

# Package ‘TimerQuant’

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**Title** Timer Quantification

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**Suggests** BiocStyle, reshape2, knitr, shinyBS

**Imports** ggplot2, grid, gridExtra, deSolve, dplyr, locfit

**VignetteBuilder** knitr

**Description** Supplementary Data package for tandem timer methods paper by Barry et al. (2015) including TimerQuant shiny applications.

**biocViews** ExperimentData, Danio\_rerio\_Data, HighThroughputImagingData, Tissue

**License** Artistic-2.0

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|                   |  |
|-------------------|--|
| analyticSolutions | <i>Analytic model solutions for fluorescence intensity</i> |
|-------------------|--|

---

### Description

Time-dependent and steady-state analytic solution to one-step model for number of mature fluorophores. Where  $f$  is given as a parameter the returned value is transformed from a molecular population into a fluorescence intensity. For the function names, 0 refers to the dark population of non-mature fluorophores, and 1 to the mature, fluorescent population. 'ss' indicates steady-state solutions.  $t_{ss}$  is the time required to reach steady-state.

### Usage

```
tss(m, k)
x0ss(p, m, k)
x1(p, m, k, t, f=1)
x1ss(p, m, k, f=1)
x1fretFP1(p, m1, m2, k, t, E=0, f=1)
x1fretFP1ss(p, m1, m2, k, E=0, f=1)
```

### Arguments

|      |   |
|------|---|
| $p$  | Protein production rate (molecules produced per unit time).   |
| $m$  | Maturation rate of fluorophore, which can be for either FP1 or FP2 (convert to maturation time with $\log(2)/m$ ).                        |
| $m1$ | Maturation rate of FP1.   |
| $m2$ | Maturation rate of FP2.   |
| $k$  | Protein degradation rate (convert to half-life with $\log(2)/k$ ).  |
| $t$  | Time (must be non-negative).  |
| $E$  | FRET coefficient representing energy transfer from FP1 to FP2.  |
| $f$  | Proportionality factor relating intensity to the number of molecules. When equal to one then the readout is number of molecules directly. |

**Value**

A numeric specifying the model solution for the given parameters.

**Author(s)**

Joseph D. Barry

**Examples**

```
t0 <- seq(0.001, 1000, by=0.1)
plot(t0, x1(p=10, m=log(2)/5, k=log(2)/100, t=t0), type="l", col="darkgreen",
      lwd=2, xlab="Time (min)", ylab="Number of mature fluorophores", cex.lab=1.4)
```

---

fitCV

*fitCV*

---

**Description**

Fits a smoothing line to coefficient of variation profiles.

**Usage**

```
fitCV(x, scaleLog10)
```

**Arguments**

**x** A dataframe with columns Time (FP maturation time) and CV (coefficient of variation of timer signal).

**scaleLog10** A logical indicating whether the points are spaced on the log10 scale or not.

**Value**

A dataframe containing fitted values and the minimum CV of the profile.

**Author(s)**

Joseph D. Barry

**Examples**

```
if (interactive()) vignette(topic="genPaperFigures", package="TimerQuant")
```

---

 FRETdata

*FRET Data*


---

### Description

A three-dimensional array of dimensions FRET value x tFT x assay type containing FRET readouts.

### Usage

FRETdata

---

genRatioHeatmap

*generate ratio heatmap*


---

### Description

Visualize timer ratios as a function of either FP1 or FP2 maturation time, and protein half-life.

### Usage

```
genRatioHeatmap(tRangeFP, Tfixed, TA, TB, channel, E, f=1, n, ramp)
```

### Arguments

|          |   |
|----------|---|
| tRangeFP | Vector containing two numerics specifying the range of maturation times to display for the chosen fluorescence channel. |
| Tfixed   | The maturation time of the FP that will remain fixed.   |
| TA       | tFT half-life in location A.  |
| TB       | tFT half-life in location B.  |
| channel  | Integer specifying fluorescence channel to be varied (1 or 2).  |
| E        | FRET value representing transfer from FP1 to FP2.   |
| f        | $f=f_2/f_1$ , the ratio of prefactors relating the number of molecules to the fluorescence intensity.                   |
| n        | Integer specifying the number of data points. Choose a higher n for a higher pixel density.                             |
| ramp     | Colour ramp, see <code>colorRampPalette</code> for more details.  |

### Value

Returns a ggplot2 heatmap.

### Author(s)

Joseph D. Barry

### Examples

```
if (interactive()) vignette(topic="genPaperFigures", package="TimerQuant")
```

---

genTimeSteadyStateHeatmap  
*Time to reach steady-state*

---

### Description

Visualize the time to reach steady-state as a function of FP2 maturation time and protein half-life.

### Usage

```
genTimeSteadyStateHeatmap(tRangeFP2, tRangeHlife, n, ramp)
```

### Arguments

|             |   |
|-------------|---|
| tRangeFP2   | Vector containing two numerics specifying the range of FP2 maturation times.                |
| tRangeHlife | Vector containing two numerics specifying the range of protein half-lives.                  |
| n           | Integer specifying the number of data points. Choose a higher n for a higher pixel density. |
| ramp        | Colour ramp, see colorRampPalette for more details.   |

### Value

Returns a ggplot2 heatmap.

### Author(s)

Joseph D. Barry

### Examples

```
if (interactive()) vignette(topic="genPaperFigures", package="TimerQuant")
```

---

|             |                         |
|-------------|-------------------------|
| getBreaks10 | <i>Get log10 breaks</i> |
|-------------|-------------------------|

---

**Description**

Return breaks for each half-decade on the log10 scale, e.g. 1, 5, 10, 50, ...

**Usage**

```
getBreaks10(x)
```

**Arguments**

x                    A vector of numbers. Breaks will be calculated across the range of x.

**Value**

A sequence of breaks useful for ticks or labels on the log10 scale.

**Author(s)**

Joseph D. Barry

**Examples**

```
getBreaks10(c(1, 100))
```

---

|              |                            |
|--------------|----------------------------|
| getSpacedSeq | <i>Get Spaced Sequence</i> |
|--------------|----------------------------|

---

**Description**

Return points nicely spaced for on the log10 scale.

**Usage**

```
getSpacedSeq(x, n)
```

**Arguments**

x                    A vector of two numbers containing the minimum and maximum of the desired sequence.

n                    The desired length of the sequence to be returned.

**Value**

A sequence of numbers with appropriate spacing for the log10 scale.

**Author(s)**

Joseph D. Barry

**Examples**

```
getSpacedSeq(c(1, 1000), n=10)
```

---

|                |                        |
|----------------|------------------------|
| maturationData | <i>Maturation Data</i> |
|----------------|------------------------|

---

**Description**

A five-dimensional array of dimensions time (in minutes) x data columns x sample x view x tFT (identified by the RFP since sfGFP is present for all) containing fluorescence intensity readouts for the fluorophore maturation curves.

**Usage**

```
maturationData
```

---

|                       |                                |
|-----------------------|--------------------------------|
| plotPrimordiumProfile | <i>Plot Primordium Profile</i> |
|-----------------------|--------------------------------|

---

**Description**

Visualizes primordium signal as a function of position with median and median absolute deviation across samples.

**Usage**

```
plotPrimordiumProfile(x, add, ylab, lwd, cex.lab, cex.axis, xlim, ylim, main,
  col, lty, alpha)
```

**Arguments**

|          |   |
|----------|---|
| x        | A matrix of data where rows are samples and columns are sequential positions. |
| add      | A logical indicating whether or not to add to the existing plot.              |
| ylab     | The y-axis label.   |
| lwd      | Integer specifying width of lines.  |
| cex.lab  | Integer specifying size of labels.  |
| cex.axis | Integer specifying size of axis labels.                                       |
| xlim     | An optional vector of length 2 specifying the limits for the x-axis.          |
| ylim     | An optional vector of length 2 specifying the limits for the y-axis.          |

|       |  |
|-------|--|
| main  | Plot title.  |
| col   | Line colour.   |
| lty   | Style of line  |
| alpha | A numeric between zero and one specifying the level of transparency for the shaded region. |

**Value**

Produces a plot of signal vs position summarizing across multiple primordium samples.

**Author(s)**

Joseph D. Barry

**Examples**

```
if (interactive()) vignette(topic="genPaperFigures", package="TimerQuant")
```

---

profileGradients      *Profile Gradients*

---

**Description**

A three-dimensional array of dimensions tFT x sample x position containing ratio readouts for migrating posterior lateral line primordia.

**Usage**

```
profileGradients
```

---

ratioSteadyState      *analytic function ratioSteadyState*

---

**Description**

Steady-state analytic solution to one-step model for the ratio of mature to non-mature fluorophores.

**Usage**

```
ratioSteadyState(T1, T2, halfLife, E=0, f=1)
```



**Arguments**

|          |   |
|----------|---|
| T1       | Maturation time of fluorescent protein 1 (FP1, fast maturing).  |
| T2       | Maturation time of fluorescent protein 2 (FP2, slow maturing).  |
| halfLife | Protein half-life.  |
| E        | FRET value representing transfer from FP1 to FP2.   |
| f        | $f=f_2/f_1$ , the ratio of prefactors relating the number of molecules to fluorescence intensity for each fluorescence channel. |

**Value**

A numeric specifying the model steady-state solution for the given parameters.

**Author(s)**

Joseph D. Barry

**Examples**

```
halfLifeSeq <- seq(1, 2000, by=0.1)
plot(halfLifeSeq, ratioSteadyState(T1=5, T2=100, halfLife=halfLifeSeq),
     type="l", lwd=2, ylim=c(0, 1), xlab="tFT half-life (min)",
     ylab="Steady-state ratio", cex.lab=1.4, log="x", col="red")
```

---

ratioTimeDependent     *analytic function ratioTimeDependent*

---

**Description**

Steady-state analytic solution to one-step model for the ratio of mature to non-mature fluorophores.

**Usage**

```
ratioTimeDependent(T1, T2, halfLife, t, E=0, f=1)
```

**Arguments**

|          |   |
|----------|---|
| T1       | Maturation time of fluorescent protein 1 (FP1, fast maturing).                                    |
| T2       | Maturation time of fluorescent protein 2 (FP2, slow maturing).                                    |
| halfLife | Protein half-life.  |
| t        | Time, which must be non-negative.   |
| E        | FRET value representing energy transfer from FP1 to FP2.  |
| f        | $f=f_2/f_1$ , the ratio of prefactors relating the number of molecules to fluorescence intensity. |

**Value**

A numeric specifying the model time-dependent solution for the given parameters.

**Author(s)**

Joseph D. Barry

**Examples**

```
tSeq <- seq(0.1, 300, by=0.1)
plot(tSeq, ratioTimeDependent(T1=5, T2=100, halfLife=30, t=tSeq, E=0, f=1), type="l", lwd=2,
     xlab="time (min)", ylab="ratio", cex.lab=1.4, col="black", ylim=c(0, 0.3))
points(tSeq, ratioTimeDependent(T1=5, T2=100, halfLife=30, t=tSeq, E=0.4, f=1), type="l", lwd=2,
      col="red")
abline(h=ratioSteadyState(T1=5, T2=100, halfLife=30, E=0, f=1), lty=2, col="black")
abline(h=ratioSteadyState(T1=5, T2=100, halfLife=30, E=0.4, f=1), lty=2, col="red")
```

---

runShinyApps

*Run R-shiny applications*

---

**Description**

Wrapper functions that run shiny apps located in extdata subdirectory of R package.

**Usage**

```
runChooseFP2App()
runTimerModellingApp()
```

**Author(s)**

Joseph D. Barry

**Examples**

```
runChooseFP2App()

runTimerModellingApp()
```

---

|        |               |
|--------|---------------|
| signal | <i>Signal</i> |
|--------|---------------|

---

**Description**

Computes timer signal (without additive noise) for a set of model parameters.

**Usage**

```
signal(T1, T2, TA, TB, E=0)
```

**Arguments**

|    |   |
|----|---|
| T1 | Maturation time of fluorescent protein 1 (fast maturing). |
| T2 | Maturation time of fluorescent protein 2 (slow maturing). |
| TA | Minimum protein half-life.                                |
| TB | Maximum protein half-life.                                |
| E  | FRET value representing transfer from FP1 to FP2.         |

**Value**

A numeric specifying the timer signal.

**Author(s)**

Joseph D. Barry

**Examples**

```
signal(T1=5, T2=60, TA=30, TB=180, E=0)
signal(T1=5, T2=60, TA=30, TB=180, E=0.5)
```

---

|                 |                               |
|-----------------|-------------------------------|
| simulatedSignal | <i>Simulated Timer Signal</i> |
|-----------------|-------------------------------|

---

**Description**

Additive error model for timer signal.

**Usage**

```
simulatedRatio(T1, T2, hLife, sigmaAdd, p, E)
simulatedSignal(T1, T2, TA, TB, sigmaAdd, p, E)
simulatedSignalN(T1, T2, TA, TB, sigmaAdd, N, p, E)
```

**Arguments**

|          |   |
|----------|---|
| T1       | Maturation time of fluorescent protein 1 (FP1, fast maturing).              |
| T2       | Maturation time of fluorescent protein 2 (FP2, slow maturing).              |
| hLife    | Protein half-life.  |
| TA       | Minimum protein half-life.  |
| TB       | Maximum protein half-life.  |
| sigmaAdd | Standard deviation of normal distribution from which noise terms are drawn. |
| p        | Protein production rate (molecules produced per unit time).                 |
| E        | FRET value representing energy transfer from FP1 to FP2.                    |
| N        | Number of simulation realizations.  |

**Value**

Returns simulated values for ratios or timer signal.

**Author(s)**

Joseph D. Barry

**Examples**

```
if (interactive()) vignette(topic="genPaperFigures", package="TimerQuant")
```

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