

# Applications of finite mixtures of regression models

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## Abstract

Package **flexmix** provides functionality for fitting finite mixtures of regression models. The available model class includes generalized linear models with varying and fixed effects for the component specific models and multinomial logit models for the concomitant variable models. This model class includes random intercept models where the random part is modelled by a finite mixture instead of a-priori selecting a suitable distribution.

The application of the package is illustrated on various datasets which have been previously used in the literature to fit finite mixtures of Gaussian, binomial or Poisson regression models. The R commands are given to fit the proposed models and additional insights are gained by visualizing the data and the fitted models as well as by fitting slightly modified models.

*Keywords:* R, finite mixture models, generalized linear models, concomitant variables.

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## 1. Introduction

Package **flexmix** provides infrastructure for flexible fitting of finite mixtures models. The design principles of the package allow easy extensibility and rapid prototyping. In addition, the main focus of the available functionality is on fitting finite mixtures of regression models, as other packages in R exist which have specialized functionality for model-based clustering, such as e.g. **mclust** (Fraley and Raftery 2002) for finite mixtures of Gaussian distributions.

Leisch (2004) gives a general introduction into the package outlining the main implementational principles and illustrating the use of the package. The paper is also contained as a vignette in the package. An example for fitting mixtures of Gaussian regression models is given in Grün and Leisch (2006). This paper focuses on examples of finite mixtures of binomial logit and Poisson regression models. Several datasets which have been previously used in the literature to demonstrate the use of finite mixtures of regression models have been selected to illustrate the application of the package.

The model class covered are finite mixtures of generalized linear model with focus on binomial logit and Poisson regressions. The regression coefficients as well as the dispersion parameters of the component specific models are assumed to vary for all components, vary between groups of components, i.e. to have a nesting, or to be fixed over all components. In addition it is possible to specify concomitant variable models in order to be able to characterize the components. Random intercept models are a special case of finite mixtures with varying and fixed effects as fixed effects are assumed for the coefficients of all covariates and varying effects for the intercept. These models are often used to capture overdispersion in the data which can occur for example if important covariates are omitted in the regression. It is then assumed

that the influence of these covariates can be captured by allowing a random distribution for the intercept.

This illustration does not only show how the package **flexmix** can be used for fitting finite mixtures of regression models but also indicates the advantages of using an extension package of an environment for statistical computing and graphics instead of a stand-alone package as available visualization techniques can be used for inspecting the data and the fitted models. In addition users already familiar with R and its formula interface should find the model specification and a lot of commands for exploring the fitted model intuitive.

## 2. Model specification

Finite mixtures of Gaussian regressions with concomitant variable models are given by:

$$H(y | \mathbf{x}, \mathbf{w}, \Theta) = \sum_{s=1}^S \pi_s(\mathbf{w}, \alpha) N(y | \mu_s(\mathbf{x}), \sigma_s^2),$$

where  $N(\cdot | \mu_s(\mathbf{x}), \sigma_s^2)$  is the Gaussian distribution with mean  $\mu_s(\mathbf{x}) = \mathbf{x}'\boldsymbol{\beta}^s$  and variance  $\sigma_s^2$ .  $\Theta$  denotes the vector of all parameters of the mixture distribution and the dependent variables are  $y$ , the independent  $\mathbf{x}$  and the concomitant  $\mathbf{w}$ .

Finite mixtures of binomial regressions with concomitant variable models are given by:

$$H(y | T, \mathbf{x}, \mathbf{w}, \Theta) = \sum_{s=1}^S \pi_s(\mathbf{w}, \alpha) \text{Bi}(y | T, \theta_s(\mathbf{x})),$$

where  $\text{Bi}(\cdot | T, \theta_s(\mathbf{x}))$  is the binomial distribution with number of trials equal to  $T$  and success probability  $\theta_s(\mathbf{x}) \in (0, 1)$  given by  $\text{logit}(\theta_s(\mathbf{x})) = \mathbf{x}'\boldsymbol{\beta}^s$ .

Finite mixtures of Poisson regressions are given by:

$$H(y | \mathbf{x}, \mathbf{w}, \Theta) = \sum_{s=1}^S \pi_s(\mathbf{w}, \alpha) \text{Poi}(y | \lambda_s(\mathbf{x})),$$

where  $\text{Poi}(\cdot | \lambda_s(\mathbf{x}))$  denotes the Poisson distribution and  $\log(\lambda_s(\mathbf{x})) = \mathbf{x}'\boldsymbol{\beta}^s$ .

For all these mixture distributions the coefficients are split into three different groups depending on if fixed, nested or varying effects are specified:

$$\boldsymbol{\beta}^s = (\boldsymbol{\beta}_1, \boldsymbol{\beta}_2^{c(s)}, \boldsymbol{\beta}_3^s)$$

where the first group represents the fixed, the second the nested and the third the varying effects. For the nested effects a partition  $\mathcal{C} = \{c_s | s = 1, \dots, S\}$  of the  $S$  components is determined where  $c_s = \{s^* = 1, \dots, S | c(s^*) = c(s)\}$ . A similar splitting is possible for the variance of mixtures of Gaussian regression models.

The function for maximum likelihood (ML) estimation with the Expectation-Maximization (EM) algorithm is **flexmix()** which is described in detail in [Leisch \(2004\)](#). It takes as arguments a specification of the component specific model and of the concomitant variable model. The component specific model with varying, nested and fixed effects can be specified with the M-step driver **FLXMRglmfix()** which has arguments **formula** for the varying, **nested**

for the nested and **fixed** for the fixed effects. **formula** and **fixed** take an argument of class "formula", whereas **nested** expects an object of class "FLXnested" or a named list specifying the nested structure with a component **k** which is a vector of the number of components in each group of the partition and a component **formula** which is a vector of formulas for each group of the partition. In addition there is an argument **family** which has to be one of **gaussian**, **binomial**, **poisson** or **Gamma** and determines the component specific distribution function as well as an **offset** argument. The argument **varFix** can be used to determine the structure of the dispersion parameters.

If only varying effects are specified the M-step driver **FLXMRglm()** can be used which only has an argument **formula** for the varying effects and also a **family** and an **offset** argument. This driver has the advantage that in the M-step the weighted ML estimation is made separately for each component which signifies that smaller model matrices are used. If a mixture model with a lot of components  $S$  is fitted to a large data set with  $N$  observations and the model matrix used in the M-step of **FLXMRglm()** has  $N$  rows and  $K$  columns, the model matrix used in the M-step of **FLXMRglmfix()** has  $SN$  rows and up to  $SK$  columns.

In general the concomitant variable model is assumed to be a multinomial logit model, i.e. :

$$\pi_s(\mathbf{w}, \boldsymbol{\alpha}) = \frac{e^{\mathbf{w}'\boldsymbol{\alpha}_s}}{\sum_{u=1}^S e^{\mathbf{w}'\boldsymbol{\alpha}_u}} \quad \forall s,$$

with  $\boldsymbol{\alpha} = (\boldsymbol{\alpha}'_s)_{s=1,\dots,S}$  and  $\boldsymbol{\alpha}_1 \equiv \mathbf{0}$ . This model can be fitted in **flexmix** with **FLXPmultinom()** which takes as argument **formula** the formula specification of the multinomial logit part. For fitting the function **nnet()** is used from package **MASS** (Venables and Ripley 2002) with the independent variables specified by the formula argument and the dependent variables are given by the a-posteriori probability estimates.

### 3. Using package flexmix

In the following datasets from different areas such as medicine, biology and economics are used. There are three subsections: for finite mixtures of Gaussian regressions, for finite mixtures of binomial regression models and for finite mixtures of Poisson regression models.

#### 3.1. Finite mixtures of Gaussian regressions

This artificial dataset with 200 observations is given in Grün and Leisch (2006). The data is generated from a mixture of Gaussian regression models with three components. There is an intercept with varying effects, an independent variable  $x_1$ , which is a numeric variable, with fixed effects and another independent variable  $x_2$ , which is a categorical variable with two levels, with nested effects. The prior probabilities depend on a concomitant variable  $w$ , which is also a categorical variable with two levels. Fixed effects are also assumed for the variance. The data is illustrated in Figure 1 and the true underlying model is given by:

$$H(y | (x_1, x_2), w, \boldsymbol{\Theta}) = \sum_{s=1}^S \pi_s(w, \boldsymbol{\alpha}) N(y | \mu_s, \sigma^2),$$

with  $\boldsymbol{\beta}^s = (\beta_{\text{Intercept}}^s, \beta_{x_1}^{c(s)}, \beta_{x_2})$ . The nesting signifies that  $c(1) = c(2)$  and  $\beta_{x_1}^{c(3)} = 0$ .

The mixture model is fitted by first loading the package and the dataset and then specifying the component specific model. In a first step a component specific model with only varying effects is specified. Then the fitting function `flexmix()` is called repeatedly using `stepFlexmix()`. Finally, we order the components such that they are in ascending order with respect to the coefficients of the variable `x1`.

```
R> set.seed(2807)
R> library("flexmix")
R> data("NregFix", package = "flexmix")
R> Model <- FLXMRglm(~ x2 + x1)
R> fittedModel <- stepFlexmix(y ~ 1, model = Model, nrep = 3, k = 3,
+   data = NregFix, concomitant = FLXPmultinom(~ w))
```

```
3 : * * *
```

```
R> fittedModel <- relabel(fittedModel, "model", "x1")
R> summary(refit(fittedModel))
```

```
$Comp.1
```

|             | Estimate | Std. Error | z value | Pr(> z )   |
|-------------|----------|------------|---------|------------|
| (Intercept) | 2.87046  | 0.13515    | 21.2394 | <2e-16 *** |
| x21         | 5.10209  | 0.20849    | 24.4716 | <2e-16 *** |
| x1          | 0.13348  | 0.10633    | 1.2553  | 0.2094     |

```
---
```

```
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
$Comp.2
```

|             | Estimate | Std. Error | z value | Pr(> z )      |
|-------------|----------|------------|---------|---------------|
| (Intercept) | 0.99358  | 0.18130    | 5.4803  | 4.245e-08 *** |
| x21         | 5.28836  | 0.25232    | 20.9590 | < 2.2e-16 *** |
| x1          | 9.89243  | 0.11778    | 83.9892 | < 2.2e-16 *** |

```
---
```

```
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
$Comp.3
```

|             | Estimate | Std. Error | z value | Pr(> z )      |
|-------------|----------|------------|---------|---------------|
| (Intercept) | -7.64055 | 0.25163    | -30.365 | < 2.2e-16 *** |
| x21         | 4.65090  | 0.38102    | 12.207  | < 2.2e-16 *** |
| x1          | 9.93667  | 0.16444    | 60.429  | < 2.2e-16 *** |

```
---
```

```
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

The estimated coefficients indicate that the components differ for the intercept, but that they are not significantly different for the coefficients of `x2`. For `x1` the coefficient of the first component is not significantly different from zero and the confidence intervals for the other two components overlap. Therefore we fit a modified model, which is equivalent to the true underlying model. The previously fitted model is used for initializing the EM algorithm:

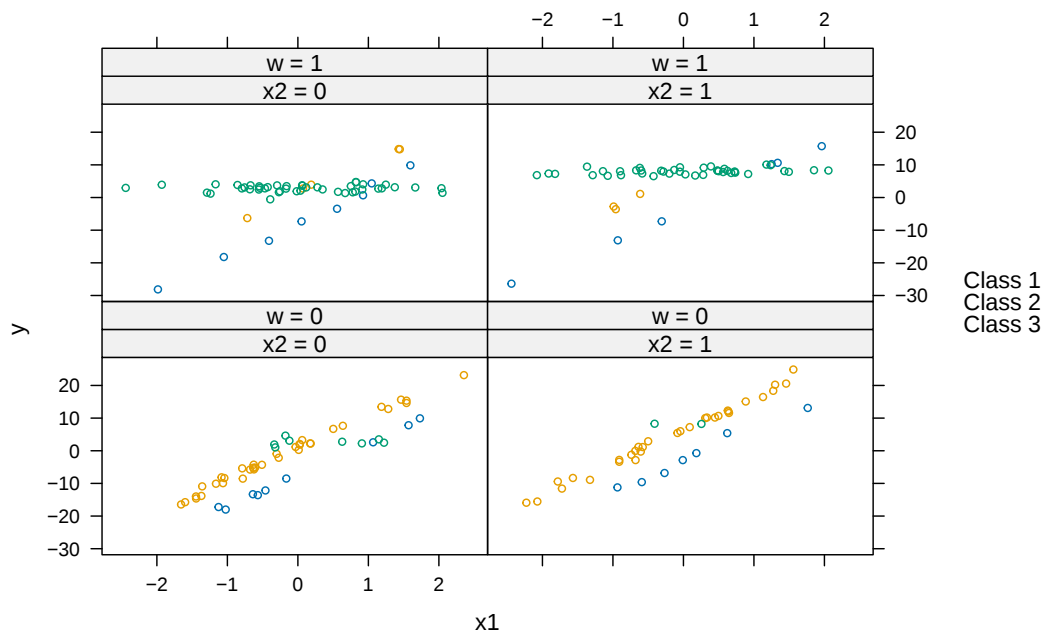


Figure 1: Sample with 200 observations from the artificial example.

```
R> Model2 <- FLXMRglmfix(fixed = ~ x2, nested = list(k = c(1, 2),
+   formula = c(~ 0, ~ x1)), varFix = TRUE)
R> fittedModel2 <- flexmix(y ~ 1, model = Model2,
+   cluster = posterior(fittedModel), data = NregFix,
+   concomitant = FLXPmultinom(~ w))
R> BIC(fittedModel)
```

```
[1] 883.5921
```

```
R> BIC(fittedModel2)
```

```
[1] 856.9122
```

The BIC suggests that the restricted model should be preferred.

```
R> summary(refit(fittedModel2))
```

```
$Comp.1
```

|             | Estimate | Std. Error | z value | Pr(> z )      |
|-------------|----------|------------|---------|---------------|
| x21         | 5.11133  | 0.14801    | 34.533  | < 2.2e-16 *** |
| (Intercept) | 2.85755  | 0.12650    | 22.590  | < 2.2e-16 *** |

```
---
```

```
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```

$Comp.2
      Estimate Std. Error  z value  Pr(>|z|)
x21      5.111327   0.148011  34.5334 < 2.2e-16 ***
x1       9.902341   0.091179 108.6027 < 2.2e-16 ***
(Intercept) 1.072193   0.141877   7.5572 4.119e-14 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

$Comp.3
      Estimate Std. Error  z value  Pr(>|z|)
x21      5.111327   0.148011  34.533 < 2.2e-16 ***
x1       9.902341   0.091179 108.603 < 2.2e-16 ***
(Intercept) -7.848359   0.197759 -39.687 < 2.2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

The coefficients are ordered such that the fixed coefficients are first, the nested varying coefficients second and the varying coefficients last.

### 3.2. Finite mixtures of binomial logit regressions

#### *Beta blockers*

The dataset is analyzed in [Aitkin \(1999a,b\)](#) using a finite mixture of binomial regression models. Furthermore, it is described in [McLachlan and Peel \(2000\)](#) on page 165. The dataset is from a 22-center clinical trial of beta-blockers for reducing mortality after myocardial infarction. A two-level model is assumed to represent the data, where centers are at the upper level and patients at the lower level. The data is illustrated in [Figure 2](#) and the model is given by:

$$H(\text{Deaths} \mid \text{Total}, \text{Treatment}, \text{Center}, \boldsymbol{\Theta}) = \sum_{s=1}^S \pi_s \text{Bi}(\text{Deaths} \mid \text{Total}, \theta_s).$$

First, the center classification is ignored and a binomial logit regression model with treatment as covariate is fitted using `glm`, i.e.  $S = 1$ :

```

R> data("betablocker", package = "flexmix")
R> betaGlm <- glm(cbind(Deaths, Total - Deaths) ~ Treatment,
+   family = "binomial", data = betablocker)
R> betaGlm

```

```

Call:  glm(formula = cbind(Deaths, Total - Deaths) ~ Treatment, family = "binomial",
  data = betablocker)

```

```

Coefficients:
(Intercept)  TreatmentTreated
      -2.1971           -0.2574

```

```
Degrees of Freedom: 43 Total (i.e. Null); 42 Residual
Null Deviance:      333
Residual Deviance: 305.8      AIC: 527.2
```

In the next step the center classification is included by allowing a random effect for the intercept given the centers, i.e. the coefficients  $\beta^s$  are given by  $(\beta_{\text{Intercept}|\text{Center}}^s, \beta_{\text{Treatment}}^s)$ . This signifies that the component membership is fixed for each center. In order to determine the suitable number of components, the mixture is fitted with different numbers of components and the BIC information criterion is used to select an appropriate model. In this case a model with three components is selected. The fitted values for the model with three components are given in Figure 2.

```
R> betaMixFix <- stepFlexmix(cbind(Deaths, Total - Deaths) ~ 1 | Center,
+   model = FLXMRglmfix(family = "binomial", fixed = ~ Treatment),
+   k = 2:4, nrep = 3, data = betablocker)
```

```
2 : * * *
3 : * * *
4 : * * *
```

```
R> betaMixFix
```

Call:

```
stepFlexmix(cbind(Deaths, Total - Deaths) ~ 1 | Center,
  model = FLXMRglmfix(family = "binomial", fixed = ~Treatment),
  data = betablocker, k = 2:4, nrep = 3)
```

|   | iter | converged | k | k0 | logLik    | AIC      | BIC      | ICL      |
|---|------|-----------|---|----|-----------|----------|----------|----------|
| 2 | 12   | TRUE      | 2 | 2  | -181.3308 | 370.6617 | 377.7984 | 380.2114 |
| 3 | 9    | TRUE      | 3 | 3  | -159.3605 | 330.7210 | 341.4262 | 343.3249 |
| 4 | 15   | TRUE      | 4 | 4  | -155.7540 | 327.5080 | 341.7815 | 345.7338 |

In addition the treatment effect can also be included in the random part of the model. As then all coefficients for the covariates and the intercept follow a mixture distribution the component specific model can be specified using `FLXMRglm()`. The coefficients are  $\beta^s = (\beta_{\text{Intercept}|\text{Center}}^s, \beta_{\text{Treatment}|\text{Center}}^s)$ , i.e. it is assumed that the heterogeneity is only between centers and therefore the aggregated data for each center can be used.

```
R> betaMix <- stepFlexmix(cbind(Deaths, Total - Deaths) ~ Treatment | Center,
+   model = FLXMRglm(family = "binomial"), k = 3, nrep = 3,
+   data = betablocker)
```

```
3 : * * *
```

```
R> summary(betaMix)
```

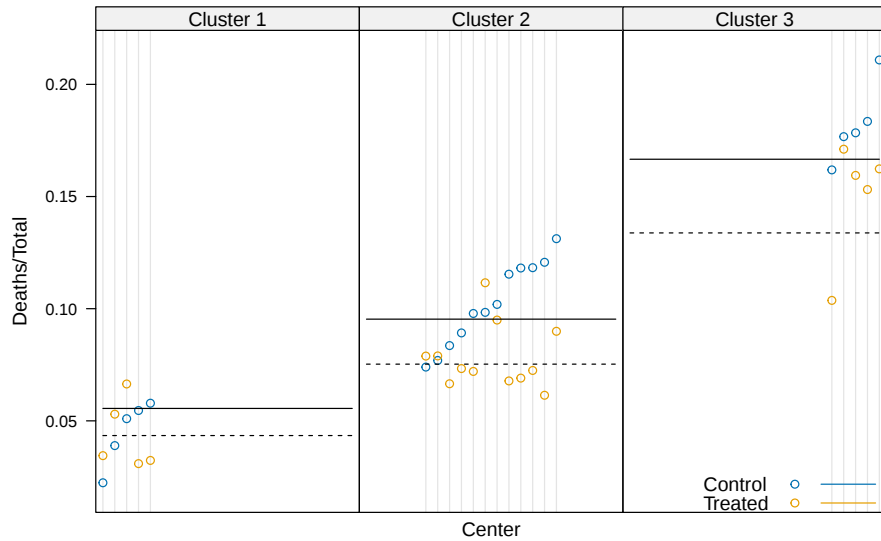


Figure 2: Relative number of deaths for the treatment and the control group for each center in the beta blocker dataset. The centers are sorted by the relative number of deaths in the control group. The lines indicate the fitted values for each component of the 3-component mixture model with random intercept and fixed effect for treatment.

Call:

```
stepFlexmix(cbind(Deaths, Total - Deaths) ~ Treatment |
  Center, model = FLXMRglm(family = "binomial"), data = betablocker,
  k = 3, nrep = 3)
```

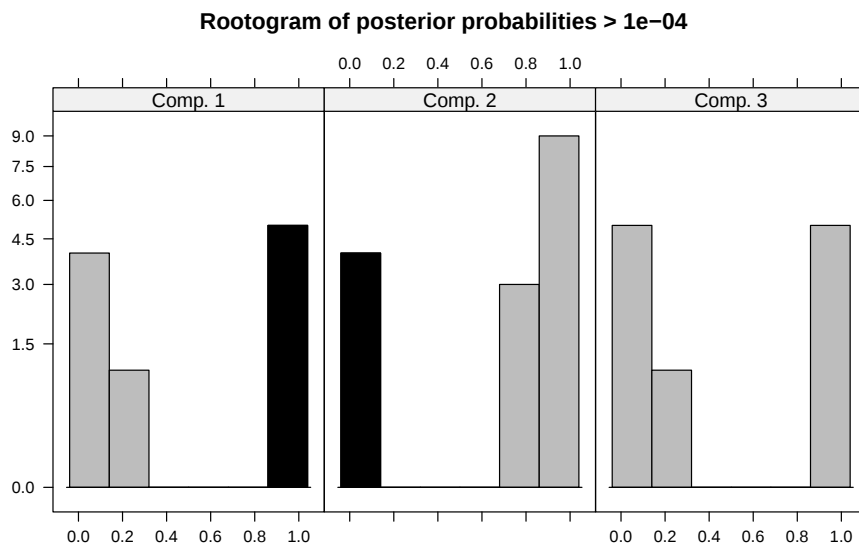
|        | prior | size | post>0 | ratio |
|--------|-------|------|--------|-------|
| Comp.1 | 0.240 | 10   | 20     | 0.500 |
| Comp.2 | 0.249 | 10   | 22     | 0.455 |
| Comp.3 | 0.511 | 24   | 32     | 0.750 |

```
'log Lik.' -158.3095 (df=8)
AIC: 332.619   BIC: 346.8925
```

The full model with a random effect for treatment has a higher BIC and therefore the smaller would be preferred.

The default plot of the returned `flexmix` object is a rootogram of the a-posteriori probabilities where observations with a-posteriori probabilities smaller than `eps` are omitted. With argument `mark` the component is specified to have those observations marked which are assigned to this component based on the maximum a-posteriori probabilities. This indicates which components overlap.

```
R> print(plot(betaMixFix_3, mark = 1, col = "grey", markcol = 1))
```



The default plot of the fitted model indicates that the components are well separated. In addition component 1 has a slight overlap with component 2 but none with component 3.

The fitted parameters of the component specific models can be accessed with:

```
R> parameters(betaMix)
```

|                       | Comp.1      | Comp.2     | Comp.3     |
|-----------------------|-------------|------------|------------|
| coef.(Intercept)      | -2.91633602 | -1.5800104 | -2.2476996 |
| coef.TreatmentTreated | -0.08047852 | -0.3248495 | -0.2630025 |

The cluster assignments using the maximum a-posteriori probabilities are obtained with:

```
R> table(clusters(betaMix))
```

```

 1  2  3
10 10 24

```

The estimated probabilities for each component for the treated patients and those in the control group can be obtained with:

```
R> predict(betaMix,
+   newdata = data.frame(Treatment = c("Control", "Treated")))
```

```

$Comp.1
      [,1]
1 0.05135190
2 0.04756999

```

```

$Comp.2
      [,1]

```

```
1 0.1707940
2 0.1295594
```

```
$Comp.3
      [,1]
1 0.09554808
2 0.07511132
```

or

```
R> fitted(betaMix)[c(1, 23), ]
```

```
      Comp.1   Comp.2   Comp.3
[1,] 0.05135190 0.1707940 0.09554808
[2,] 0.04756999 0.1295594 0.07511132
```

A further analysis of the model is possible with function `refit()` which returns the estimated coefficients together with the standard deviations, z-values and corresponding p-values:

```
R> summary(refit(getModel(betaMixFix, "3")))
```

```
$Comp.1
              Estimate Std. Error  z value  Pr(>|z|)
TreatmentTreated -0.258163   0.049901  -5.1735 2.297e-07 ***
(Intercept)      -2.250160   0.040529 -55.5204 < 2.2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
$Comp.2
              Estimate Std. Error  z value  Pr(>|z|)
TreatmentTreated -0.258163   0.049901  -5.1735 2.297e-07 ***
(Intercept)      -2.833679   0.075079 -37.7428 < 2.2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
$Comp.3
              Estimate Std. Error  z value  Pr(>|z|)
TreatmentTreated -0.258163   0.049901  -5.1735 2.297e-07 ***
(Intercept)      -1.609726   0.055735 -28.8819 < 2.2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

The printed coefficients are ordered to have the fixed effects before the varying effects.

### *Mehta et al. trial*

This dataset is similar to the beta blocker dataset and is also analyzed in [Aitkin \(1999b\)](#). The dataset is visualized in Figure 3. The observation for the control group in center 15 is slightly conspicuous and might classify as an outlier.

The model is given by:

$$H(\text{Response} | \text{Total}, \Theta) = \sum_{s=1}^S \pi_s \text{Bi}(\text{Response} | \text{Total}, \theta_s),$$

with  $\beta^s = (\beta_{\text{Intercept}|\text{Site}}^s, \beta_{\text{Drug}}^s)$ . This model is fitted with:

```
R> data("Mehta", package = "flexmix")
R> mehtaMix <- stepFlexmix(cbind(Response, Total - Response) ~ 1 | Site,
+   model = FLXMRglmfix(family = "binomial", fixed = ~ Drug),
+   control = list(minprior = 0.04), nrep = 3, k = 3, data = Mehta)
```

```
3 : * * *
```

```
R> summary(mehtaMix)
```

Call:

```
stepFlexmix(cbind(Response, Total - Response) ~ 1 | Site,
  model = FLXMRglmfix(family = "binomial", fixed = ~ Drug),
  control = list(minprior = 0.04), data = Mehta, k = 3,
  nrep = 3)
```

|        | prior  | size | post>0 | ratio |
|--------|--------|------|--------|-------|
| Comp.1 | 0.0456 | 2    | 4      | 0.500 |
| Comp.2 | 0.5012 | 22   | 44     | 0.500 |
| Comp.3 | 0.4532 | 20   | 42     | 0.476 |

```
'log Lik.' -66.8056 (df=6)
AIC: 145.6112   BIC: 156.3163
```

One component only contains the observations for center 15 and in order to be able to fit a mixture with such a small component it is necessary to modify the default argument for `minprior` which is 0.05. The fitted values for this model are given separately for each component in Figure 3.

If also a random effect for the coefficient of Drug is fitted, i.e.  $\beta^s = (\beta_{\text{Intercept}|\text{Site}}^s, \beta_{\text{Drug}|\text{Site}}^s)$ , this is estimated by:

```
R> mehtaMix <- stepFlexmix(cbind(Response, Total - Response) ~ Drug | Site,
+   model = FLXMRglm(family = "binomial"), k = 3, data = Mehta, nrep = 3,
+   control = list(minprior = 0.04))
```

```
3 : * * *
```

```
R> summary(mehtaMix)
```

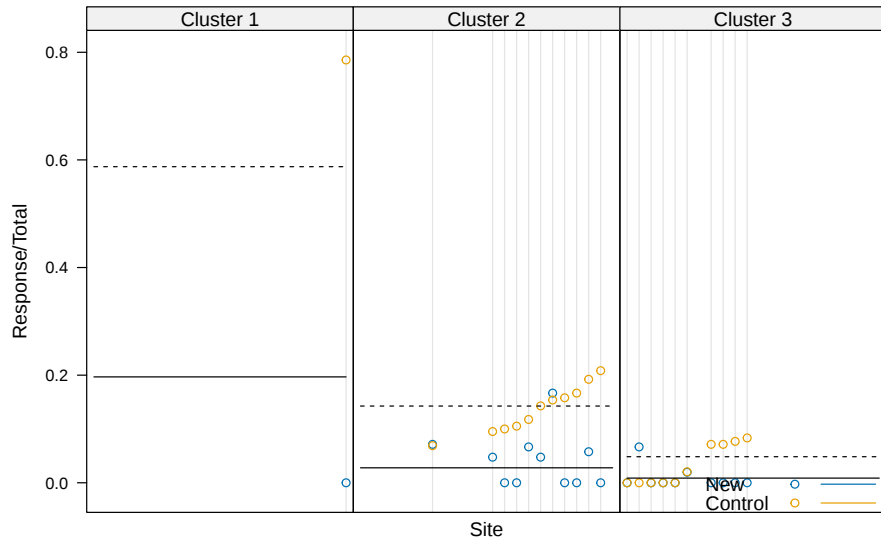


Figure 3: Relative number of responses for the treatment and the control group for each site in the Mehta et al. trial dataset together with the fitted values. The sites are sorted by the relative number of responses in the control group.

Call:

```
stepFlexmix(cbind(Response, Total - Response) ~ Drug |
  Site, model = FLXMRglm(family = "binomial"), data = Mehta,
  control = list(minprior = 0.04), k = 3, nrep = 3)
```

|        | prior  | size | post>0 | ratio |
|--------|--------|------|--------|-------|
| Comp.1 | 0.5084 | 22   | 42     | 0.524 |
| Comp.2 | 0.0455 | 2    | 2      | 1.000 |
| Comp.3 | 0.4462 | 20   | 42     | 0.476 |

```
'log Lik.' -62.02723 (df=8)
AIC: 140.0545 BIC: 154.328
```

The BIC is smaller for the larger model and this indicates that the assumption of an equal drug effect for all centers is not confirmed by the data.

Given Figure 3 a two-component model with fixed treatment is also fitted to the data where site 15 is omitted:

```
R> Mehta.sub <- subset(Mehta, Site != 15)
R> mehtaMix <- stepFlexmix(cbind(Response, Total - Response) ~ 1 | Site,
+   model = FLXMRglmfix(family = "binomial", fixed = ~ Drug),
+   data = Mehta.sub, k = 2, nrep = 3)
```

```
2 : * * *
```

```
R> summary(mehtaMix)
```

Call:

```
stepFlexmix(cbind(Response, Total - Response) ~ 1 | Site,
  model = FLXMRglmfix(family = "binomial", fixed = ~Drug),
  data = Mehta.sub, k = 2, nrep = 3)
```

|        | prior | size | post>0 | ratio |
|--------|-------|------|--------|-------|
| Comp.1 | 0.472 | 20   | 42     | 0.476 |
| Comp.2 | 0.528 | 22   | 42     | 0.524 |

```
'log Lik.' -56.5844 (df=4)
AIC: 121.1688 BIC: 128.1195
```

### *Tribolium*

A finite mixture of binomial regressions is fitted to the *Tribolium* dataset given in Wang and Puterman (1998). The data was collected to investigate whether the adult *Tribolium* species *Castaneum* has developed an evolutionary advantage to recognize and avoid eggs of its own species while foraging, as beetles of the genus *Tribolium* are cannibalistic in the sense that adults eat the eggs of their own species as well as those of closely related species.

The experiment isolated a number of adult beetles of the same species and presented them with a vial of 150 eggs (50 of each type), the eggs being thoroughly mixed to ensure uniformity throughout the vial. The data gives the consumption data for adult *Castaneum* species. It reports the number of *Castaneum*, *Confusum* and *Madens* eggs, respectively, that remain uneaten after two day exposure to the adult beetles. Replicates 1, 2, and 3 correspond to different occasions on which the experiment was conducted. The data is visualized in Figure 4 and the model is given by:

$$H(\text{Remaining} | \text{Total}, \Theta) = \sum_{s=1}^S \pi_s(\text{Replicate}, \alpha) \text{Bi}(\text{Remaining} | \text{Total}, \theta_s),$$

with  $\beta^s = (\beta_{\text{Intercept}}^s, \beta_{\text{Species}}^s)$ . This model is fitted with:

```
R> data("tribolium", package = "flexmix")
R> TribMix <- stepFlexmix(cbind(Remaining, Total - Remaining) ~ 1,
+   k = 2:3, model = FLXMRglmfix(fixed = ~ Species, family = "binomial"),
+   concomitant = FLXPmultinom(~ Replicate), data = tribolium)

2 : * * *
3 : * * *
```

The model which is selected as the best in Wang and Puterman (1998) can be estimated with:

```
R> modelWang <- FLXMRglmfix(fixed = ~ I(Species == "Confusum"),
+   family = "binomial")
R> concomitantWang <- FLXPmultinom(~ I(Replicate == 3))
R> TribMixWang <- stepFlexmix(cbind(Remaining, Total - Remaining) ~ 1,
+   data = tribolium, model = modelWang, concomitant = concomitantWang,
+   k = 2)
```

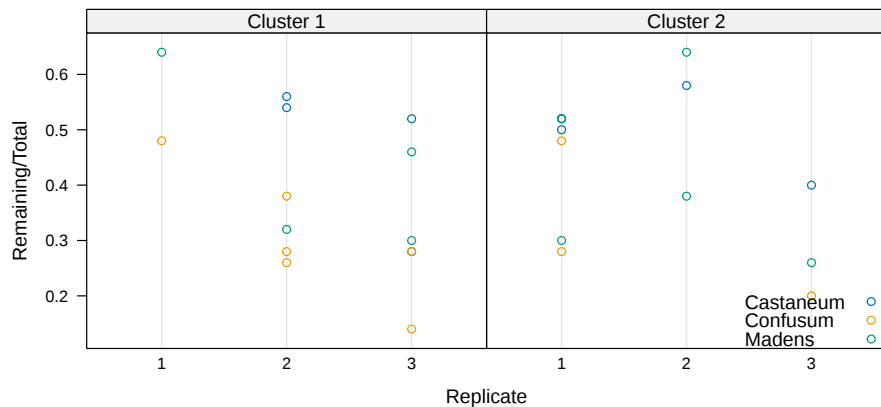


Figure 4: Relative number of remaining beetles for the number of replicate. The different panels are according to the cluster assignments based on the a-posteriori probabilities of the model suggested in Wang and Puterman (1998).

2 : \* \* \*

```
R> summary(refit(TribMixWang))
```

\$Comp.1

|                              | Estimate | Std. Error | z value | Pr(> z )  |
|------------------------------|----------|------------|---------|-----------|
| I(Species == "Confusum")TRUE | -0.56046 | 0.22985    | -2.4384 | 0.01475   |
| (Intercept)                  | -0.64544 | 0.13260    | -4.8674 | 1.131e-06 |

```
I(Species == "Confusum")TRUE *
(Intercept) ***
```

---

Signif. codes: 0 '\*\*\*' 0.001 '\*\*' 0.01 '\*' 0.05 '.' 0.1 ' ' 1

\$Comp.2

|                              | Estimate | Std. Error | z value | Pr(> z )  |
|------------------------------|----------|------------|---------|-----------|
| I(Species == "Confusum")TRUE | -0.56046 | 0.22985    | -2.4384 | 0.01475 * |
| (Intercept)                  | 0.19447  | 0.10117    | 1.9222  | 0.05459 . |

---

Signif. codes: 0 '\*\*\*' 0.001 '\*\*' 0.01 '\*' 0.05 '.' 0.1 ' ' 1

Wang and Puterman (1998) also considered a model where they omit one conspicuous observation. This model can be estimated with:

```
R> TribMixWangSub <- stepFlexmix(cbind(Remaining, Total - Remaining) ~ 1,
+   k = 2, data = tribolium[-7,], model = modelWang,
+   concomitant = concomitantWang)
```

2 : \* \* \*

*Trypanosome*

The data is used in [Follmann and Lambert \(1989\)](#). It is from a dosage-response analysis where the proportion of organisms belonging to different populations shall be assessed. It is assumed that organisms belonging to different populations are indistinguishable other than in terms of their reaction to the stimulus. The experimental technique involved inspection under the microscope of a representative aliquot of a suspension, all organisms appearing within two fields of view being classified either alive or dead. Hence the total numbers of organisms present at each dose and the number showing the quantal response were both random variables. The data is illustrated in [Figure 5](#).

The model which is proposed in [Follmann and Lambert \(1989\)](#) is given by:

$$H(\text{Dead} | \Theta) = \sum_{s=1}^S \pi_s \text{Bi}(\text{Dead} | \theta_s),$$

where  $\text{Dead} \in \{0, 1\}$  and with  $\beta^s = (\beta_{\text{Intercept}}^s, \beta_{\log(\text{Dose})}^s)$ . This model is fitted with:

```
R> data("trypanosome", package = "flexmix")
R> TrypMix <- stepFlexmix(cbind(Dead, 1-Dead) ~ 1, k = 2, nrep = 3,
+   data = trypanosome, model = FLXMRglmfix(family = "binomial",
+   fixed = ~ log(Dose)))
```

```
2 : * * *
```

```
R> summary(refit(TrypMix))
```

```
$Comp.1
```

|             | Estimate | Std. Error | z value | Pr(> z )      |
|-------------|----------|------------|---------|---------------|
| log(Dose)   | 124.895  | 25.261     | 4.9441  | 7.648e-07 *** |
| (Intercept) | -196.324 | 39.591     | -4.9588 | 7.094e-07 *** |

```
---
```

```
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
$Comp.2
```

|             | Estimate | Std. Error | z value | Pr(> z )      |
|-------------|----------|------------|---------|---------------|
| log(Dose)   | 124.895  | 25.261     | 4.9441  | 7.648e-07 *** |
| (Intercept) | -205.864 | 41.803     | -4.9247 | 8.450e-07 *** |

```
---
```

```
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

The fitted values are given in [Figure 5](#) together with the fitted values of a generalized linear model in order to facilitate comparison of the two models.

### 3.3. Finite mixtures of Poisson regressions

*Fabric faults*

The dataset is analyzed using a finite mixture of Poisson regression models in [Aitkin \(1996\)](#). Furthermore, it is described in [McLachlan and Peel \(2000\)](#) on page 155. It contains 32

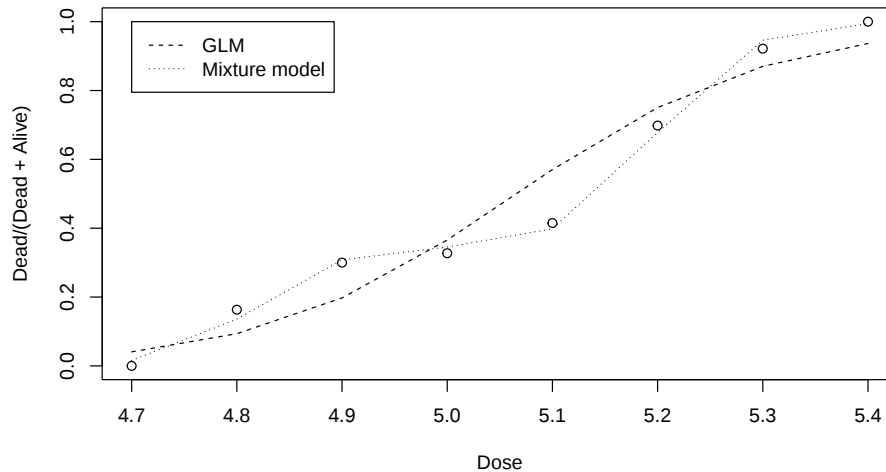


Figure 5: Relative number of deaths for each dose level together with the fitted values for the generalized linear model (“GLM”) and the random intercept model (“Mixture model”).

observations on the number of faults in rolls of a textile fabric. A random intercept model is used where a fixed effect is assumed for the logarithm of length:

```
R> data("fabricfault", package = "flexmix")
R> fabricMix <- stepFlexmix(Faults ~ 1, model = FLXMRglmfix(family="poisson",
+   fixed = ~ log(Length)), data = fabricfault, k = 2, nrep = 3)
```

```
2 : * * *
```

```
R> summary(fabricMix)
```

Call:

```
stepFlexmix(Faults ~ 1, model = FLXMRglmfix(family = "poisson",
  fixed = ~log(Length)), data = fabricfault, k = 2,
  nrep = 3)
```

|        | prior | size | post>0 | ratio |
|--------|-------|------|--------|-------|
| Comp.1 | 0.796 | 27   | 32     | 0.844 |
| Comp.2 | 0.204 | 5    | 32     | 0.156 |

```
'log Lik.' -86.33119 (df=4)
AIC: 180.6624    BIC: 186.5253
```

```
R> summary(refit(fabricMix))
```

```
$Comp.1
```

| Estimate | Std. Error | z value | Pr(> z ) |
|----------|------------|---------|----------|
|          |            |         |          |

```
log(Length) 0.79913      0.23491  3.4019 0.0006692 ***
(Intercept) -3.12797     1.51934 -2.0588 0.0395167 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
$Comp.2
```

```
      Estimate Std. Error z value Pr(>|z|)
log(Length) 0.79913      0.23491  3.4019 0.0006692 ***
(Intercept) -2.36202     1.59146 -1.4842 0.1377594
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
R> Lnew <- seq(0, 1000, by = 50)
R> fabricMix.pred <- predict(fabricMix, newdata = data.frame(Length = Lnew))
```

The intercept of the first component is not significantly different from zero for a significance level of 0.05. We therefore also fit a modified model where the intercept is a-priori set to zero for the first component. This nested structure is given as part of the model specification with argument `nested`.

```
R> fabricMix2 <- flexmix(Faults ~ 0, data = fabricfault,
+   cluster = posterior(fabricMix),
+   model = FLXMRglmfix(family = "poisson", fixed = ~ log(Length),
+   nested = list(k=c(1,1), formula=list(~0,~1))))
R> summary(refit(fabricMix2))
```

```
$Comp.1
```

```
      Estimate Std. Error z value Pr(>|z|)
log(Length) 0.308000     0.013437 22.922 < 2.2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
$Comp.2
```

```
      Estimate Std. Error z value Pr(>|z|)
log(Length) 0.308000     0.013437 22.9215 < 2.2e-16 ***
(Intercept) 0.921282     0.132720  6.9415 3.878e-12 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
R> fabricMix2.pred <- predict(fabricMix2,
+   newdata = data.frame(Length = Lnew))
```

The data and the fitted values for each of the components for both models are given in Figure 6.

### Patent

The patent data given in Wang, Cockburn, and Puterman (1998) consist of 70 observations on patent applications, R&D spending and sales in millions of dollar from pharmaceutical

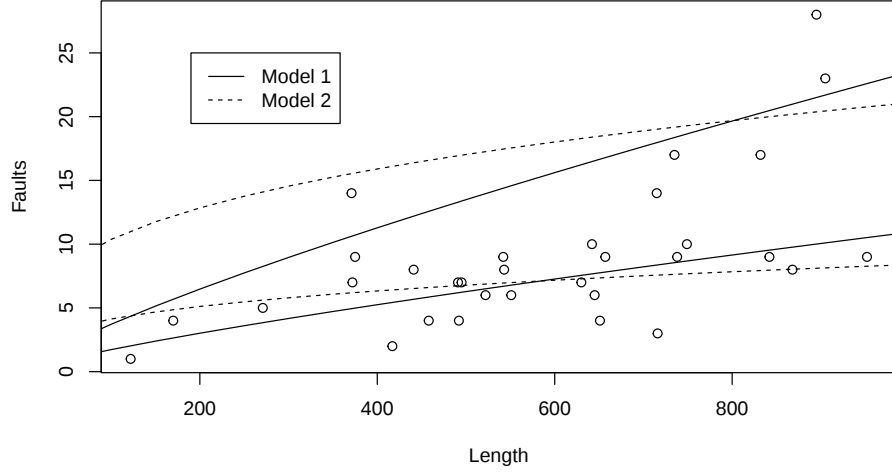


Figure 6: Observed values of the fabric faults dataset together with the fitted values for the components of each of the two fitted models.

and biomedical companies in 1976 taken from the National Bureau of Economic Research R&D Masterfile. The observations are displayed in Figure 7. The model which is chosen as the best in Wang *et al.* (1998) is given by:

$$H(\text{Patents} | \lg\text{RD}, \text{RDS}, \Theta) = \sum_{s=1}^S \pi_s(\text{RDS}, \alpha) \text{Poi}(\text{Patents} | \lambda_s),$$

and  $\beta^s = (\beta_{\text{Intercept}}^s, \beta_{\lg\text{RD}}^s)$ .

The model is fitted with:

```
R> data("patent", package = "flexmix")
R> ModelPat <- FLXMRglm(family = "poisson")
R> FittedPat <- stepFlexmix(Patents ~ lgRD, k = 3, nrep = 3,
+   model = ModelPat, data = patent, concomitant = FLXPmultinom(~ RDS))
```

```
3 : * * *
```

```
R> summary(FittedPat)
```

Call:

```
stepFlexmix(Patents ~ lgRD, model = ModelPat, data = patent,
  concomitant = FLXPmultinom(~RDS), k = 3, nrep = 3)
```

|        | prior | size | post>0 | ratio |
|--------|-------|------|--------|-------|
| Comp.1 | 0.615 | 45   | 63     | 0.714 |
| Comp.2 | 0.184 | 13   | 47     | 0.277 |

```
Comp.3 0.201    12    48 0.250
```

```
'log Lik.' -197.6753 (df=10)
AIC: 415.3506    BIC: 437.8355
```

The fitted values for the component specific models and the concomitant variable model are given in Figure 7. The plotting symbol of the observations corresponds to the induced clustering given by `clusters(FittedPat)`.

This model is modified to have fixed effects for the logarithmized R&D spendings, i.e.  $(\beta)^s = (\beta_{\text{Intercept}}^s, \beta_{\text{lgRD}}^s)$ . The already fitted model is used for initialization, i.e. the EM algorithm is started with an M-step given the a-posteriori probabilities.

```
R> ModelFixed <- FLXMRglmfix(family = "poisson", fixed = ~ lgRD)
R> FittedPatFixed <- flexmix(Patents ~ 1, model = ModelFixed,
+   cluster = posterior(FittedPat), concomitant = FLXPmultinom(~ RDS),
+   data = patent)
R> summary(FittedPatFixed)
```

Call:

```
flexmix(formula = Patents ~ 1, data = patent, cluster = posterior(FittedPat),
        model = ModelFixed, concomitant = FLXPmultinom(~RDS))
```

|        | prior | size | post>0 | ratio |
|--------|-------|------|--------|-------|
| Comp.1 | 0.361 | 25   | 63     | 0.397 |
| Comp.2 | 0.203 | 14   | 52     | 0.269 |
| Comp.3 | 0.436 | 31   | 54     | 0.574 |

```
'log Lik.' -216.824 (df=8)
AIC: 449.6479    BIC: 467.6359
```

The fitted values for the component specific models and the concomitant variable model of this model are also given in Figure 7.

With respect to the BIC the full model is better than the model with the fixed effects. However, fixed effects have the advantage that the different components differ only in their baseline and the relation between the components in return of investment for each additional unit of R&D spending is constant. Due to a-priori domain knowledge this model might seem more plausible. The fitted values for the constrained model are also given in Figure 7.

### Seizure

The data is used in Wang, Puterman, Cockburn, and Le (1996) and is from a clinical trial where the effect of intravenous gamma-globulin on suppression of epileptic seizures is studied. There are daily observations for a period of 140 days on one patient, where the first 27 days are a baseline period without treatment, the remaining 113 days are the treatment period. The model proposed in Wang *et al.* (1996) is given by:

$$H(\text{Seizures} \mid (\text{Treatment}, \log(\text{Day}), \log(\text{Hours})), \Theta) = \sum_{s=1}^S \pi_s \text{Poi}(\text{Seizures} \mid \lambda_s),$$

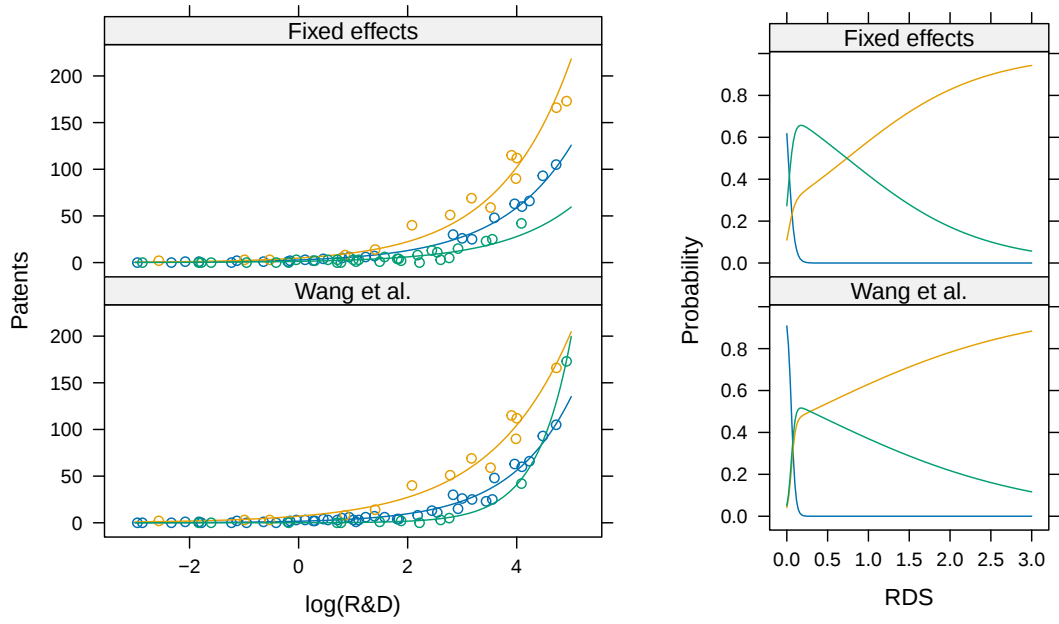


Figure 7: Patent data with the fitted values of the component specific models (left) and the concomitant variable model (right) for the model in Wang *et al.* and with fixed effects for  $\log(\text{R\&D})$ . The plotting symbol for each observation is determined by the component with the maximum a-posteriori probability.

where  $(\beta)^s = (\beta_{\text{Intercept}}^s, \beta_{\text{Treatment}}^s, \beta_{\log(\text{Day})}^s, \beta_{\text{Treatment}:\log(\text{Day})}^s)$  and  $\log(\text{Hours})$  is used as offset. This model is fitted with:

```
R> data("seizure", package = "flexmix")
R> seizMix <- stepFlexmix(Seizures ~ Treatment * log(Day), data = seizure,
+   k = 2, nrep = 3, model = FLXMRglm(family = "poisson",
+   offset = log(seizure$Hours)))
```

```
2 : * * *
```

```
R> summary(seizMix)
```

Call:

```
stepFlexmix(Seizures ~ Treatment * log(Day), data = seizure,
  model = FLXMRglm(family = "poisson", offset = log(seizure$Hours)),
  k = 2, nrep = 3)
```

|        | prior | size | post>0 | ratio |
|--------|-------|------|--------|-------|
| Comp.1 | 0.724 | 103  | 115    | 0.896 |
| Comp.2 | 0.276 | 37   | 101    | 0.366 |

```
'log Lik.' -376.1762 (df=9)
AIC: 770.3525   BIC: 796.8272
```

```
R> summary(refit(seizMix))
```

\$Comp.1

|                       | Estimate  | Std. Error | z value | Pr(> z )      |
|-----------------------|-----------|------------|---------|---------------|
| (Intercept)           | 2.070226  | 0.092252   | 22.441  | < 2.2e-16 *** |
| TreatmentYes          | 7.432200  | 0.548865   | 13.541  | < 2.2e-16 *** |
| log(Day)              | -0.270550 | 0.042320   | -6.393  | 1.626e-10 *** |
| TreatmentYes:log(Day) | -2.276359 | 0.147857   | -15.396 | < 2.2e-16 *** |

---

Signif. codes: 0 '\*\*\*' 0.001 '\*\*' 0.01 '\*' 0.05 '.' 0.1 ' ' 1

\$Comp.2

|                       | Estimate | Std. Error | z value | Pr(> z )      |
|-----------------------|----------|------------|---------|---------------|
| (Intercept)           | 2.84422  | 0.25898    | 10.9825 | < 2.2e-16 *** |
| TreatmentYes          | 1.30319  | 0.54448    | 2.3935  | 0.016690 *    |
| log(Day)              | -0.40593 | 0.10014    | -4.0537 | 5.04e-05 ***  |
| TreatmentYes:log(Day) | -0.43139 | 0.15265    | -2.8261 | 0.004712 **   |

---

Signif. codes: 0 '\*\*\*' 0.001 '\*\*' 0.01 '\*' 0.05 '.' 0.1 ' ' 1

A different model with different contrasts to directly estimate the coefficients for the jump when changing between base and treatment period is given by:

```
R> seizMix2 <- flexmix(Seizures ~ Treatment * log(Day/27),
+   data = seizure, cluster = posterior(seizMix),
+   model = FLXMRglm(family = "poisson", offset = log(seizure$Hours)))
R> summary(seizMix2)
```

Call:

```
flexmix(formula = Seizures ~ Treatment * log(Day/27),
  data = seizure, cluster = posterior(seizMix), model = FLXMRglm(family = "poisson",
    offset = log(seizure$Hours)))
```

|        | prior | size | post>0 | ratio |
|--------|-------|------|--------|-------|
| Comp.1 | 0.724 | 103  | 115    | 0.896 |
| Comp.2 | 0.276 | 37   | 101    | 0.366 |

```
'log Lik.' -376.1762 (df=9)
AIC: 770.3524   BIC: 796.8272
```

```
R> summary(refit(seizMix2))
```

\$Comp.1

|                          | Estimate  | Std. Error | z value  | Pr(> z )      |
|--------------------------|-----------|------------|----------|---------------|
| (Intercept)              | 1.178452  | 0.072453   | 16.2650  | < 2.2e-16 *** |
| TreatmentYes             | -0.070116 | 0.116887   | -0.5999  | 0.5486        |
| log(Day/27)              | -0.270600 | 0.042324   | -6.3935  | 1.621e-10 *** |
| TreatmentYes:log(Day/27) | -2.276249 | 0.147854   | -15.3953 | < 2.2e-16 *** |

---  
Signif. codes: 0 '\*\*\*' 0.001 '\*\*' 0.01 '\*' 0.05 '.' 0.1 ' ' 1

\$Comp.2

|                          | Estimate  | Std. Error | z value | Pr(> z )      |
|--------------------------|-----------|------------|---------|---------------|
| (Intercept)              | 1.506044  | 0.091612   | 16.4394 | < 2.2e-16 *** |
| TreatmentYes             | -0.118471 | 0.140926   | -0.8407 | 0.40054       |
| log(Day/27)              | -0.406176 | 0.100100   | -4.0577 | 4.956e-05 *** |
| TreatmentYes:log(Day/27) | -0.431134 | 0.152620   | -2.8249 | 0.00473 **    |

---  
Signif. codes: 0 '\*\*\*' 0.001 '\*\*' 0.01 '\*' 0.05 '.' 0.1 ' ' 1

A different model which allows no jump at the change between base and treatment period is fitted with:

```
R> seizMix3 <- flexmix(Seizures ~ log(Day/27)/Treatment, data = seizure,
+   cluster = posterior(seizMix), model = FLXMRglm(family = "poisson",
+   offset = log(seizure$Hours)))
R> summary(seizMix3)
```

Call:

```
flexmix(formula = Seizures ~ log(Day/27)/Treatment, data = seizure,
```

```

cluster = posterior(seizMix), model = FLXMRglm(family = "poisson",
  offset = log(seizure$Hours)))

      prior size post>0 ratio
Comp.1 0.722  102    115 0.887
Comp.2 0.278   38    101 0.376

'log Lik.' -376.6495 (df=7)
AIC: 767.2991   BIC: 787.8906

R> summary(refit(seizMix3))

$Comp.1
              Estimate Std. Error  z value  Pr(>|z|)
(Intercept)      1.150003    0.058217  19.7537 < 2.2e-16 ***
log(Day/27)       -0.283878    0.036969  -7.6788 1.606e-14 ***
log(Day/27):TreatmentYes -2.311510    0.134828 -17.1441 < 2.2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

$Comp.2
              Estimate Std. Error  z value  Pr(>|z|)
(Intercept)      1.458918    0.067241 21.6968 < 2.2e-16 ***
log(Day/27)       -0.447634    0.081633  -5.4835 4.17e-08 ***
log(Day/27):TreatmentYes -0.458721    0.145578  -3.1510 0.001627 **
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

With respect to the BIC criterion the smaller model with no jump is preferred. This is also the more intuitive model from a practitioner's point of view, as it does not seem to be plausible that starting the treatment already gives a significant improvement, but improvement develops over time. The data points together with the fitted values for each component of the two models are given in Figure 8. It can clearly be seen that the fitted values are nearly equal which also supports the smaller model.

### *Ames salmonella assay data*

The ames salmonella assay dataset was used in Wang *et al.* (1996). They propose a model given by:

$$H(y | x, \Theta) = \sum_{s=1}^S \pi_s \text{Poi}(y | \lambda_s),$$

where  $\beta^s = (\beta_{\text{Intercept}}^s, \beta_x, \beta_{\log(x+10)})$ . The model is fitted with:

```

R> data("salmonellaTA98", package = "flexmix")
R> salmonMix <- stepFlexmix(y ~ 1, data = salmonellaTA98, k = 2, nrep = 3,
+   model = FLXMRglmfix(family = "poisson", fixed = ~ x + log(x + 10)))

```

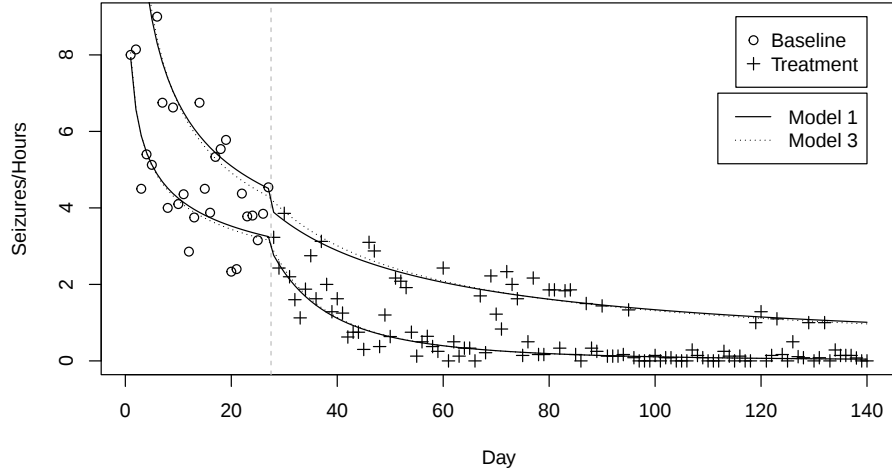


Figure 8: Observed values for the seizure dataset together with the fitted values for the components of the two different models.

2 : \* \* \*

## 4. Conclusions and future work

Package **flexmix** can be used to fit finite mixtures of regressions to datasets used in the literature to illustrate these models. The results can be reproduced and additional insights can be gained using visualization methods available in R. The fitted model is an object in R which can be explored using `show()`, `summary()` or `plot()`, as suitable methods have been implemented for objects of class "flexmix" which are returned by `flexmix()`.

In the future it would be desirable to have more diagnostic tools available to analyze the model fit and compare different models. The use of resampling methods would be convenient as they can be applied to all kinds of mixtures models and would therefore suit well the purpose of the package which is flexible modelling of various finite mixture models. Furthermore, an additional visualization method for the fitted coefficients of the mixture would facilitate the comparison of the components.

## Computational details

All computations and graphics in this paper have been done using R version 4.6.1 with the packages **lattice** 0.22-9, **flexmix** 2.3-21, **compiler** 4.6.1, **modeltools** 0.2-24, **tools** 4.6.1, **nnet** 7.3-21, **mvtnorm** 1.4-2, **ellipse** 0.5.0, **diptest** 0.77-2, **stats4** 4.6.1.

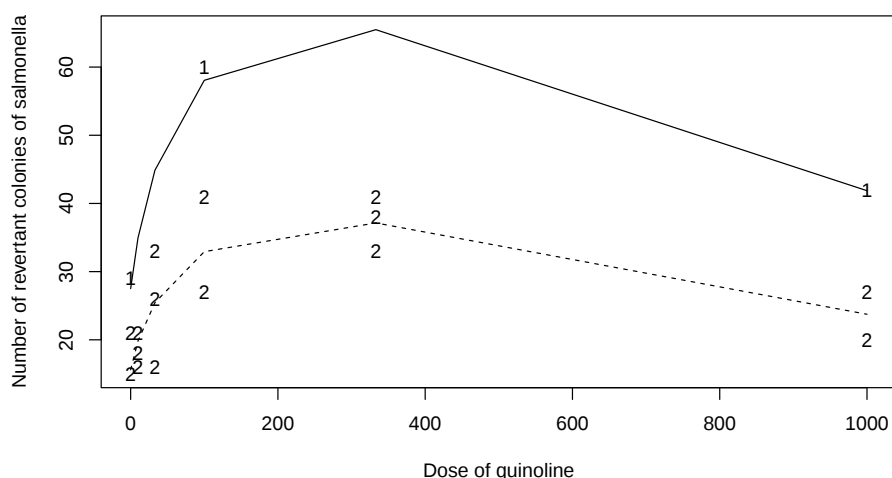


Figure 9: Means and classification for assay data according to the estimated posterior probabilities based on the fitted model.

## Acknowledgments

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