Case study: *L. monocytogenes* in cold-smoked salmon

R. POUILLOT, M.-L. DELIGNETTE-MULLER, M. CORNU

August 8, 2011

The objective of this case study is to assess the risk of invasive listeriosis from consumption of cold-smoked salmon in France. The process of interest lays from the end of the production line in the factory, when the cold-smoked salmon is vacuum-packed, to the consumption.

The data and the model are adapted to illustrate the use of `mc2d`: the results will not and *should not* be interpreted as an assessment of the actual risk of listeriosis from consumption of cold-smoked salmon. Interested readers could refer to [3] and [2] for a complete risk assessment on that issue.

The model will be developed in a first section, without considering variability or uncertainty (deterministic model). Variability will then be introduced in a second section, and a last section will consider variability and a part of the data uncertainty.

1 The Model

In this section, no variability nor uncertainty is considered. We assess the final level of *L. monocytogenes* in the product, the exposure and the risk of invasive listeriosis for an "average" individual of the "healthy" French population[1].

During the logistic, the retail and the home step, a bacterial growth is modeled considering *i*) the fluctuating temperature during the various stages and; *ii*) the bacterial competition with the food flora. We use the models developed and/or used in [3]. The data are adapted from [3] and [1]:

- The DMS model predicts the bacterial growth during a stage of duration d, when the temperature is fluctuating, with an intra-stage average temperature m_T and an intra-stage standard deviation of the temperature s_T. It is written:

$$N_1 = \min\left(N_0 + \frac{\mu_{ref}}{\ln(10)} \times d \times \frac{\left(s_T^2 + (m_T - T_{min})^2\right)}{(T_{ref} - T_{min})^2},\ N_{max}\right) \quad (1)$$

  if $m_T > T_{min}$, with N_1 the $\log_{10}$ concentration of bacteria ($\log_{10}$ (CFU/g)) in the product at the end of the stage, N_0 the $\log_{10}$ concentration of bacteria ($\log_{10}$ (CFU/g)) in the product at the beginning of the stage, μ_{ref} the specific growth rate (day^{-1}) at a reference temperature T_{ref} (°C), T_{min} the minimal temperature (°C) of growth and N_{max} the maximum achievable concentration in the product ($\log_{10}$ (CFU/g)). If $m_T \leq T_{min}$, $N_1 = N_0$.

- We will use $T_{ref} = 25$°C. We have in this section $N_{max} = 7.27\log_{10}(\text{CFU/g})$;
- The model for *L. monocytogenes* uses $\mu_{ref,Lm} = 6.2\,\text{day}^{-1}$ and $T_{min,Lm} = -2.9$°C;
- The same model is used for the food flora, with $\mu_{ref,ff} = 4.1\,\text{day}^{-1}$ and $T_{min,ff} = -4.5$°C;
- The growth model for the bacterial competition consider the Jameson effect, i.e. consider that the bacterial growth of *L. monocytogenes and* the growth of the food flora are stopped as soon as one population reaches N_{max}.

[1] Yes, it makes no sense, but it will help us introducing smoothly the model.

In practice, one will evaluate d_{Lm} and d_{ff}, the time needed for *L. monocytogenes* or the food flora to reach N_{max}, respectively, and model a growth for the given stage during an effective duration of $\min(d, d_{Lm}, d_{ff})$. The time needed to reach N_{max} is evaluated by inverting (1):

$$d_{(N_1=N_{max})} = (N_{max} - N_0) \times \frac{\ln(10)}{\mu_{ref}} \times \frac{(T_{ref} - T_{min})^2}{\left(s_T^2 + (m_T - T_{min})^2\right)}$$

The other assumptions are:

- A cold-smoked salmon package is homogeneously contaminated with *L. monocytogenes* at the end of the production at a level of 0.1 CFU/g;
- The food flora level at the end of the production is $10^{2.78}$ CFU/g;
- The time-temperature profile is:
  - 1.1 days at an average temperature of 3.2°C from the factory to the retail (logistic step), with an intra-stage standard deviation of the temperature of 2.1 °C;
  - 4.7 days at an average temperature of 5.5°C at retail with an intra-stage standard deviation of the temperature of 1.0 °C;
  - 4.3 days at an average temperature of 8.2°C in the consumer's home with an intra-stage standard deviation of the temperature of 2.0 °C;
- An healthy, non elderly, non pregnant individual eats 35g of this product;
- The individual dose-response model for this population is a one hit model

  $$\Pr(\text{Illness} \mid D) = 1 - (1 - r)^D$$

  with $r = 4.7 \times 10^{-14}$ for an individual from this healthy sub-population. The populational dose-response that evaluates the mean risk for a population exposed to food where the number of bacteria follows a Poisson distribution of mean paramer D is the exponential dose-response

  $$\Pr(\text{Illness} \mid D) = 1 - \exp(r \times D)$$

The question is "What is the risk for this 'average' individual?". One way to write this model is as following:

```
> Nmax <- 7.3
> murefLm <- 6.2
> TminLm <- -2.9
> murefFF <- 4.1
> TminFF <- -4.5
> Lm0 <- log10(1)
> FF0 <- 2.78
> d1 <- 1.1
> mT1 <- 3.2
> sdT1 <- 2.1
> d2 <- 4.7
> mT2 <- 5.5
> sdT2 <- 1
> d3 <- 4.3
> mT3 <- 8.2
> sdT3 <- 2
> conso <- 35
> r <- 4.7e-14
```

```
> modGrowth <- function(duration, mTemp, sdTemp, N0Lm, murefLm, TminLm, N0FF,
+     murefFF, TminFF, Nmax, Tref = 25) {
+     N0Lm <- pmin(N0Lm, Nmax)
+     N0FF <- pmin(N0FF, Nmax)
+     dLm <- (Nmax - N0Lm) * log(10)/murefLm * (Tref - TminLm)^2/(sdTemp^2 + (mTemp -
+         TminLm)^2)
+     dLm <- ifelse(mTemp < TminLm & N0Lm != Nmax, Inf, dLm)
+     dFF <- (Nmax - N0FF) * log(10)/murefFF * (Tref - TminFF)^2/(sdTemp^2 + (mTemp -
+         TminFF)^2)
+     dFF <- ifelse(mTemp < TminFF & N0FF != Nmax, Inf, dFF)
+     realDuration <- pmin(duration, dLm, dFF)
+     xLm <- N0Lm + (mTemp > TminLm) * murefLm/log(10) * (sdTemp^2 + (mTemp -
+         TminLm)^2)/((Tref - TminLm)^2) * realDuration
+     xFF <- N0FF + (mTemp > TminFF) * murefFF/log(10) * (sdTemp^2 + (mTemp -
+         TminFF)^2)/((Tref - TminFF)^2) * realDuration
+     return(list(xLm = xLm, xFF = xFF))
+ }
> x1 <- modGrowth(d1, mT1, sdT1, Lm0, murefLm, TminLm, FF0, murefFF, TminFF, Nmax)
> x2 <- modGrowth(d2, mT2, sdT2, x1$xLm, murefLm, TminLm, x1$xFF, murefFF, TminFF,
+     Nmax)
> x3 <- modGrowth(d3, mT3, sdT3, x2$xLm, murefLm, TminLm, x2$xFF, murefFF, TminFF,
+     Nmax)
> x3

$xLm
[1] 3.21

$xFF
[1] 5.35

> conta <- 10^x3$xLm
> conta

[1] 1637

> expo <- conso * conta
> expo

[1] 57281

> risk <- 1 - (1 - r)^expo
> risk

[1] 2.69e-09
```

`modGrowth` is a convenient function for the growth model. Within this function `dLm` is the time needed for *L. monocytogenes* to reach `Nmax`, `dFF` is the time needed for the food flora to reach `Nmax` and, `realDuration` is the effective time of growth during the stage. Note that:

- this function is "vectorized", meaning that it can deal with a vector for any of its parameters, returning consequently a vector. This is a strength of R, notably for Monte-Carlo simulations, but it requests a bit of knowledge on the way to code the functions. As an example: `pmin`, a function that takes one or more vectors as arguments and return a single vector giving the "parallel" minima of the vectors is used instead of the more classical function `min` function, that would return the maximum or minimum of *all* the values. Another example is the use of the `ifelse` instead of `if`;

- it is also written to handle *all* specific cases that could occur in the Monte-Carlo simulation, such as $N_0 \geq N_{max}$ or $m_T \leq T_{min}$ or both, for any or both bacterial populations.

`x1`, `x2` and `x3` are the bacterial concentrations at the end of the logistic, the retail and the home step, respectively.

2 Including Variability

We now specify now some variability distributions for some inputs, following [1] and [3]. We first have to call the needed libraries, and define the desired number of iterations:

```
> library(fitdistrplus)
> library(mc2d)
> ndvar(10001)
```

```
[1] 10001
```

2.1 Specifying Variability Distribution

2.1.1 Initial Contamination

For the initial contamination levels in *L. monocytogenes*, we have a set of 62 enumeration data from a representative sample of packages of cold smoked salmon positive in detection: 43 samples have less than 0.2 CFU/g, 7 samples have 0.2 CFU/g, 4 samples have 0.4 CFU/g, 2 samples have 0.6 CFU/g, and the other values are 0.3, 1.0, 1.6, 2.4, 5.4 and 7.0 CFU/g [3]. We will use the `fitdistrplus` package to fit a normal distribution on the $\log_{10}$ of these values, taking into account the censored values. Using the fitted parameters, we model thereafter these initial concentrations in contaminated packages through a normal distribution truncated[2] on $[-2, \infty)$ $\log_{10}$ (CFU/g).

For the food flora, we use the distribution proposed by [1], $N_{0ff} \sim N(2.78, 1.14)$.

```
> dataC <- data.frame(left = c(rep(NA, 43), rep(0.2, 7), 0.3, rep(0.4, 4), 1,
+     1.6, 0.6, 0.6, 2.4, 5.4, 7), right = c(rep(0.2, 43), rep(0.2, 7), 0.3, rep(0.4,
+     4), 1, 1.6, 0.6, 0.6, 2.4, 5.4, 7))
> fit <- fitdistcens(log10(dataC), "norm")
> fit
```

```
Fitting of the distribution ' norm ' on censored data by maximum likelihood
Parameters:
     estimate
mean   -1.117
sd      0.764
```

```
> Lm0V <- mcstoc(rnorm, mean = fit$est["mean"], sd = fit$est["sd"], rtrunc = TRUE,
+     linf = -2)
> FF0V <- mcstoc(rnorm, mean = 2.78, sd = 1.14)
```

Note that, by default, the type of alea that is modeled is "variability" (`type="V"`).

2.1.2 Growth Parameters

Distributions are derived from [1]:

- N_{max} follows a normal distribution with mean 7.27 $\log_{10}$ CFU/g and standard deviation 0.86 $\log_{10}$ CFU/g;
- The specific growth rate at the reference temperature of 25°C for *L. monocytogenes* follows a normal distribution with mean 6.24 day^{-1} and standard deviation 0.75 day^{-1} truncated on $[0, \infty)$. The minimal growth temperature follows a normal distribution with mean -2.86°C and standard deviation 1.93°C;

[2] so that at least one CFU is included in one 100g package

Table 1: Time Temperature Profiles

Stage	Mean Temperature (°C)	Intra-Stage Variance of T (°C)	time (days)
logistic	normal(3.2, 2.2) truncated on [-3;25]	$\Gamma(1.16, 4.61)$	Exponential(1.1)
retail	normal(5.5, 2.2) truncated on [-3;25]	$\Gamma(0.65, 2.09)$	Exponential(4.7)
consumer	normal(8.2, 3.8) truncated on [-3; 25]	$\Gamma(0.35, 19.7)$	Exponential(4.3)

- The specific growth rate at the reference temperature of 25°C for the food flora follows a normal distribution with mean 4.12 day^{-1} and standard deviation 1.97 day^{-1} truncated on $[0, \infty)$. The minimal growth temperature follows a normal distribution with mean -4.52°C and standard deviation 7.6°C.

```
> NmaxV <- mcstoc(rnorm, mean = 7.27, sd = 0.86)
> murefLmV <- mcstoc(rnorm, mean = 6.24, sd = 0.75, rtrunc = TRUE, linf = 0)
> TminLmV <- mcstoc(rnorm, mean = -2.86, sd = 1.93)
> murefFFV <- mcstoc(rnorm, mean = 4.12, sd = 1.97, rtrunc = TRUE, linf = 0)
> TminFFV <- mcstoc(rnorm, mean = -4.52, sd = 7.66)
```

2.1.3 Time-Temperature Profiles

The time temperature profiles in the three steps are modelled using the distribution provided in the table 1 (adapted from [3] from representative data from France)[3]. We assume a shelf life of 28 days. A simple way to model this shelf life will be to have $d_1 + d_2 + d_3 \leq 28$ days, with d_1 the duration of the logistic stage, d_2 the duration of the retail stage and d_3 the duration of the consumer stage[4];

```
> d1V <- mcstoc(rexp, rate = 1/1.1)
> mT1V <- mcstoc(rnorm, mean = 3.2, sd = 2.2, rtrunc = TRUE, linf = -3, lsup = 25)
> sdT1V <- sqrt(mcstoc(rgamma, shape = 1.16, scale = 4.61))
> d2V <- mcstoc(rexp, rate = 1/4.7, rtrunc = TRUE, lsup = 28 - d1)
> mT2V <- mcstoc(rnorm, mean = 5.5, sd = 2.2, rtrunc = TRUE, linf = -3, lsup = 25)
> sdT2V <- sqrt(mcstoc(rgamma, shape = 0.65, scale = 2.09))
> d3V <- mcstoc(rexp, rate = 1/4.3, rtrunc = TRUE, lsup = 28 - (d1 + d2))
> mT3V <- mcstoc(rnorm, mean = 8.2, sd = 3.8, rtrunc = TRUE, linf = -3, lsup = 25)
> sdT3V <- sqrt(mcstoc(rgamma, shape = 0.35, scale = 19.7))
```

2.1.4 Serving Size

As for the serving size, we consider, from observed data, a discrete empirical distribution with values [3]: V={10, 12, 19, 20, 30, 34, 40, 50, 60, 67.5, 80, 100, 250} grams, observed F={11, 1, 1 ,29, 12, 1, 41, 4, 4, 1, 4, 1, 1} time, respectively.

```
> consoV <- mcstoc(rempiricalD, values = c(10, 12, 19, 20, 30, 34, 40, 50, 60,
+     67.5, 80, 100, 250), prob = c(11, 1, 1, 29, 12, 1, 41, 4, 4, 1, 4, 1, 1))
```

2.2 Applying the Model

The model may then be evaluated straightforwardly:

```
> r <- mcdata(4.7e-14, type = "0")
> x1V <- modGrowth(d1V, mT1V, sdT1V, Lm0V, murefLmV, TminLmV, FF0V, murefFFV,
+     TminFFV, NmaxV)
> x2V <- modGrowth(d2V, mT2V, sdT2V, x1V$xLm, murefLmV, TminLmV, x1V$xFF, murefFFV,
```

[3] Γ is the Gamma distribution parameterized as $\Gamma(shape, scale)$. The Exponential(x) ditribution is the exponential distribution with mean x.

[4] See the code for a way to model this shelf life using truncated distributions.

```
+     TminFFV, NmaxV)
> x3V <- modGrowth(d3V, mT3V, sdT3V, x2V$xLm, murefLmV, TminLmV, x2V$xFF, murefFFV,
+     TminFFV, NmaxV)
> contaV <- 10^x3V$xLm
> expoV <- consoV * contaV
> riskV <- 1 - exp(-r * expoV)
> Lm1 <- mc(Lm0V, FF0V, NmaxV, murefLmV, TminLmV, murefFFV, TminFFV, d1V, mT1V,
+     sdT1V, d2V, mT2V, sdT2V, d3V, mT3V, sdT3V, consoV, r, contaV, expoV, riskV)
> Lm1
```

	node	mode	nsv	nsu	nva	variate	min	mean	median	max	Nas	type	outm
1	Lm0V	numeric	10001	1	1	1	-2.00e+00	-9.30e-01	-9.88e-01	1.76e+00	0	V	each
2	FF0V	numeric	10001	1	1	1	-1.28e+00	2.78e+00	2.78e+00	6.85e+00	0	V	each
3	NmaxV	numeric	10001	1	1	1	3.97e+00	7.26e+00	7.27e+00	1.06e+01	0	V	each
4	murefLmV	numeric	10001	1	1	1	2.85e+00	6.24e+00	6.25e+00	9.25e+00	0	V	each
5	TminLmV	numeric	10001	1	1	1	-1.01e+01	-2.83e+00	-2.85e+00	3.69e+00	0	V	each
6	murefFFV	numeric	10001	1	1	1	1.31e-02	4.19e+00	4.17e+00	1.13e+01	0	V	each
7	TminFFV	numeric	10001	1	1	1	-3.51e+01	-4.52e+00	-4.46e+00	2.66e+01	0	V	each
8	d1V	numeric	10001	1	1	1	5.36e-05	1.10e+00	7.69e-01	9.69e+00	0	V	each
9	mT1V	numeric	10001	1	1	1	-2.98e+00	3.20e+00	3.15e+00	1.14e+01	0	V	each
10	sdT1V	numeric	10001	1	1	1	3.37e-02	2.08e+00	1.96e+00	6.57e+00	0	V	each
11	d2V	numeric	10001	1	1	1	1.70e-03	4.69e+00	3.29e+00	2.67e+01	0	V	each
12	mT2V	numeric	10001	1	1	1	-2.53e+00	5.53e+00	5.50e+00	1.35e+01	0	V	each
13	sdT2V	numeric	10001	1	1	1	1.60e-03	9.66e-01	8.63e-01	4.76e+00	0	V	each
14	d3V	numeric	10001	1	1	1	3.84e-04	4.16e+00	2.95e+00	2.22e+01	0	V	each
15	mT3V	numeric	10001	1	1	1	-2.98e+00	8.24e+00	8.21e+00	2.26e+01	0	V	each
16	sdT3V	numeric	10001	1	1	1	1.31e-06	1.91e+00	1.41e+00	1.16e+01	0	V	each
17	consoV	numeric	10001	1	1	1	1.00e+01	3.55e+01	4.00e+01	2.50e+02	0	V	each
18	r	numeric	1	1	1	1	4.70e-14	4.70e-14	4.70e-14	4.70e-14	0	0	each
19	contaV	numeric	10001	1	1	1	1.16e-02	4.24e+06	2.22e+01	5.04e+09	0	V	each
20	expoV	numeric	10001	1	1	1	1.70e-01	1.24e+08	6.84e+02	1.01e+11	0	V	each
21	riskV	numeric	10001	1	1	1	7.99e-15	5.81e-06	3.21e-11	4.73e-03	0	V	each

```
> sLm1 <- mc(contaV = Lm1$contaV, expoV = Lm1$expoV, riskV = Lm1$riskV)
> summary(sLm1, probs = c(0, 0.5, 0.75, 0.95, 1))
```

```
contaV :
        mean      sd    Min  50% 75%     95%      Max   nsv Na's
NoUnc 4235073 7.7e+07 0.0116 22.2 875 2120394 5.04e+09 10001    0

expoV :
         mean       sd  Min 50%   75%      95%      Max   nsv Na's
NoUnc 1.24e+08 1.89e+09 0.17 684 27774 71813973 1.01e+11 10001    0

riskV :
         mean       sd      Min      50%      75%      95%     Max   nsv Na's
NoUnc 5.81e-06 8.89e-05 7.99e-15 3.21e-11 1.31e-09 3.38e-06 0.00473 10001    0
```

`Lm1` is a `mc` object that contains all the parameters and outputs. We extract some of these outputs in `sLm1` to provide a short summary.

2.3 Final Estimate

If 6.5% of cold-smoked salmon package are contaminated, if 49,090,000 Frenchs are part of the "non susceptible" population and if, on average, those people consume some smoked salmon 6.4 times per year, the expected number

of cases of listeriosis from consumption of cold smoked salmon in this population is estimated through:

```
> meanRisk <- mcapply(riskV, "var", mean)
> expectedN <- round(0.065 * unmc(meanRisk) * 6.4 * 49090000)
> expectedN
```

```
[1] 119
```

3 Including (a Part of the) Uncertainty

We eventually include both variability and uncertainty in the model. For this example, we will only consider the uncertainty linked to the initial contamination, the growth parameters and the prevalence.

3.1 Specifying Uncertainty

3.1.1 Initial Contamination

The uncertainty surrounding the initial contamination levels of the *L. monocytogenes* will be modeled using a bootstrap procedure, obtained straightforwardly with the help of the `fitdistrplus` package and its `bootdistcens` function. Before this, we define the number of iterations needed in the uncertainty dimension.

```
> ndunc(101)
```

```
[1] 101
```

```
> bootLm0 <- bootdistcens(fit, niter = ndunc())
> MLm0 <- mcdata(bootLm0$est$mean, type = "U")
> SLm0 <- mcdata(bootLm0$est$sd, type = "U")
> Lm0VU <- mcstoc(rnorm, type = "VU", mean = MLm0, sd = SLm0, rtrunc = TRUE, linf = -2)
```

In order to consider uncertainty for the food flora initial contamination, we have, from [1], a set of uncertain hyperparameters, M_{N0ff} and σ_{N0ff}, that are used as parameters for the uncertain *and* variable parameter N_{0ff}:

$$\begin{aligned} N_{0ff} &\sim N(M_{N0ff}, \sigma_{N0ff}) \\ M_{N0ff} &\sim N(2.78, 0.265) \\ \ln(\sigma_{N0ff}) &\sim N(0.114, 0.172) \end{aligned}$$

This hierarchical simulation is written with `mc2d`:

```
> MLm0FF <- mcstoc(rnorm, type = "U", mean = 2.78, sd = 0.265)
> SLm0FF <- mcstoc(rlnorm, type = "U", meanlog = 0.114, sdlog = 0.172)
> FF0VU <- mcstoc(rnorm, type = "VU", mean = MLm0FF, sd = SLm0FF)
```

3.1.2 Growth Parameters

The uncertainty around $\mu_{ref,Lm}$, $T_{min,Lm}$, $\mu_{ref,ff}$, $T_{min,ff}$ and N_{max} are modeled similarly through the specification of hyperparameters [1][5]:

$$\begin{aligned}
\mu_{ref,Lm} &\sim N(M_{\mu ref,Lm}, \sigma_{\mu ref,Lm}) \\
M_{\mu ref,Lm} &\sim \Gamma(shape : 69.7, scale : 0.0896) \\
\ln(\sigma_{\mu ref,Lm}) &\sim N(1.03, 0.191)
\end{aligned}$$

$$\begin{aligned}
T_{min,Lm} &\sim N(M_{Tmin,Lm}, \sigma_{Tmin,Lm}) \\
M_{Tmin,Lm} &\sim N(-2.86, 0.459) \\
\ln(\sigma_{Tmin,Lm}) &\sim N(0.638, 0.208)
\end{aligned}$$

$$\begin{aligned}
\mu_{ref,ff} &\sim N(M_{\mu ref,ff}, \sigma_{\mu ref,ff}) \\
M_{\mu ref,ff} &\sim \Gamma(shape : 32.5, scale : 0.127) \\
\ln(\sigma_{\mu ref,ff}) &\sim N(-0.656, 0.221)
\end{aligned}$$

$$\begin{aligned}
T_{min,ff} &\sim N(M_{Tmin,ff}, \sigma_{Tmin,ff}) \\
M_{Tmin,ff} &\sim N(-4.52, 1.23) \\
\ln(\sigma_{Tmin,ff}) &\sim N(2.00, 0.257)
\end{aligned}$$

$$\begin{aligned}
N_{max} &\sim N(M_{Nmax}, \sigma_{Nmax}) \\
M_{Nmax} &\sim N(7.27, 0.276) \\
\ln(\sigma_{Nmax}) &\sim N(-0.172, 0.218)
\end{aligned}$$

with $\mu_{ref} > 0$ and $T_{min} < 25$. We simply translated the preceeding distributions:

```
> MmurefLm <- mcstoc(rgamma, type = "U", shape = 69.7, scale = 0.0896)
> SmurefLm <- mcstoc(rlnorm, type = "U", meanlog = 1.03, sdlog = 0.191)
> murefLmVU <- mcstoc(rnorm, type = "VU", mean = MmurefLm, sd = SmurefLm, rtrunc = TRUE,
+     linf = 0)
> MTminLm <- mcstoc(rnorm, type = "U", mean = -2.86, sd = 0.459)
> STminLm <- mcstoc(rlnorm, type = "U", meanlog = 0.638, sdlog = 0.208)
> TminLmVU <- mcstoc(rnorm, type = "VU", mean = MTminLm, sd = STminLm, rtrunc = TRUE,
+     lsup = 25)
> MmurefFF <- mcstoc(rgamma, type = "U", shape = 32.5, scale = 0.127)
> SmurefFF <- mcstoc(rlnorm, type = "U", meanlog = -0.656, sdlog = 0.221)
> murefFFVU <- mcstoc(rnorm, type = "VU", mean = MmurefFF, sd = SmurefFF, rtrunc = TRUE,
+     linf = 0)
> MTminFF <- mcstoc(rnorm, type = "U", mean = -4.52, sd = 1.23)
> STminFF <- mcstoc(rlnorm, type = "U", meanlog = 2, sdlog = 0.257)
> TminFFVU <- mcstoc(rnorm, type = "VU", mean = MTminFF, sd = STminFF, rtrunc = TRUE,
+     lsup = 25)
> MNmax <- mcstoc(rnorm, type = "U", mean = 7.27, sd = 0.276)
> SNmax <- mcstoc(rlnorm, type = "U", meanlog = -0.172, sdlog = 0.218)
> NmaxVU <- mcstoc(rnorm, type = "VU", mean = MNmax, sd = SNmax)
```

[5]Note that there was a typo in [1] that lead to an error in [3]: the standard-error for $\ln(\sigma_{\mu ref,Lm})$ is 1.03 and not -1.03 as written in [1]. We will use here the correct value.

3.1.3 Prevalence

The prevalence level of contaminated cold-smoked salmon packages (6.5%) was estimated from 41 positive packages out of 626 tested [3]. We assume a sensitivity and a specificity of the method of 100%. We model the data uncertainty around the true prevalence of contaminated package using a bayesian reasonning, with a Beta(1, 1) distribution as a prior. The number of expected cases may be estimated using:

```
> prevU <- mcstoc(rbeta, type = "U", shape1 = 41 + 1, shape2 = 626 - 41 + 1)
```

3.2 Applying the Model

Applying the model is just a copy-paste from the previous version (+ we change the name of the parameters).

```
> x1VU <- modGrowth(d1V, mT1V, sdT1V, Lm0VU, murefLmVU, TminLmVU, FF0VU, murefFFVU,
+     TminFFVU, NmaxVU)
> x2VU <- modGrowth(d2V, mT2V, sdT2V, x1VU$xLm, murefLmVU, TminLmVU, x1VU$xFF,
+     murefFFVU, TminFFVU, NmaxVU)
> x3VU <- modGrowth(d3V, mT3V, sdT3V, x2VU$xLm, murefLmVU, TminLmVU, x2VU$xFF,
+     murefFFVU, TminFFVU, NmaxVU)
> contaVU <- 10^x3VU$xLm
> expoVU <- consoV * contaVU
> riskVU <- 1 - exp(-r * expoVU)
> Lm2 <- mc(Lm0VU, FF0VU, NmaxVU, murefLmVU, TminLmVU, murefFFVU, TminFFVU, d1V,
+     mT1V, sdT1V, d2V, mT2V, sdT2V, d3V, mT3V, sdT3V, consoV, r, contaVU, expoVU,
+     riskVU)
> Lm2
```

	node	mode	nsv	nsu	nva	variate	min	mean	median	max	Nas	type	outm
1	Lm0VU	numeric	10001	101	1	1	-2.00e+00	-9.37e-01	-9.93e-01	3.68e+00	0	VU	each
2	FF0VU	numeric	10001	101	1	1	-4.82e+00	2.76e+00	2.76e+00	9.58e+00	0	VU	each
3	NmaxVU	numeric	10001	101	1	1	2.11e+00	7.28e+00	7.28e+00	1.27e+01	0	VU	each
4	murefLmVU	numeric	10001	101	1	1	1.00e-04	6.45e+00	6.36e+00	2.43e+01	0	VU	each
5	TminLmVU	numeric	10001	101	1	1	-1.44e+01	-2.83e+00	-2.84e+00	8.70e+00	0	VU	each
6	murefFFVU	numeric	10001	101	1	1	4.81e-03	4.21e+00	4.21e+00	8.24e+00	0	VU	each
7	TminFFVU	numeric	10001	101	1	1	-5.90e+01	-4.39e+00	-4.35e+00	2.50e+01	0	VU	each
8	d1V	numeric	10001	1	1	1	5.36e-05	1.10e+00	7.69e-01	9.69e+00	0	V	each
9	mT1V	numeric	10001	1	1	1	-2.98e+00	3.20e+00	3.15e+00	1.14e+01	0	V	each
10	sdT1V	numeric	10001	1	1	1	3.37e-02	2.08e+00	1.96e+00	6.57e+00	0	V	each
11	d2V	numeric	10001	1	1	1	1.70e-03	4.69e+00	3.29e+00	2.67e+01	0	V	each
12	mT2V	numeric	10001	1	1	1	-2.53e+00	5.53e+00	5.50e+00	1.35e+01	0	V	each
13	sdT2V	numeric	10001	1	1	1	1.60e-03	9.66e-01	8.63e-01	4.76e+00	0	V	each
14	d3V	numeric	10001	1	1	1	3.84e-04	4.16e+00	2.95e+00	2.22e+01	0	V	each
15	mT3V	numeric	10001	1	1	1	-2.98e+00	8.24e+00	8.21e+00	2.26e+01	0	V	each
16	sdT3V	numeric	10001	1	1	1	1.31e-06	1.91e+00	1.41e+00	1.16e+01	0	V	each
17	consoV	numeric	10001	1	1	1	1.00e+01	3.55e+01	4.00e+01	2.50e+02	0	V	each
18	r	numeric	1	1	1	1	4.70e-14	4.70e-14	4.70e-14	4.70e-14	0	0	each
19	contaVU	numeric	10001	101	1	1	1.01e-02	1.27e+07	1.71e+01	5.74e+11	0	VU	each
20	expoVU	numeric	10001	101	1	1	1.01e-01	4.65e+08	5.23e+02	2.87e+13	0	VU	each
21	riskVU	numeric	10001	101	1	1	4.77e-15	2.08e-05	2.46e-11	7.41e-01	0	VU	each

```
> sLm2 <- mc(contaVU = Lm2$contaVU, expoVU = Lm2$expoVU, riskVU = Lm2$riskVU)
> summary(sLm2, probs = c(0, 0.5, 0.75, 0.95, 1))

contaVU :
           mean       sd    Min   50%   75%      95%      Max   nsv Na's
```

```
median  7747666 1.12e+08 0.0112 15.47   904  4502760 7.23e+09 10001    0
mean   12664880 3.23e+08 0.0116 24.25  2796  9383534 2.58e+10 10001    0
2.5%    1138646 1.23e+07 0.0101  6.19   201   393180 4.77e+08 10001    0
97.5%  49254487 1.66e+09 0.0142 97.54 19262 38670270 1.54e+11 10001    0

expoVU :
          mean       sd   Min  50%    75%      95%      Max   nsv Na's
median 2.76e+08 4.96e+09 0.149  485  27767 1.41e+08 3.33e+11 10001    0
mean   4.65e+08 1.32e+10 0.160  730  86312 2.92e+08 1.08e+12 10001    0
2.5%   4.26e+07 5.50e+08 0.105  189   6310 1.25e+07 2.33e+10 10001    0
97.5%  1.99e+09 6.77e+10 0.257 2864 593488 1.17e+09 6.20e+12 10001    0

riskVU :
          mean       sd      Min      50%      75%      95%     Max   nsv Na's
median 1.29e-05 2.32e-04 6.99e-15 2.28e-11 1.31e-09 6.65e-06 0.01554 10001    0
mean   2.08e-05 5.35e-04 7.50e-15 3.43e-11 4.06e-09 1.37e-05 0.04225 10001    0
2.5%   2.00e-06 2.58e-05 4.94e-15 8.89e-12 2.97e-10 5.88e-07 0.00109 10001    0
97.5%  8.96e-05 2.81e-03 1.21e-14 1.35e-10 2.79e-08 5.49e-05 0.25263 10001    0
```

The summary provides the estimate of the mean, the standard deviation, the minimum, the median ... and a 95% credible interval. The estimate is the median of the 101 values obtained in the uncertainty dimension. The credible interval lays between the 2.5^{th} and the 97.5^{th} percentiles obtained in the uncertainty dimension.

3.3 Final Estimate

The uncertainty around the number of expected cases is estimated using:

```
> meanRiskU <- mcapply(riskVU, "var", mean)
> expectedNU <- round(prevU * meanRiskU * 6.4 * 49090000)
> summary(expectedNU)

node :
       NoVar
median   271
mean     434
2.5%      41
97.5%   1987
```

This is an estimate of the uncertainty around the number of cases linked to the uncertainty around the initial contamination, the bacterial growth parameter and the sampling uncertainty for positive packages. A lot of other uncertainties exist but are not considered here, notably the uncertainty around the dose-response model and parameters. See [3, 2] for a complete analysis. The study of the model through a Tornado chart in the variability dimension leads to the Figure 1. It suggests a big impact of the growth rate of *L. monocytogenes*, of the storage duration during the consumer step, and of the initial level of *L. monocytogenes*. The Tornado chart in the uncertainty dimension leads to the Figure 2 and suggests the impact of the uncertainty around N_{max} on the mean risk, and thus the expected number of cases.

```
> torn <- tornado(Lm2)
> torn

Spearman's rho statistic
Output:  riskVU
$riskVU
       Lm0VU   FF0VU NmaxVU murefLmVU TminLmVU murefFFVU TminFFVU    d1V   mT1V    sdT1V   d2V
median 0.302 -0.0827 0.0712     0.464   -0.236  -0.02911   0.1194 0.0462 0.0336  0.00420 0.282
```

```
mean   0.297 -0.0889 0.0753     0.456   -0.237  -0.03067   0.1267 0.0454 0.0332  0.00344 0.282
2.5%   0.202 -0.1568 0.0298     0.346   -0.341  -0.05707   0.0458 0.0257 0.0196 -0.01158 0.230
97.5%  0.379 -0.0341 0.1382     0.547   -0.158  -0.00699   0.2254 0.0622 0.0485  0.01786 0.334
        mT2V    sdT2V   d3V  mT3V  sdT3V consoV contaVU expoVU
median 0.156  0.00744 0.414 0.260 0.0289  0.125   0.991      1
mean   0.157  0.00716 0.416 0.259 0.0293  0.125   0.990      1
2.5%   0.131 -0.00785 0.337 0.219 0.0162  0.105   0.986      1
97.5%  0.185  0.02028 0.490 0.309 0.0417  0.149   0.994      1
```

```
> tornunc <- tornadounc.mc(Lm2, quant = NULL)
> tornunc

Tornado on uncertainty
Spearman's rho statistic
Output:  riskVU
$riskVU
            mean LmOVU sd LmOVU mean FFOVU sd FFOVU mean NmaxVU sd NmaxVU mean murefLmVU
mean riskVU      0.145   0.0356    -0.0855   -0.168       0.652     0.724          0.415
sd riskVU        0.137  -0.0157    -0.0167   -0.180       0.500     0.804          0.287
            sd murefLmVU mean TminLmVU sd TminLmVU mean murefFFVU sd murefFFVU mean TminFFVU
mean riskVU        0.282        0.0188     -0.0633        -0.1837       0.0567         0.153
sd riskVU          0.167        0.0762     -0.1426        -0.0859       0.0288         0.126
            sd TminFFVU mean contaVU sd contaVU mean expoVU sd expoVU
mean riskVU    -0.00535        0.993      0.930       1.000     0.934
sd riskVU      -0.00935        0.928      0.969       0.937     1.000
```

`quant=NULL` request an analysis only on the mean risk, and not on some qunatiles.

```
> plot(torn)
> plot(tornunc, stat = "mean risk")
```

As a conclusion, this example illustrates how predictive growth models may be implemented within `mc2d`...

References

[1] M.-L. Delignette-Muller, M.˜Cornu, R.˜Pouillot, and J.-B. Denis. Use of bayesian modelling in risk assessment: application to growth of *Listeria monocytogenes* and food flora in cold-smoked salmon. *International Journal of Food Microbiology*, 106(2):195–208, 2006.

[2] R.˜Pouillot, V.˜Goulet, M.˜L. Delignette-Muller, A.˜Mahe, and M.˜Cornu. Quantitative risk assessment of listeria monocytogenes in french cold-salmon : Ii. risk characterization. *Risk Analysis*, 29(6):806–819, 2009.

[3] R.˜Pouillot, N.˜Miconnet, A.-L. Afchain, M.-L. Delignette-Muller, A.˜Beaufort, L.˜Rosso, J.-B. Denis, and M.˜Cornu. Quantitative risk assessment of listeria monocytogenes in french cold-salmon : I. quantitative exposure assessment. *Risk Analysis*, 27(3):683–700, 2007.

Figure 1: Tornado chart for the *L. monocytogenes* example (Variability).

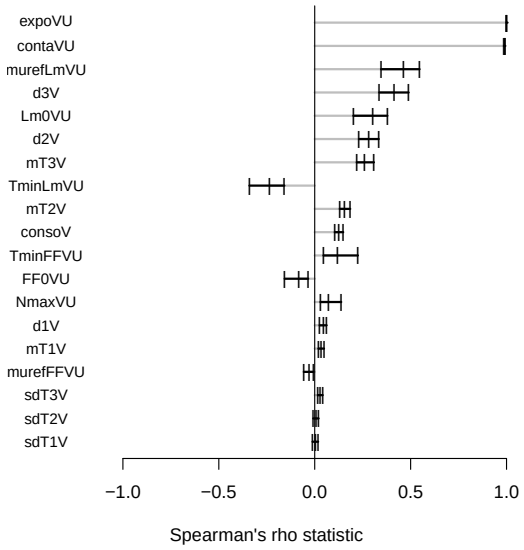

Figure 2: Tornado chart for the *L. monocytogenes* example (Uncertainty).