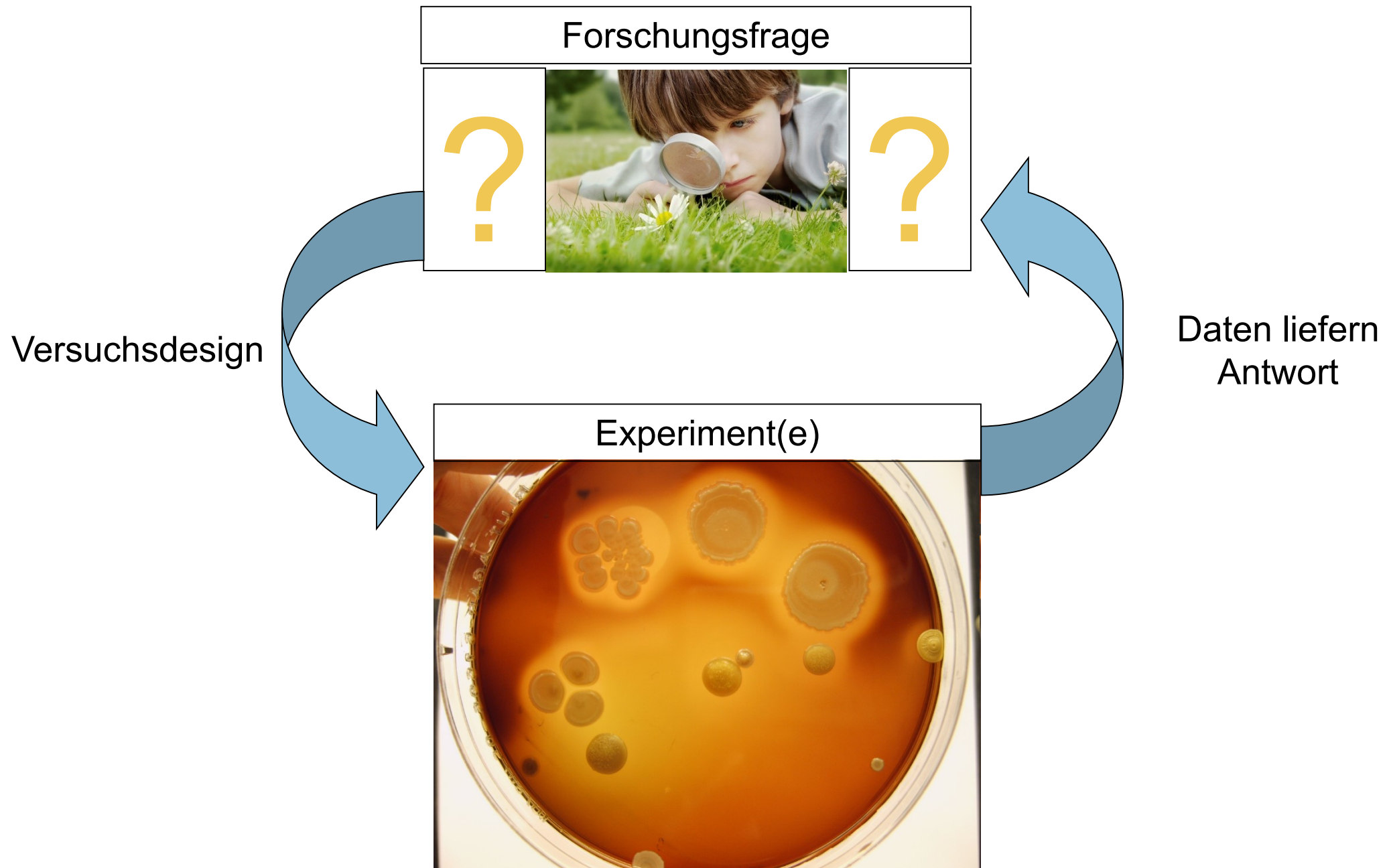


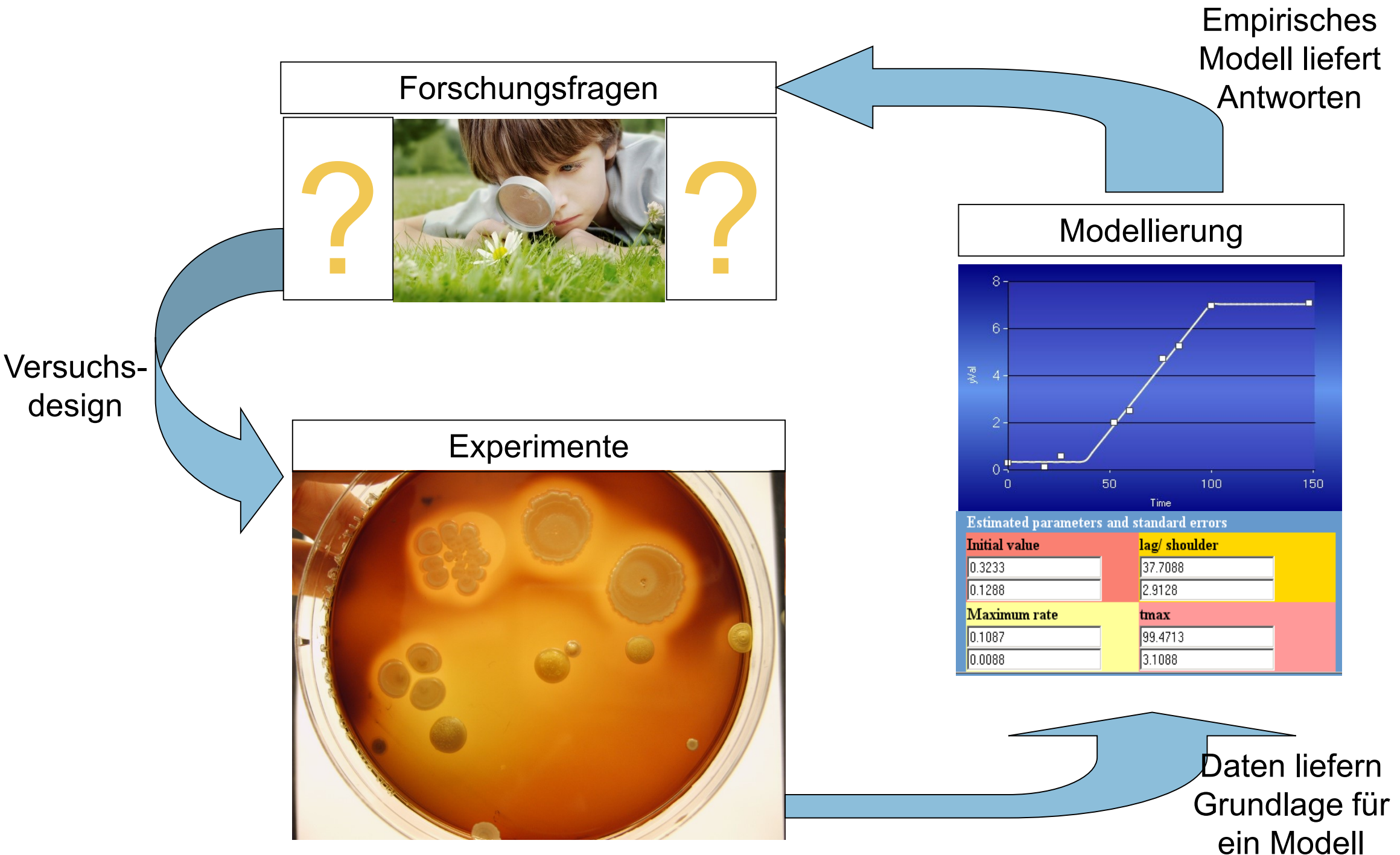
Tools und Ressourcen aus dem Bereich der prädiktiven Mikrobiologie

Matthias Filter

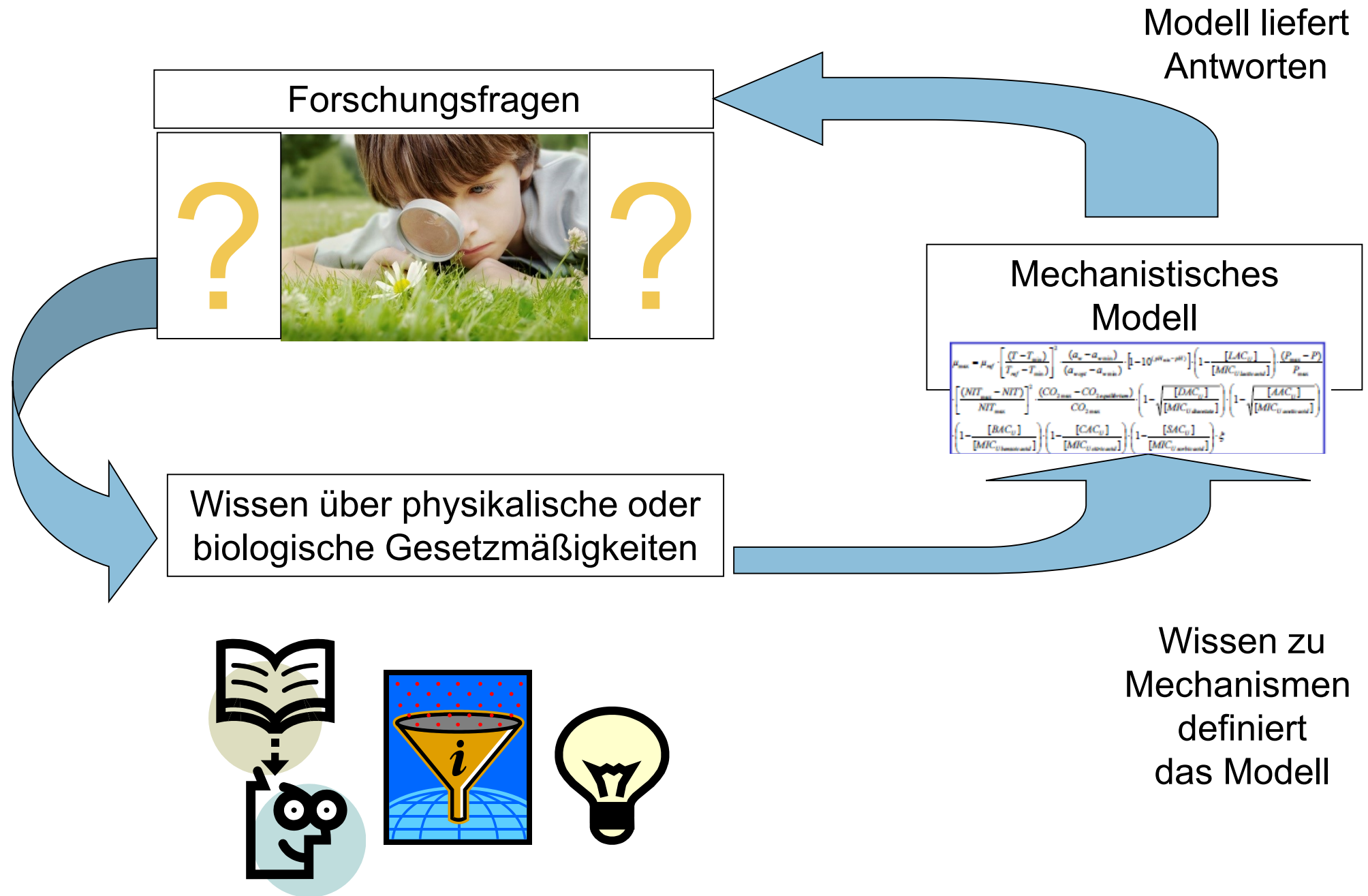
Was ist „Prädiktive Mikrobiologie“? – Szenario 1



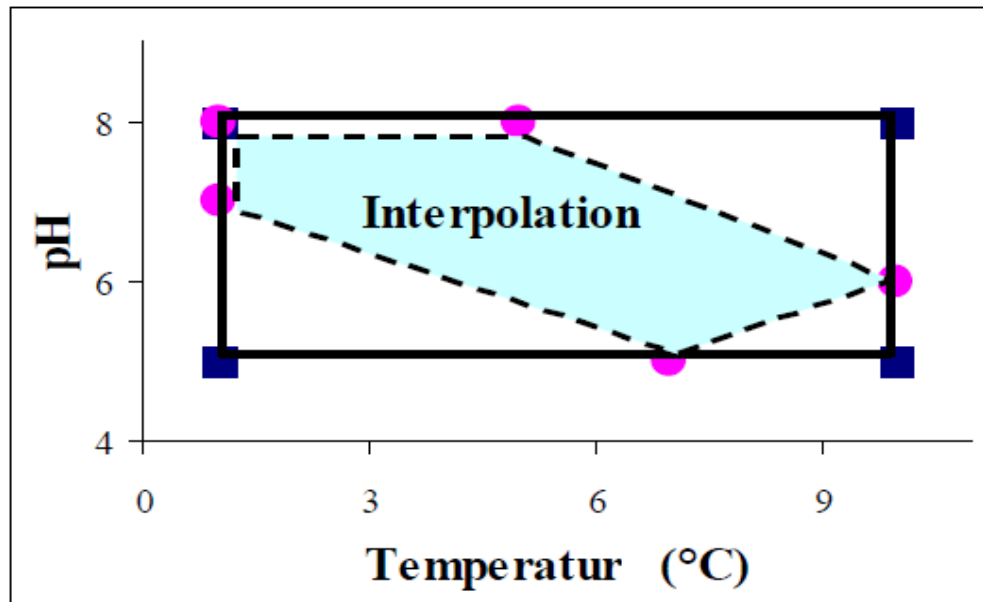
Was ist „Prädiktive Mikrobiologie“? – Szenario 2 (häufig)



Was ist „Prädiktive Mikrobiologie“? – Szenario 3 (selten)



Nachteil empirischer Modelle



Vorhersagen, die auf der **Interpolation** zwischen Messwerten beruhen:

=> **OK**

Vorhersagen, die außerhalb des Messbereichs liegen (**Extrapolation**)

=> **Nicht zu empfehlen !**

Bezieht sich u.a. auch auf

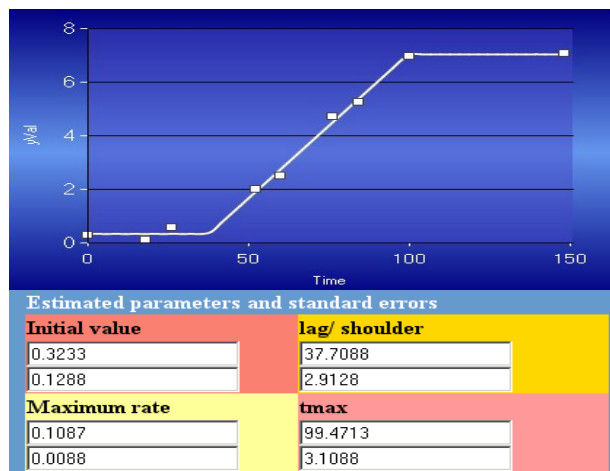
- Lebensmittelmatrizes
- Physiologischen Zellstatus
- Kultivierungshistorie
- Begleitflora u.v.m.

Grundsätzlich gilt:

(sowohl für empirische als auch mechanistische Modelle):

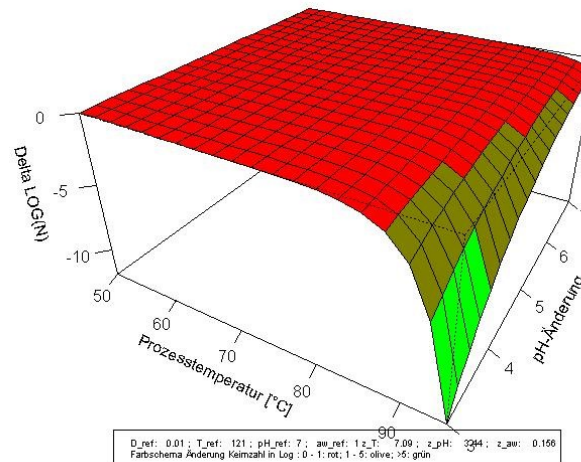
Die Validierung von Modellen mit unabhängigen Daten ist essenziell.

Gängige Nomenklatur prädiktiver mikrobieller Modelle



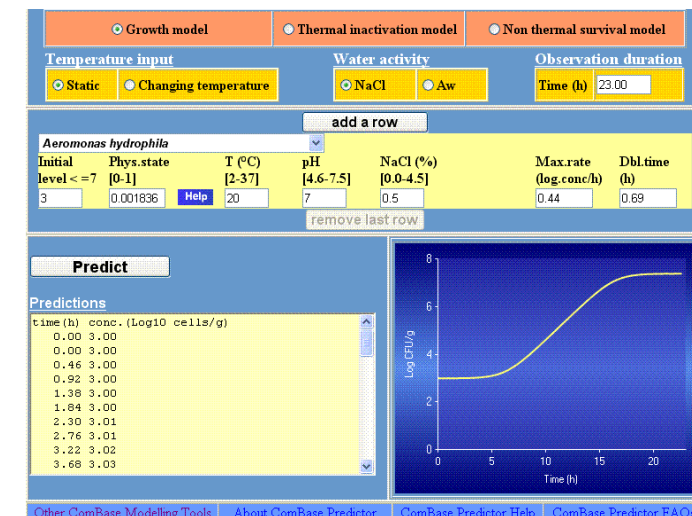
Primär-Modelle

beschreiben die **zeitliche** Veränderung der Menge / Konzentration eines Agens unter **konstanten** Umweltbedingungen (z.B. Temperatur, pH, NaCl, CO2 etc.)



Sekundär-Modelle

beschreiben die Abhängigkeit der Parameter in Primärmodellen (z.B. Wachstumsrate, Dauer der Lag-Phase etc.) von den Umweltbedingungen



Tertiär-Modelle

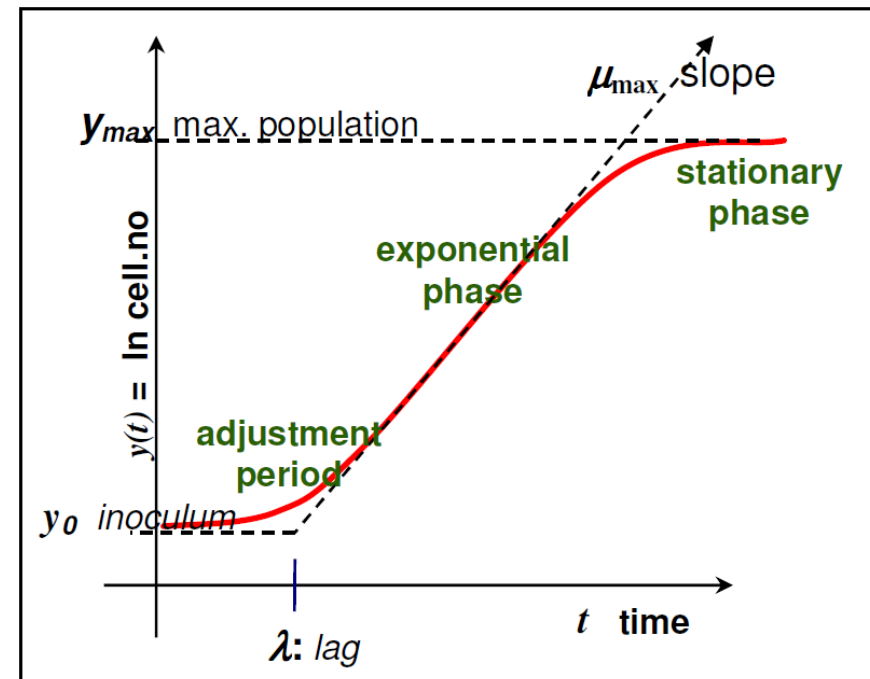
integrieren Primär- und Sekundärmodelle in eine nutzerfreundliche Software mit der Prädiktionen (Prognosen) zu vom Nutzer vorgegebenen Umweltbedingungen erstellt werden

Primäre Wachstumsmodelle

Lag phase: Zeit, die Zellen zur Anpassung an neue Umgebung benötigen
Shoulder : Maximale Populationsdichte

Populäre Gleichungen:

- Buchanan Three Phase Linear
- Logistic
- Gompertz
- **Baranyi**
- McKellar
- etc.



http://www2.sci.u-szeged.hu/fokozatok/PDF/Baranyi_Jozsef/Disszertacio.pdf

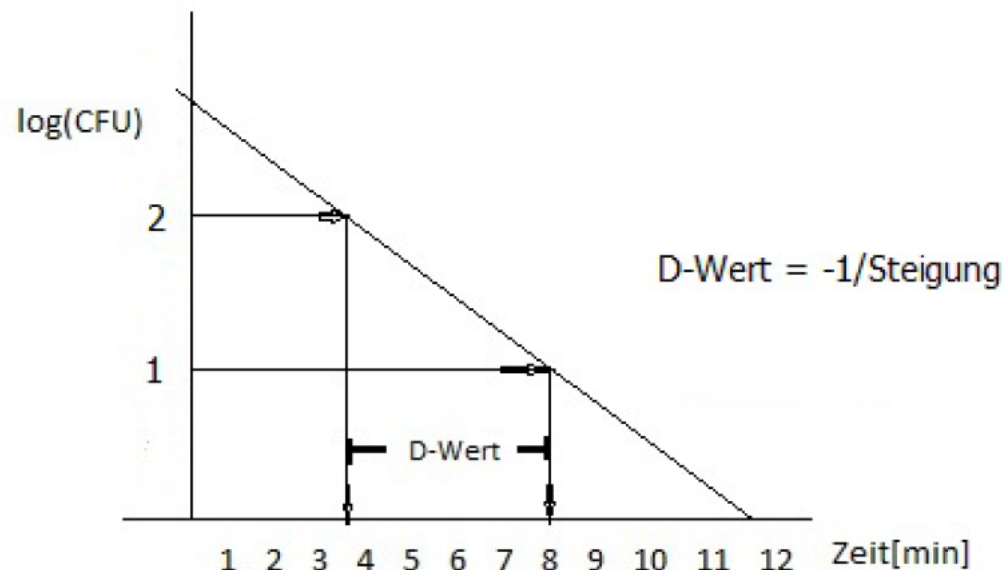
Primäre Inaktivierungsmodelle

Beispiel: Bigelow-Konzept

D-Wert : Zeit zur Reduktion der Keimzahl um 90% (1 Log-Stufe)
bei konstanten Umweltbedingungen (z.B. Temperatur, pH ...)

$$N_t = N_0 \times 10^{\frac{-t}{D_T}}$$

$$\log(N_t) = \log(N_0) - \frac{t}{D_T}$$



Sekundärmodelle

- Beispiel: "Cardinal Parameter Type Modell"



Predictive model for *Listeria monocytogenes*

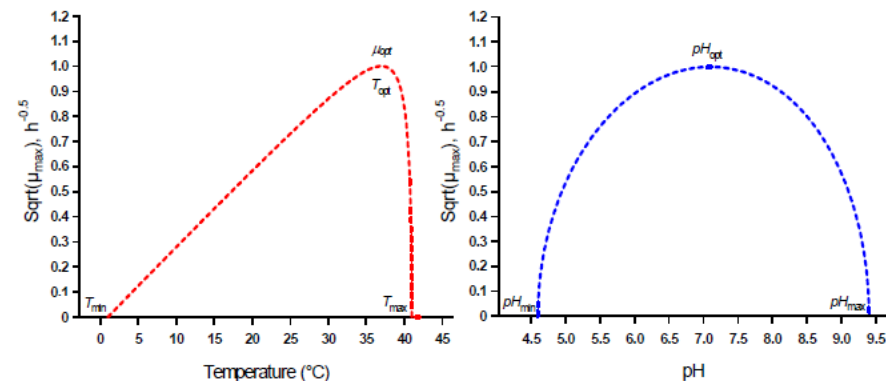
- Growth and growth boundary model for *L. monocytogenes* in lightly preserved seafood (Mejlholm and Dalgaard, 2009)

- Temperature
- pH
- NaCl/water activity
- Smoke components (phenol)
- Nitrite
- CO₂
- Acetic acid
- Benzoic acid
- Citric acid
- Diacetat
- Lactic acid
- Sorbic acid
- Interactions between all these parameters

$$\mu_{max} = \mu_{ref} \cdot \left[\frac{(T - T_{min})^2}{T_{ref} - T_{min}} \right] \cdot \frac{(a_w - a_{wmin})}{(a_{wref} - a_{wmin})} \cdot [1 - 10^{(pH_{max} - pH)}] \cdot \left(1 - \frac{[LAC_U]}{[MIC_U \text{ lactic acid}]} \right) \cdot \frac{(P_{max} - P)}{P_{max}}$$

$$\cdot \left[\frac{(NIT_{max} - NIT)^2}{NIT_{max}} \right] \cdot \frac{(CO_{2max} - CO_{2equilibrium})}{CO_{2max}} \cdot \left(1 - \sqrt{\frac{[DAC_U]}{[MIC_U \text{ diacetic acid}]}} \right) \cdot \left(1 - \sqrt{\frac{[AAC_U]}{[MIC_U \text{ acetic acid}]}} \right)$$

$$\cdot \left(1 - \frac{[BAC_U]}{[MIC_U \text{ benzoic acid}]} \right) \cdot \left(1 - \frac{[CAC_U]}{[MIC_U \text{ citric acid}]} \right) \cdot \left(1 - \frac{[SAC_U]}{[MIC_U \text{ sorbic acid}]} \right) \cdot \xi$$



Prädiktive Mikrobiologie - Anwendungsbereiche

Behörden / Risikobewerter:

Grundlage für wissenschafts-basierten Risikobewertungen

Grundlage für die Ableitung von Risikomanagement-Richtlinien, z.B.

- Festlegung von “Food Safety Objectives”
- Festlegung von “microbiological criteria”

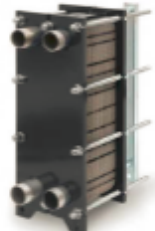
Lebensmittelunternehmen:

- Unterstützt die Planung, Implementierung und Validierung von „Food Safety Plans“ und die Optimierung von Kontrollstrategien
- Unterstützt bei der Minimierung der Zahl mikrobieller Tests und der Entscheidungsfindung zu Fragen aus dem Bereich Lebensmittelhaltbarkeit und –sicherheit
- Unterstützt bei der effizienten Entwicklung neuer Produkte und Rezepturen („safe innovation“)

Prädiktive Mikrobiologie - Anwendungsbeispiele

Some Examples of Application in Unilever to Support Safety by Design



	Driver	Model	Factors	Tools
	Sodium reduction	Survival of <i>Salmonella</i> spp. at ambient temp.	%NaCl, %KCl (a_w between 0.76 and 0.92)	• In-house model development (Matlab) • ComBase (data) • Scientific literature (data)
	Energy reduction in ice cream production	Thermal inactivation of vegetative infectious pathogens	Time-temperature, a_w	• In-house models • ComBase (models) • Pathogen Modeling Program (models) • Scientific literature (data)
	Milder-tasting, less acidic dressings	Survival of <i>E. coli</i> O157:H7, <i>Salmonella</i> spp., <i>L. monocytogenes</i>	Temperature, pH, %NaCl, %acetic acid, %K-sorbate	• In-house model development (Matlab) • ComBase (data) • Scientific literature (data)

Courtesy:

ALEJANDRO AMEZQUITA, Unilever

IAFP Annual Meeting 2014: „What are the Industry Needs for Tools for Microbial Modeling and Risk-based Decision Making?“

Matthias Filter, BfR-Symposium: *Listeria monocytogenes*, 17.11.2020

Seite 11

Prädiktive Mikrobiologie – Verfügbare Software

FoodRisk-Labs

FoodChain-Lab

Predictive Microbial Modeling Lab (PMM-Lab)

FoodProcess-Lab

Food Safety Knowledge Lab (FSK-Lab)

BfR-NewsRadar

Open Food Safety Model Repository

BfR & EFSA Safety Tools

RAKIP Web Portal

RAKIP Model Repository & Web Services

RAKIP Harmonization Resources

Food Safety Knowledge Exchange (FSKX) Format

RAKIP News and Roadmap

Predictive Microbial Modelling and QMRA Software Directory

ORION One Health EJP

External Tools

Predictive Microbial Modelling and QMRA Software Directory

A listing of tools available for predictive quantitative microbial risk assessment

Model repositories

- Baseline Software Tool
- ComBase
- GroPIN
- Interactive online Catalogue on Risk /
- Microbial Responses Viewer (MRV)
- openFSMR – a community driven sea
- crobial models
- Pathogen Modeling Program (PMP)
- RAKIP Web Portal

Predictive microbial modellin

Fitting tools

- DMFit
- FILTRES
- GInaFit
- IPMP
- nlsMicrobio (R package)
- Bioinactivation (R package)
- Bioinactivation FE

Prediction tools

- Baseline Software Tool
- Bioinactivation FE
- Bioinactivation SE
- ComBase Predictor
- Dairy products safety predic
- DMRI – predictive models fo
- E. coli Inactivation in Fermei
- EcSF – E. coli SafeFerment
- Food Spoilage and Safety Pr
- FISHMAP
- GroPIN
- Listeria Control Model 2012
- Listeria Meat Model
- Microbial Responses Viewer
- MicroHibro: Predictive Mod
- MLA Refrigeration Index Cal
- PMM-Lab
- Process lethality determinat
- Perfringens Predictor
- Praedicere
- Salmonella predictions
- Shelf Stability Predictor
- SWEETSHELF
- Sym'Previus
- Therm 2.0

Tools for quantitative microbial risk assessment

- A swift Quantitative Microbiological Risk Assessment tool (sQMRA)
- FDA-iRISK
- FSK-Lab
- MicroHibro: Risk Model
- Risk Ranger
- @Risk

Other resources

- ComBase
- Emerging Zoonoses Information and Priority systems (EZIPs)
- EFSA Comprehensive European Food Consumption Database
- EFSA zoonoses, antimicrobial resistance and food-borne out-
- breaks
- FDA's Fresh Produce Risk Ranking Tool
- Food Commodity Intake Database (FCID)
- FoodProcess-Lab
- FOSCOLLAB: a global platform for food safety data and informa-
- tion
- FRISBEE
- NIZO Premia
- PredOxyPack
- The European Surveillance System (TESSy)
- Tool for Risk based Microbiological Criteria (TRiMiCri)

<https://foodrisklabs.bfr.bund.de/predictive-microbial-modelling-and-qmra-software-directory/>

ComBase – größte öffentlich zugängliche Sammlung experimenteller Daten

ComBase

Home About ComBase team Donate data FAQ Contact us SUPPORT COMBASE

ComBase

Browser

Broth Models

Food Models

DMFit

Resources

Help

Search results [262 records]

Organism (Ascending)

41. *Listeria monocytogenes/innocua* in non-dairy cream

Food category: Other or unknown type of dairy
Food name: Non-dairy cream
Temp (°C): 15
Aw: 0.7
pH: 7
Conditions: Not specified
Source: Food Standards Agency funded data generated at the former FMBRA, Chorleywood (today Champden and Chorleywood Food Research Association), UK
Record views: 4
Record downloads: 3
Date added: Not available

Max.rate(log conc/h) Fit data

42. *Listeria monocytogenes/innocua* in non-dairy cream

Food category: Other or unknown type of dairy
Food name: Non-dairy cream
Temp (°C): 15
Aw: 0.6
pH: 5.5
Conditions: Not specified
Source: Food Standards Agency funded data generated at the former FMBRA, Chorleywood (today Champden and Chorleywood Food Research Association), UK
Record views: 3
Record downloads: 1
Date added: Not available

Max.rate(log conc/h) Fit data

43. *Listeria monocytogenes/innocua* in non-dairy cream

Food category: Other or unknown type of dairy
Food name: Non-dairy cream
Temp (°C): 15
Aw: 0.7
pH: 5.5
Conditions: Not specified
Source: Food Standards Agency funded data generated at the former FMBRA, Chorleywood (today Champden and Chorleywood Food Research Association), UK
Record views: 4
Record downloads: 3
Date added: Not available

Max.rate(log conc/h) Fit data

<https://www.combase.cc>

„Suchmaschine“ für prädiktive Modelle

openFSMR open Food Safety Model Repository
a community driven search engine for predictive microbial models

Created by BfR and

Search Organsim Environment

listeria monocytogenes **listeria innocua**

PMF-Organism	PMF-Environment	Model-
Listeria monocytogenes, Listeria innocua	Culture medium	Growth
Listeria monocytogenes, Listeria innocua	Culture medium	Growth
Listeria monocytogenes, Listeria innocua	Culture medium	Growth
Listeria monocytogenes, Listeria innocua	Culture medium	Growth
Listeria monocytogenes, Listeria innocua	Culture medium	Growth
Listeria monocytogenes, Listeria innocua	Culture medium	Survival
Listeria monocytogenes, Listeria innocua	Culture medium	Inactivation
Listeria innocua	Fruits/Vegetables	Growth
Listeria monocytogenes	Fruits/Vegetables	Growth
Vibrio parahaemolyticus	Seafood	Growth

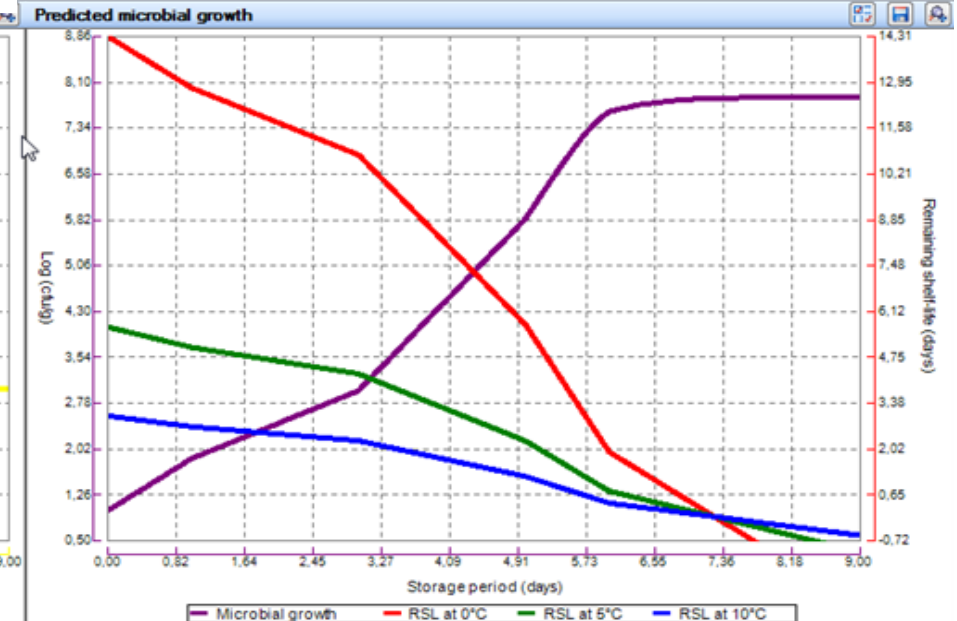
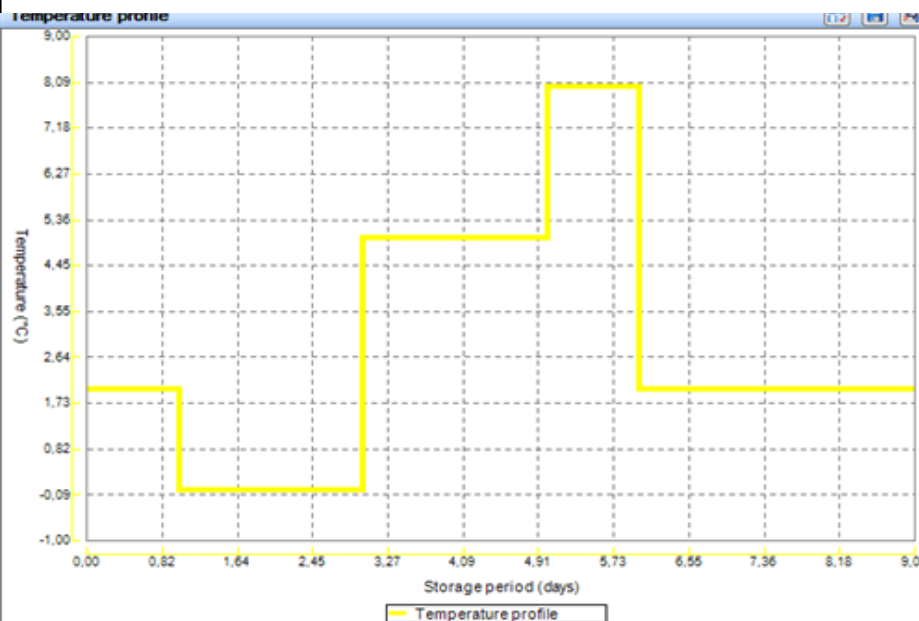
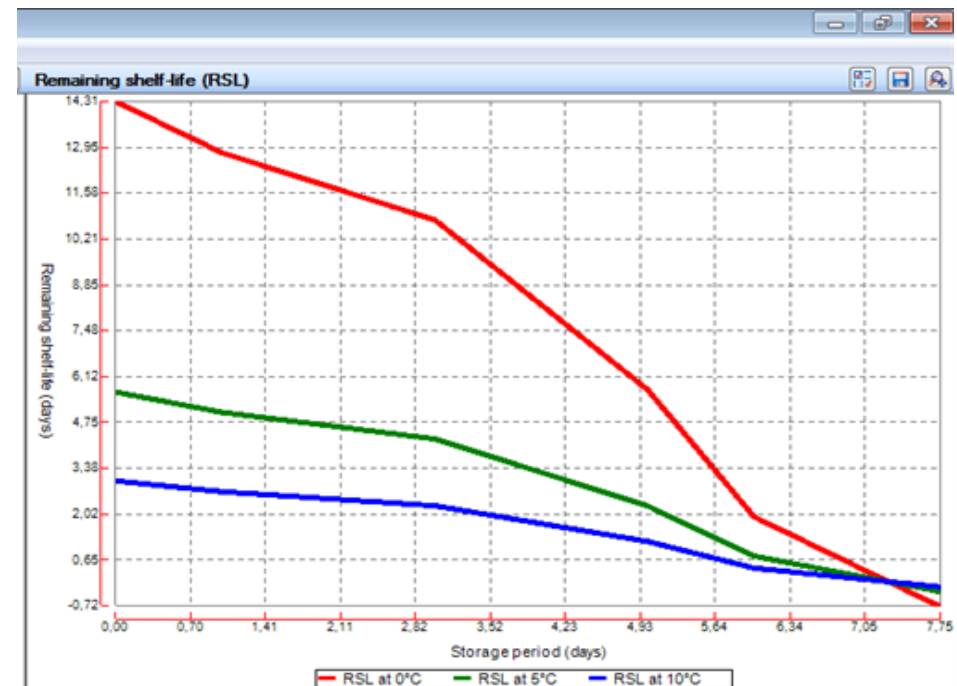
CombasePredictor_Growth_ListeriaMonocytogenes/innocua

DOLU	2019-03-29T00:00
Model-Name	CombasePredictor_Growth_ListeriaMonocytogenes/innocua
PMF-Organism	Listeria monocytogenes, Listeria innocua
PMF-Environment	Culture medium
Model-Creator	ComBase Consortium; ifr.combase@ifr.ac.uk
Model-CurationStatus	long term use
Model-Type	Growth
Model-Foodprocess	Storage
Model-DependentVariables	Concentration, Rate, Generation time
Model-DependentVariablesUnits	log10(count/g)
Model-IndependentVariables	temp, pH, aw, NaCl, sodium_nitrite
Software	Combase
Software-Link	Link
Software-Accessibility	Public, registration required
Software-StochasticModeling?	yes
Software-PredictionConditions	Static, dynamic
Atmosphere	0.0
init_level+Min	0.0
init_level+Max	7.0
init_level+Unit	Log10(count/g)
time+Min	0.0
time+Unit	h
temp+Min	1.0
temp+Max	40
temp+Unit	°C

<https://foodrisklabs.bfr.bund.de/openfsmr/>

Nützliche Tools: Food Spoilage and Safety Predictor

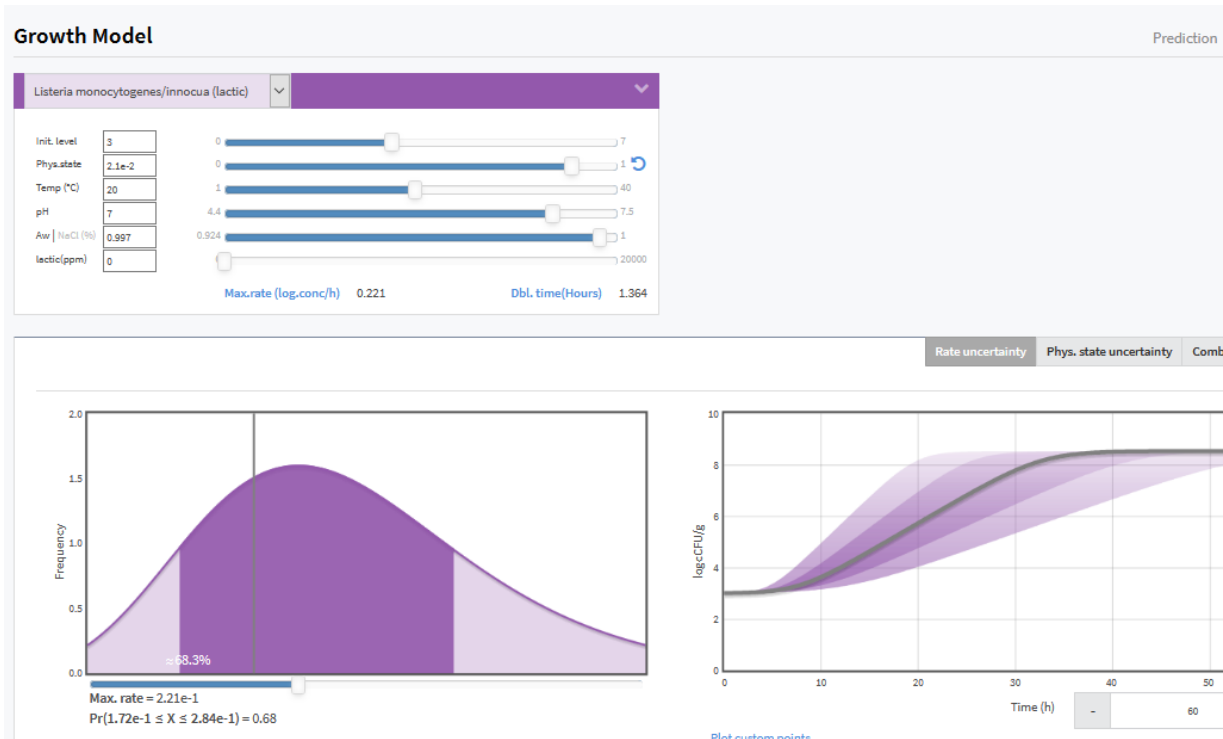
- [-] Food Spoilage and Safety Predictor (FSSP)
 - [-] Relative rate of spoilage (RRS) models
 - [+] Fresh seafood from temperate waters
 - [+] Fresh seafood from tropical waters
 - [+] Cold-smoked salmon
 - [+] Cooked and brined shrimps
 - [+] RRS models with user-defined temperature characteristics
 - [+] Comparison of observed and predicted RRS data
 - [-] Microbial spoilage models (MSM)
 - [+] Photobacterium phosphoreum
 - [+] H₂S-producing Shewanella
 - [+] MS models with user-defined parameter values
 - [+] Comparison of observed and predicted data
 - [-] Psychrotolerant Lactobacillus spp. (LAB)
 - [+] Growth of Lactobacillus in seafood and meat products
 - [-] Histamine formation models
 - [+] Morganella psychrotolerans - growth and histamine formation
 - [+] Morganella morganii and M. psychrotolerans - growth and histamine formation
 - [-] Listeria monocytogenes in chilled seafood and meat products
 - [+] Growth of L. monocytogenes
 - [+] Growth boundary of L. monocytogenes
 - [-] Listeria monocytogenes and lactic acid bacteria (LAB)
 - [+] Growth of L. monocytogenes and LAB in chilled seafood and meat products
 - [-] Listeria monocytogenes and lactic acid bacteria (LAB) in cottage cheese
 - [+] Growth of Listeria monocytogenes in cottage cheese in combination with LAB (starter or aroma culture)
 - [-] Generic growth models
 - [+] Generic models for growth of microorganisms



RSL for tempo. profile (d):7.25 Temp. (°C):2 RSL 0 °C (d):-INF RSL 5 °C (d):-INF RSL 10 °C (d):-INF Log(cfu/g):1.01

<http://fssp.food.dtu.dk/>

Nützliche Tools: ComBase Predictor & CB+ Premium



Model	Temp _{min}	Temp _{max}	pH _{min}	pH _{max}	Aw _{min}	ef4 _{max}
<i>Aeromonas hydrophila</i>	2	37	4.6	7.5	0.974	0
<i>Bacillus cereus</i> with CO2(%)	5	34	4.9	7.4	0.94	60
<i>Bacillus licheniformis</i>	13	34	4	7.6	0.907	0
<i>Bacillus subtilis</i>	10	34	4.3	7.8	0.933	0
<i>Clostridium botulinum</i> (non-prot.)	4	30	5.1	7.5	0.974	0
<i>Clostridium botulinum</i> (prot.)	14	40	4.7	7.2	0.954	0
<i>Clostridium perfringens</i>	15	52	5	8	0.971	0
<i>Escherichia coli</i> with CO2(%)	10	42	4.5	7.5	0.961	100
<i>Listeria monocytogenes/innocua</i> with CO2(%)	1	40	4.3	7.5	0.924	100
<i>Listeria monocytogenes/innocua</i> with nitrite(ppm)	1	40	4.4	7.5	0.924	200
<i>Listeria monocytogenes/innocua</i> with lactic(ppm)	1	40	4.4	7.5	0.924	20000
<i>Listeria monocytogenes/innocua</i> with acetic(ppm)	1	40	4.4	7.5	0.924	10000
<i>Staphylococcus aureus</i>	7.5	30	4.3	7.1	0.907	0
salmonellae with CO2(%)	7	40	3.9	7.4	0.973	100
salmonellae with nitrite(ppm)	7	40	3.9	7.4	0.973	200
<i>Shigella flexneri</i> with nitrite (ppm)	15	37	5.5	7.5	0.971	1000
<i>Yersinia enterocolitica</i> with CO2(%)	-1	37	4.4	7.2	0.957	80
<i>Yersinia enterocolitica</i> with lactic(ppm)	-1	37	4.4	7.2	0.957	10000
<i>Brochothrix thermosphacta</i>	0	30	5.5	7	0.95	0
<i>Pseudomonas</i> spp	0	20	5	7.4	0.961	0

<https://www.combase.cc>

<https://www.cbpremium.org/>

Nützliche Tools: Pathogen Modeling Program (PMP)

You are here: [PMP Home](#) / PMP Online

SELECT A PATHOGEN MODEL ▶

Growth Model: *Listeria monocytogenes* (Broth Culture, Aerobic)

Input Conditions

Environment:
☒ aerobic ☐ anaerobic

Temperature in:
☒ °C ☐ °F

Temperature
Range: 4.0 to 37.0 °C
19.0

pH
Range: 4.5 to 7.5
5.0

Sodium Chloride
Range: 0.5 to 10.5 (% [g/dL])
5.5

Sodium Nitrite
Range: 0 to 150 ppm
0

Initial Level
Range: 3.0 to 5.9 log(CFU/ml)
3

CALCULATE GROWTH DATA

Modeled Growth

Hours	log(CFU/ml)
0	3.0
100	3.0 (Lag)
110	3.0 (Lag)
200	9.57 (No Lag)
300	9.57 (Lag)

Modeled Growth Parameters

- Lag Phase Duration: 109.79 (hours)
- Generation Time: 6.52 (hours)
- Growth Rate: 0.046 (log(cfu/ml)/h)
- Max Population Density: 9.57 (log(cfu/ml))

Growth Models

Aeromonas hydrophila
Bacillus cereus
Clostridium botulinum
Clostridium perfringens
Escherichia coli O157:H7
Listeria monocytogenes
Salmonellae
Salmonella typhimurium
Shigella flexneri
Staphylococcus aureus 196E
Yersinia enterocolitica

Cooling / Growth Models

Clostridium botulinum
Clostridium perfringens

Survival Models

Escherichia coli O157:H7
Listeria monocytogenes
Salmonellae
Staphylococcus aureus 196E

Thermal Inactivation Models

Non-proteolytic Clostridium botulinum
Escherichia coli O157:H7
Listeria monocytogenes

Radiation Models

Escherichia coli O157:H7
Salmonella typhimurium

<https://pmp.errc.ars.usda.gov/PMPOnline.aspx>

Matthias Filter, BfR-Symposium: *Listeria monocytogenes*, 17.11.2020

Seite 17

 **BfR**

Nützliche Tools: Microbial Response Viewer

Listeria monocytogenes/innocua

Food



Culture Medium (5474)



Beef (511)



Pork



Additives



Other or unknown type of meat (381)



Seafood (419)



Milk (483)



Cheese



Dessert food (62)



Sauce/Dressing (12)



Vegetable or fruit and their products (255)



Bread

← Lactic Acid Listeria monocytogenes / innocua

Condition

Axis

temp - aw

temp - pH

pH - aw

aw

<0.70

0.75±0.05

0.85±0.05

0.95±0.05

0.955±0.005

0.965±0.005

0.975±0.005

0.985±0.005

0.995±0.005

Plot

Growth

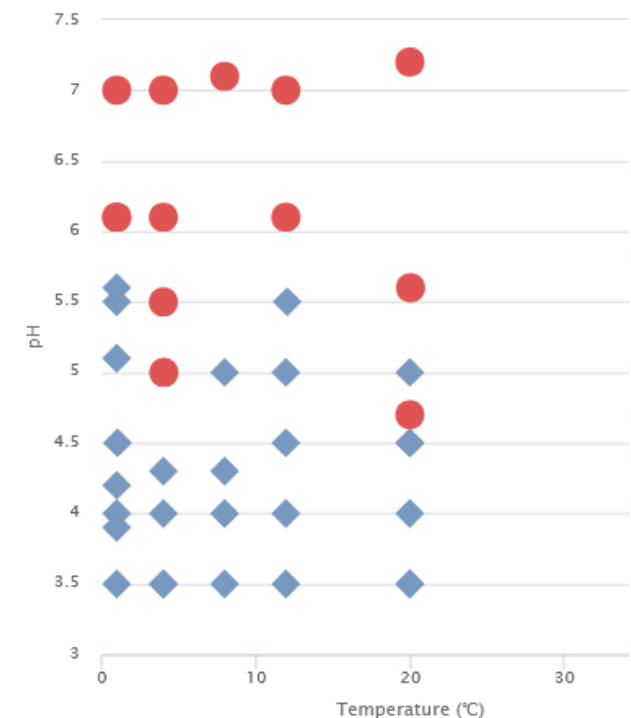
No growth

Both

* To switch the axis of the chart, click or touch "temp-aw", "temp-pH", and "pH-aw" buttons

* Click or touch a data point to show related data list

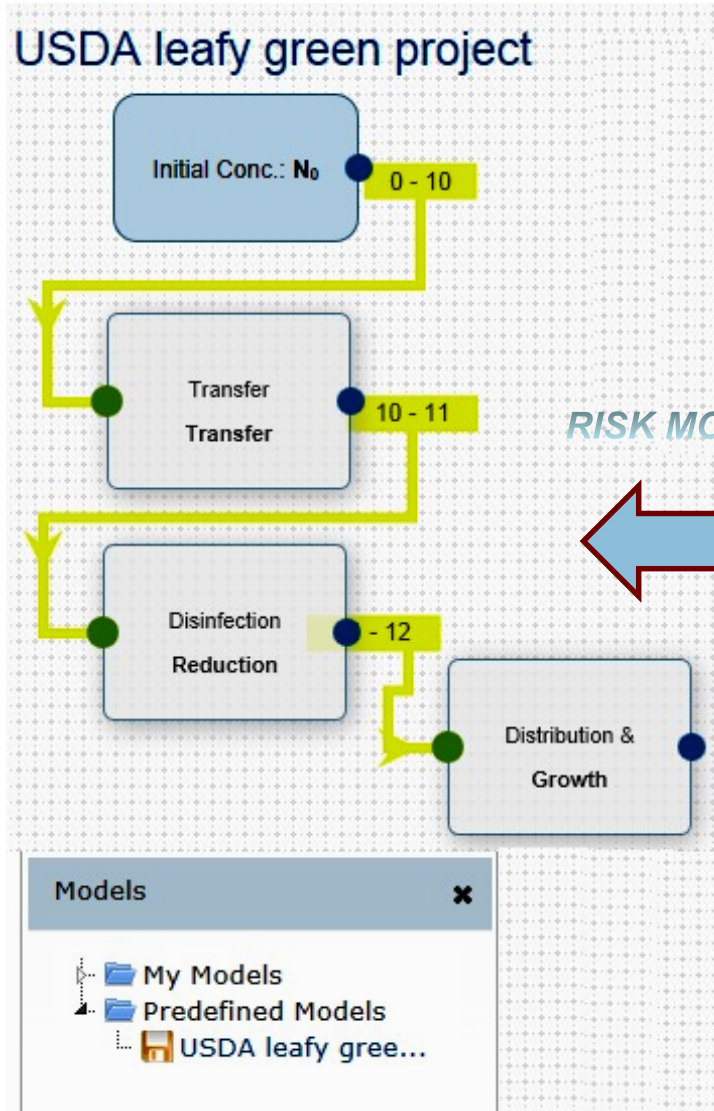
2000ppm



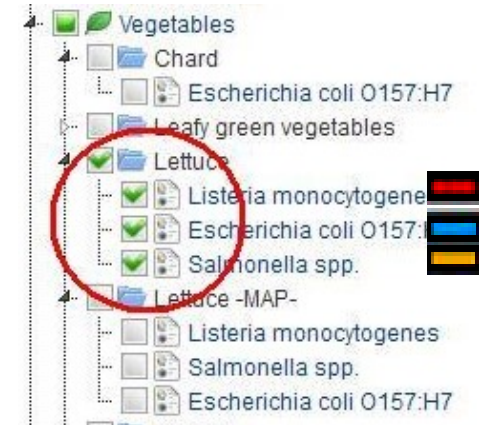
<http://mrviewer.info/>

Nützliche Tools: microHibro

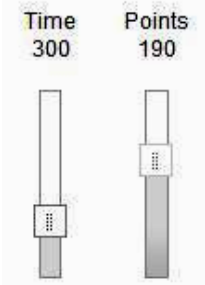
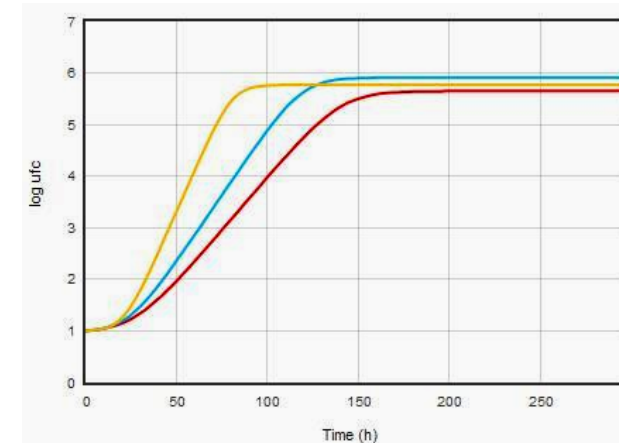
microHibro



RISK MODEL

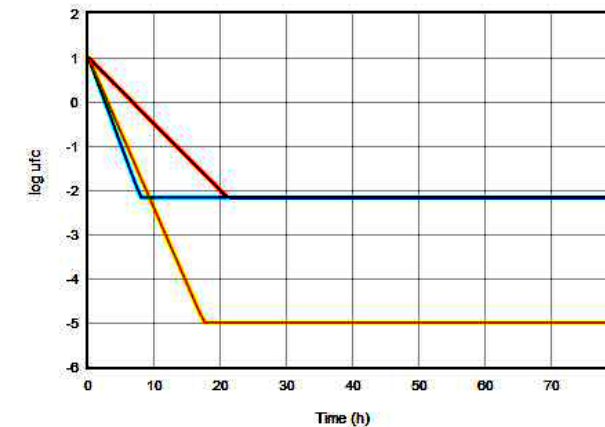


GROWTH



microHibro

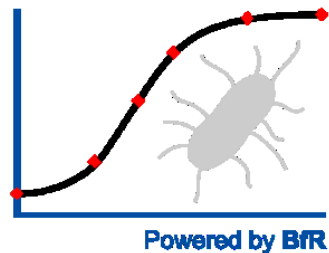
INACTIVATION



<http://www.microhibro.com/>

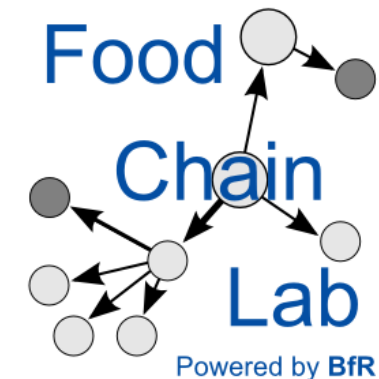
Nützliche Tools: BfR FoodRisk-Labs Tools

PMM-Lab



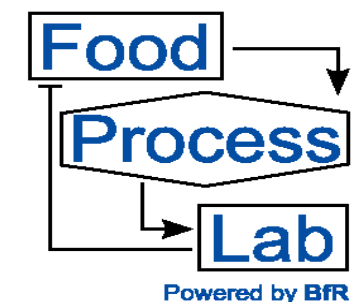
**Wachstum- /
Inaktivierungs-
Modellierung**

**Rückverfolgung
von
Lebensmitteln**



**QMRA-
Modelle &
Austauschformate**

**Prozess-
Modellierung &
Simulation**



Generelle Hinweise zur Nutzung prädiktiver Modelle

- Je nach Anwendungsszenario sollte VOR der Nutzung geprüft werden, ob ein Modell für das jeweils betrachtete Lebensmittel und die gegebenen Prozessbedingungen anwendbar ist
- Trotz der Vielzahl an verfügbare Modellen gilt, Modelle können nicht alle Einflussgrößen berücksichtigen, z. B.
 - natürliche mikrobielle Flora und Interaktion von MO
 - rheologische / strukturelle Eigenschaften der LM
 - Stamm-spezifische Unterschiede
- Zur Nutzung der diversen Tools ist i.d.R. Fachwissen zur korrekten Interpretation der Vorhersagen notwendig
- Modell-Autoren / Tool-Entwickler übernehmen keinerlei Gewährleistung / Haftung

“All models are wrong, but some of them are useful” (Box, G. E. P. (1979), "Robustness in the strategy of scientific model building", in Launer, R. L.; Wilkinson, G. N. (eds.) *Robustness in Statistics*, Academic Press, pp. 201–236, doi:10.1016/B978-0-12-438150-6.50018-2, ISBN 9781483263366.)

Danke für Ihre Aufmerksamkeit

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