## ${\bf 1}\quad Constant And Multiplicative Gaussian Error Model \\$

An error model which assumes that the model error is a mixture between a Gaussian base-level noise and a Gaussian heteroscedastic noise.

A mixture between a Gaussian base-level noise and a Gaussian heteroscedastic noise assumes that the observable biomarker X is related to the :class:'MechanisticModel' output by

$$X(t, \psi, \sigma_{\text{base}}, \sigma_{\text{rel}}) = x^{\text{m}} + (\sigma_{\text{base}} + \sigma_{\text{rel}}x^{\text{m}}) \epsilon$$

where  $x^{\mathrm{m}}:=x^{\mathrm{m}}(t,\psi)$  is the mechanistic model output with parameters  $\psi$ , and  $\epsilon$  is a i.i.d. standard Gaussian random variable

$$\epsilon \sim \mathcal{N}(0,1)$$
.

As a result, this model assumes that the observed biomarker values  $x^{\text{obs}}$  are realisations of the random variable X.

At each time point t the distribution of the observable biomarkers can be expressed in terms of a Gaussian distribution

$$p(x|\psi, \sigma_{\rm base}, \sigma_{\rm rel}) = \frac{1}{\sqrt{2\pi}\sigma_{\rm tot}} \exp{\left(-\frac{(x-x^{\rm m})^2}{2\sigma_{\rm tot}^2}\right)},$$

where  $\sigma_{\text{tot}} = \sigma_{\text{base}} + \sigma_{\text{rel}} x^{\text{m}}$ .

Extends :class:'ErrorModel'.

## 2 GaussianErrorModel

An error model which assumes that the model error follows a Gaussian distribution

A Gaussian error model assumes that the observable biomarker X is related to the :class:'MechanisticModel' output by

$$X(t, \psi, \sigma) = x^{\mathrm{m}} + \sigma \epsilon,$$

where  $x^{\mathrm{m}}:=x^{\mathrm{m}}(t,\psi)$  is the mechanistic model output with parameters  $\psi$ , and  $\epsilon$  is a i.i.d. standard Gaussian random variable

$$\epsilon \sim \mathcal{N}(0,1)$$
.

As a result, this model assumes that the observed biomarker values  $x^{\text{obs}}$  are realisations of the random variable X.

At each time point t the distribution of the observable biomarkers can be expressed in terms of a Gaussian distribution

$$p(x|\psi,\sigma) = \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{(x-x^{\mathrm{m}})^2}{2\sigma^2}\right).$$

Extends :class:'ErrorModel'.

## 3 LogNormalErrorModel

An error model which assumes that the model error follows a Log-normal distribution.

A log-normal error model assumes that the observable biomarker X is related to the :class:'MechanisticModel' output by

$$X(t, \psi, \sigma_{\log}) = y e^{\mu + \sigma_{\log} \varepsilon},$$

where  $y := y(t, \psi)$  is the mechanistic model output with parameters  $\psi$ , and  $\varepsilon$  is a i.i.d. standard Gaussian random variable

$$\varepsilon \sim \mathcal{N}(0,1)$$
.

Here,  $\sigma_{\log}$  is the standard deviation of  $\log X$  and  $\mu := -\sigma_{\log}^2/2$  is chosen such that

$$\mathbb{E}[X] = y.$$

As a result, this model assumes that the observed biomarker values  $x^{\text{obs}}$  are realisations of the random variable X.

At each time point t the distribution of the observable biomarkers can be expressed in terms of a log-normal distribution

$$p(x|\psi, \sigma_{\log}) = \frac{1}{\sqrt{2\pi}\sigma_{\log}x} \exp\left(-\frac{\left(\log x - \log y + \sigma_{\log}^2/2\right)^2}{2\sigma_{\log}^2}\right).$$

Extends :class:'ErrorModel'.

## 4 MultiplicativeGaussianErrorModel

An error model which assumes that the model error is a Gaussian heteroscedastic noise.

A Gaussian heteroscedastic noise model assumes that the observable biomarker X is related to the :class:'MechanisticModel' output by

$$X(t, \psi, \sigma_{\rm rel}) = x^{\rm m} + \sigma_{\rm rel} x^{\rm m} \epsilon,$$

where  $x^{\mathrm{m}} := x^{\mathrm{m}}(t, \psi)$  is the mechanistic model output with parameters  $\psi$ , and  $\epsilon$  is a i.i.d. standard Gaussian random variable

$$\epsilon \sim \mathcal{N}(0,1)$$
.

As a result, this model assumes that the observed biomarker values  $x^{\text{obs}}$  are realisations of the random variable X.

At each time point t the distribution of the observable biomarkers can be expressed in terms of a Gaussian distribution

$$p(x|\psi, \sigma_{\text{base}}, \sigma_{\text{rel}}) = \frac{1}{\sqrt{2\pi}\sigma_{\text{tot}}} \exp\left(-\frac{(x-x^{\text{m}})^2}{2\sigma_{\text{tot}}^2}\right),$$

where  $\sigma_{\rm tot} = \sigma_{\rm rel} x^{\rm m}$ . Extends :class:'ErrorModel'.