Package 'Ritc'

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Type Package

Title Isothermal Titration Calorimetry (ITC) Data Analysis

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Depends minpack.lm

Description Implements the simulation and regression of
integrated Isothermal Titration Calorimetry (ITC) data using
the most commonly used one-to-one binding reaction model.

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Contents

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data_inputparam1 *An example set of input parameter data for the function* fititcdata

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Description

This is a group of nine ITC parameters organized in a dataframe.

The first is the file name of the csv file exported from Origin7 data sheet

The second group of four is experimental set parameters including

P0: protein concentration in cell in mM (the binding partner in cell even if it is not a protein)

L0: ligand concentration in cell in mM (the binding partner in syringe even if it is not ligand)

Asyr: ligand cocentration in syringe in mM (the binding partner in syringe even if it is not ligand)

V0: the volume of the ITC cell in ml

The third group of four is estimates of the fitting parameters including

K: the binding constant in 1/M

DH: the binding enthalpy in cal/mole

N: the binding stoichiometry ratio, ligand/protein

HD: heat of dilution in ucal for each injection

It is the content of the inputparam.txt file in the extdata folder:

file_name, B110711CD4.CSV

P0, 0.00159

L0, 0

Asyr, 0.0181

V0, 1.4347

K, 3E7

DH, -65000

HD, 0.05

N, 0.9

Usage

```
data(data_inputparam1)
```

Format

A data frame with 9 observations on the following 2 variables.

V1 a character vector of parameter names

V2 a character vector of parameter values

Examples

```
data(data_inputparam1)
```

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data_origin1 *An example set of ITC data as exported by Origin7 data sheet*

Description

This is the content of the B110711CD4.txt file in the extdata folder, imported as a dataframe.

Usage

```
data(data_origin1)
```

Format

A data frame with observations on the following 7 variables.

DH a character vector

INJV a character vector

Xt a character vector

Mt a character vector

XMt a character vector

NDH a character vector

B a character vector

Examples

```
data(data_origin1)
```

---

fititcdata *Fit and plot ITC data*

Description

The fititcdata function reads in integrated Isothermal Titration Calorimetry (ITC) data as exported from Origin, experimental and fitting parameters from input text files, fit the data to a one-to-one binding model, and plot the data and fitting results in an exported pdf file and esp file. The pdf file contains the plotted diagram and the numeric parameters below the diagram, while the esp file contains only the diagram.

Usage

```
fititcdata(x, y)
```

Arguments

x   a character string of the name of the text file in csv format that has the input
                          data.

y   a character string of the partial name of the output files that will be attached with
                          "0.pdf" and "1.eps".

Details

The input file contains the input parameters for ITC fitting to one to one binding model. This file
is read in as a csv file. An example file "inputparam.txt" is provided in the 'extdata' subdirectory
(folder). Keep the format when modifying.

Nine lines of data in three groups should be listed in the file:

The first group is one line, for the file name of the csv file exported from Origin7.

The second group is experimental set parameters including

P0: protein concentration in cell in mM (the binding partner in cell even if it is not a protein)

L0: ligand concentration in cell in mM (the binding partner in syringe even if it is not ligand)

Asyr: ligand cocentration in syringe in mM (the binding partner in syringe even if it is not ligand)

V0: the volume of the ITC cell in ml

The third group is estimates of the fitting parameters including

K: the binding constant in 1/M

DH: the binding enthalpy in cal/mole

N: the binding stoichiometry ratio, ligand/protein

HD: heat of dilution in ucal for each injection

The following 9 non-blank lines are the content of the inputparam.txt file: file_name, B110711CD4.CSV

P0, 0.00159

L0, 0

Asyr, 0.0181

V0, 1.4347

K, 3E7

DH, -65000

HD, 0.05

N, 0.9

The output file name should not be the same as existing file names, otherwise it will be overwritten.
This can happen especially when calling the function repeatedly with the same second argument.

Value

A vector of the fitting coefficients with names: $"K"$ $"DH"$ $"HD"$ $"N"$

Author(s)

Yingyun Liu

References

Freire, E. 1998 Statistical thermodynamic linkage between conformational and binding equilibria. *Adv. Protein Chem* **51**, 255-279.

Tellinghuisen, J. 2007 Calibration in isothermal titration calorimetry: heat and cell volume from heat of dilution of NaCl(aq). *Anal. Biochem* **360**, 47-55.

Elzhov,T.V., Mullen, K.M. 2010 CRAN - package minpack.lm

See Also

nls.lm, itcONE11

Examples

```
data(data_inputparam1);
data(data_origin1);

## using the loaded data to generate the input parameter file
write.table(data_inputparam1, "inputparam2.txt", quote=FALSE,
col.names=FALSE, row.names=FALSE, sep=", ");

## using the loaded data to generate an Origin7 data file as input
write.csv(data_origin1, "B110711CD4.CSV", quote=FALSE, row.names=FALSE)

## perform fitting
param0 <- fititcdata(x = "inputparam2.txt", y = "itcout");
```

---

importorigin	*Import data from Origin7 ITC data sheet*

Description

The `importorigin` function imports integreted ITC data from csv files. The source csv files can be generated, for example, by exportation from spreadsheets generated after integration in Origin7 ITC module.

Usage

```
importorigin(x)
```

Arguments

x   a character string of the name of the text file in csv format exported from Origin7 ITC data sheet

Value

A list with each column in the input file as one component. Elements in each component are converted to the numeric type. NAs are generated if non-numerical values are present. NAs at the end of each component are deleted. These components are in the list if imported from Origin7: DH,INJV,Xt,Mt,XMt,NDH,B

DH	heat exchange in mcals for each injection
INJV	injection volume in ul for each injection
Xt	ligand concentration in the ITC cell before each injection
Mt	protein concentration in the ITC cell before each injection
XMt	the molar ratio of ligand to protein in the ITC cell after each injection
NDH	heat exchange in cal/mole for each injection
B	heat exchange in cal/mole for each injection, fitting results from Origin7

Note

Origin7 with ITC module is software from Microcal Inc.

References

MicroCal Inc. 1998 ITC Data Analysis in Origin Tutorial Guide, Version **5.0**

See Also

itcONE11

Examples

```
data(data_origin1);

## using the loaded data to generate an Origin7 data file as input
write.csv(data_origin1, "origin_data.csv", quote=FALSE, row.names=FALSE)

## import data
x1 <- importorigin("origin_data.csv");
```

---

itcONE11 *Simulate an ITC reaction with one to one binding model*

Description

The itcONE11 function calculates the heat exchange for each ITC injection with a given reaction system and reaction parameters as input. Here a given reaction system should be two binding partners with known binding affinity and binding enthalpy. The two binding partners should bind to each other according to the one-to-one binding model, although the binding stoichiometry (N) can be adjusted to account for partial inactivity of one binding partner.

Usage

```
itcONE11(varpar = list(K = 1e+06, DH = -20000, HD = 0.1, N = 0.5),
stapar = list(P0 = 0.01, L0 = 0, Asyr = 0.2, V0 = 1.4195), injV0)
```

Arguments

varpar   A list of four parameters:

K, The binding constant, in 1/M, as in K=[AB]/[A]/[B];

H, The binding enthalpy, in calories;

HD, The dilution heat for each injection;

N, The stoichiometry, or the fraction of protein being active in ITC cell;

stapar   A list of four parameters:

P0, The initial protein concentration in ITC cell, in mM;

L0, The initial ligand concentration in ITC cell, in mM;

Asyr, The initial ligand concentration in syringe, in mM;

V0, The volume of ITC cell, in ml;

injV0   A vector of injection volumes for each ITC injection, in ul

Value

A vector of heat exchange per mole of injectant for each injection, in cal/mole

References

Freire, E. 1998 Statistical thermodynamic linkage between conformational and binding equilibria. *Adv. Protein Chem* **51**, 255-279.

Tellinghuisen, J. 2007 Calibration in isothermal titration calorimetry: heat and cell volume from heat of dilution of NaCl(aq). *Anal. Biochem* **360**, 47-55.

See Also

fititcdata, XMt_func

Examples

```
a <- list(K = 1e7, DH = -23000, HD = 0.1, N = 0.9);

b <- list(P0 = 0.02, L0 = 0, Asyr = 0.2, V0 = 1.4195);

injv <- rep(10,30);

dh1 <- itcONE11(varpar=a, stapar=b, injV0=injv);
```

| residNDH11 | *Residual function for fitting ITC heat data to one-to-one binding model* |

Description

This is the residual function required by the `nls.lm` function from the `minpack.lm` package.

Usage

```
residNDH11(p = list(K = 1e+06, DH = -20000, HD = 0.1, N = 0.5),
NDH0, q = list(P0 = 0.01, L0 = 0, Asyr = 0.2, V0 = 1.4195), injV1)
```

Arguments

p	This is the list of fitting parameters with initial values:
	K: the binding constant in 1/M;
	DH: the binding enthalpy in cal/mole;
	HD: heat of dilution in ucal for each injection;
	N: the binding stoichiometry ratio, ligand/protein;
NDH0	Vector of integrated injection heat measured by ITC instrument
q	This is a list of ITC experimental parameters:
	P0: protein concentration in cell in mM (the binding partner in cell even if it is not a protein);
	L0: ligand concentration in cell in mM (the binding partner in syringe even if it is not ligand);
	Asyr: ligand cocentration in syringe in mM (the binding partner in syringe even if it is not ligand);
	V0: the volume of the ITC cell in ml;
injV1	A vector of injection volumes in ul of each ITC injection

Value

A vector of the residual heat for each ITC injection, or the differences between the experimental heat and the calculated heat using the binding modela and the given values of the fitting parameters

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rmlastna	*Delete trailing NA values from a vector*

Description

If there are NA values at the end of a vector, this function deletes them and returns the rest of the vector. This is used to clean up the data imported from Origin7 data sheets.

Usage

```
rmlastna(x)
```

Arguments

x   A vector

Value

A vector with a non-NA value as the last element

Examples

```
x <- rep(2, 20);

y <- rep(NA, 10);

z <- c(x, y);

zx <- rmlastna(z);
```

XMt_func	*Calculation of concentrations of reaction components in ITC cell after each injection*

Description

The `XMt_func` function calculates concentrations of reaction components in ITC cell after each injection based on the input ITC parameters. The molar ratio of the two binding components after each injection is also calculated. This value is usually used as the x-axis in ITC plots. This function is used in ITC simulations and plots.

Usage

```
XMt_func(stapar = list(P0 = 0.01, L0 = 0, Asyr = 0.2,
V0 = 1.4195), injV0)
```

Arguments

stapar	A list of four parameters:
	P0, The initial protein concentration in ITC cell, in mM;
	L0, The initial ligand concentration in ITC cell, in mM;
	Asyr, The initial ligand concentration in syringe, in mM;
	V0, The volume of ITC cell, in ml;
injV0	A vector of injection volumes for each ITC injection, in ul

Value

A list with three vectors:

Mt	vector of protein concentration in cell after each injection
Xt	vector of ligand concentration in cell after each injection
XMt	vector of molar ratio [ligand]/[protein] in cell after each injection

References

Freire, E. 1998 Statistical thermodynamic linkage between conformational and binding equilibria. *Adv. Protein Chem* **51**, 255-279.

Tellinghuisen, J. 2007 Calibration in isothermal titration calorimetry: heat and cell volume from heat of dilution of NaCl(aq). *Anal. Biochem* **360**, 47-55.

See Also

itcONE11

Examples

```
a <- list(P0=0.01, L0=0, Asyr=0.2, V0=1.4195);

injv <- rep(10,30);

dh2 <- XMt_func(stapar=a, injV0=injv);
```

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