# Analyzing Thermal Proteome Profiling experiments by NPARC (Non-Parametric Analysis of Response Curves)

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**Abstract**

This document demonstrates how to analyze TPP-TR (temperature range) experiments by the NPARC approach. NPARC is a recent extension to the *TPP* package. It offers a novel methodology to model the temperature dependent melting behavior of each protein, and to detect significant changes in this behaviour due to changes in experimental conditions like drug treatment [1].

In brief, the melting curve of each protein is represented by natural splines, either once for all conditions (null model), or separately for different experimental conditions (alternative model). Condition specific effects are then detected by testing for significant improvements in goodnes-of-fit of the alternative model relative to the null model.

## Contents

# 1 Installation and input data

This document describes the analysis of TPP-TR data by the NPARC approach. General information regarding package installation and format of the input data is provided in the complementary introductory vignette.

# 2 Getting started

First, we load the *TPP* package by

```
library("TPP")
```

Note that this command only works if the package has been correctly installed beforehand, as described in the introductory vignette.

Next, we load the example data for the analysis (treatment of K562 cells using the clinical HDAC inhibitor panobinostat[2]):

```
data("hdacTR_smallExample")
```

This command loads two objects:

1. hdacTR_data: a list of data frames that contain the measurements to be analyzed,
2. hdacTR_config: a configuration table with details about each experiment.

Now we define the desired output path for the results:

```
resultPath = file.path(getwd(), 'NPARC_Vignette_Example')
```

We start the workflow by typing

```
TRresults <- analyzeTPPTR(configTable = hdacTR_config, data = hdacTR_data,
                          method = "splinefit", nCores = 2, resultPath = resultPath,
                          plotCurves = FALSE)
```

Here, the new methodology is activated by the argument `method = "splinefit"` (available since package version 3.0.0)

# References

[1] Mikhail M Savitski, Friedrich BM Reinhard, Holger Franken, Thilo Werner, Maria Fälth Savitski, Dirk Eberhard, Daniel Martinez Molina, Rozbeh Jafari, Rebecca Bakszt Dovega, Susan Klaeger, et al. Tracking cancer drugs in living cells by thermal profiling of the proteome. *Science*, 346(6205):1255784, 2014.

[2] Holger Franken, Toby Mathieson, Dorothee Childs, Gavain Sweetman, Thilo Werner, Wolfgang Huber, and Mikhail M Savitski. Thermal proteome profiling for unbiased identification of drug targets and detection of downstream effectors. *Nature protocols*, 10(10):1567 − 1593, 2015.