SimThyr CLI 4.0

Manual

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Preface

Thyroid hormones act on virtually any cell of the vertebrate organism. They play a central role in metabolic coordination and differentiation. Robust control of thyroid homeostasis is therefore essential for survival, differentiation and reproduction [1].

In 1936, only seven years after the discovery of the thyrotropic hormone TSH by Aron in the year 1929, Karl Fellinger suggested a negative feedback effect of thyroid hormones on thyrotropic cells of the pituitary [2]. W. T. Salter probably independently postulated the existence of a control loop linking the pituitary and thyroid gland in 1940. His idea was inspired by the then recent description of the two gonadotropic feedback control loops. Only a few years later, Astwood and Hoskins could reveal both the existence and the pathophysiological relevance of this thyrotropic feedback control system. In 1968, Panda and Turner succeeded in a quantitative description of the interdependence of thyroxine and TSH levels, but the first mathematical models of the feedback loop had already been developed up to 12 years earlier [3-6].

Over the years, cybernetic models of thyroid homeostasis were increasingly improved, a success that was enabled by enhanced mathematical modelling methodology as well as growing empirical data. As a consequence of this continued evolution some of the newest models are also suitable for medical decision-making [1, 7-11]. However, due to nonlinear interactions, none of these cybernetic models can simultaneously describe static and dynamic behaviour. This gap may be filled with computer simulations that additionally facilitate an intuitive insight into the dynamics of thyrotropic feedback.

One of the more popular simulation programs for the pituitary thyroid feedback control is SimThyr. Based on a parametrically isomorphic model of the overall system [1, 12-15] SimThyr looks back on more than 25 years of continued development and a plethora of publications cited in PubMed and Web of Science [11-16]. Today, SimThyr is a user-friendly "virtual thyroid" program for modern desktop and server operating systems. Applications of SimThyr cover research, including development of hypotheses, and education of students in biology and medicine, nurses and patients.

Software, source code and additional documentation of SimThyr are available from http://simthyr.sf.net.

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Introduction

SimThyr is a continuous simulator for pituitary-thyroid homeostasis. Pre-compiled Software is available for several mainstream operating systems, and it can also be compiled for additional platforms. SimThyr was developed in Object Pascal with Lazarus and Free Pascal. Source code is provided for all supported platforms and may also be used in order to compile SimThyr for additional platforms.

This document describes the version of SimThyr for command line interfaces (CLI). Please refer to the handbook and reference information for standard SimThyr for usage of the version for graphical user interfaces (GUI).

System Requirements

SimThyr CLI 4.0 should work on every operating system supporting user interaction in dialog mode with a terminal-based interface and software development with modern Object Pascal implementations. This includes nearly every desktop computer, including MS Windows, macOS and most Linux distributions as well as supercomputers, mini, midrange and mainframe systems.

Precompiled binaries are available for macOS and Windows. In order to use SimThyr on other systems please download the source code and compile it for your processor and operating system with Lazarus / Free Pascal.

Installation

Precompiled versions should be copied to the desired location of the file system. Please check the access permissions and make sure that the file is executable.

If precompiled binaries are not available for your platform, please download the source code and compile it for your processor and operating system with Lazarus / Free Pascal.

Uninstalling SimThyr

Before uninstalling SimThyr make sure that the program is not running. Then follow the directions of your operating system to delete the executable.

As required, you may also want to delete scenarios and preferences files.

Source Code

Source code is available from http://sourceforge.net/projects/simthyr. For compiling SimThyr from source please follow the directions given there.

SimThyr Guided Tour

Starting SimThyr

SimThyr is started by entering the command name `SimThyr` in a command line window or *via* a terminal. In many cases, and usually in new installations, it may be necessary to precede the name with a fully qualified folder path description, e. g.:

`/Users/John/Projects/Thyroid/Simulations/SimThyr/simthyr`

Of course, you may want to simply enter `simthyr` to run the program. In order to make this happen you have to add SimThyr's directory to the search path. The following examples show how to do this on Mac workstations, but the steps are very similar in other Unix implementations and in Linux.
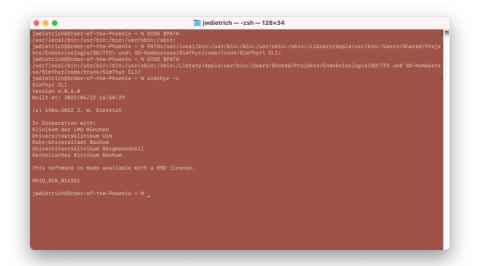
To add SimThyr's directory to the default path simply enter:

`echo $PATH`, copy the result to the clipboard and enter `PATH = `*`<your copied PATH>:<path to SimThyr>`*.

In a concrete example this may be e.g.:

```
echo $PATH
/usr/local/bin:/usr/bin:/bin:/usr/sbin:/sbin:/Library/Apple/usr/bin

PATH=/usr/local/bin:/usr/bin:/bin:/usr/sbin:/sbin:/Library/Apple/usr
/bin:/Users/John/Projects/Thyroid/Simulations/SimThyr/
```
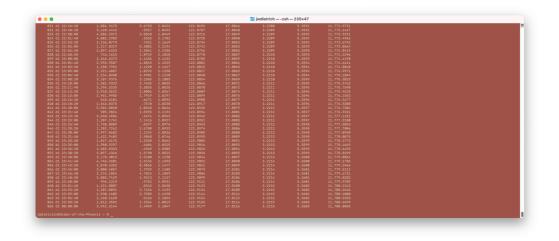

The procedure described above adds SimThyr's location *temporarily* to the search path, so that it is only valid for the current terminal session. In a new session (e. g. after opening a new terminal window) the original default `PATH` is set again. Please follow the instructions of your operating system to *permanently* add SimThyr's

directory to the search path. Usually this is done by editing `.zshrc`, `.bash_profile` or `.bashrc` files in your home directory.

First simulation

For a first simulation enter simply `simthyr` (or a full path qualifier, as described above, if necessary) and hit the enter key. This starts a simulation run under standard conditions for 24 hours:

Small deviations from the depicted results above may ensue from simulated random effects.

You may want to pipeline the results to the `more` filter to get a page-wise display with

`simthyr | more`

Scenarios

Simulation scenarios, e. g. containing a set of structure parameters in certain thyroid disorders, may be stored as XML files and reused. This may be a valuable option for research use, talks or educational purposes. Examples for useful scenarios are sets of structure parameters in certain thyroid disorders and influencing factors in some conditions like pregnancy or critical illness.

Saved scenarios are also an excellent medium to make *in-silico* experiments better reproducible. An increasing number of journals requires submission of open scientific data as a supplement to submitted manuscripts. Scenarios may be helpful for this purpose.

SimThyr CLI uses the same scenario XML file format as the standard GUI versions of SimThyr for macOS, Windows or Linux. You may use a SimThyr GUI version to conveniently edit a scenario file.

Command-line Options

SimThyr takes the following options from the command line:

`-e`

> Show a table with predicted hormone concentrations in equilibrium.

`-i` *switch*

> Starts simulation with (*switch* = "+") or without (*switch* = "-") initial conditions from predicted equilibrium. Standard behaviour is simulation with predicted initial conditions.

`-n` *switch*

> Simulates with (*switch* = "+") or without (*switch* = "-") superimposed noise of the TRH input. Standard behaviour is simulation with noise.

`-p`

> List the values of structure parameters.

`-v`

> Writes version and copyright to the console or terminal.

`-d`

> Provides diagnostic information (e. g. dimensions of the terminal window).

`--duration`

> Simulates the evolution of hormone concentration over the specified time. Examples are:

> | | |
> |---|---|
> | `simthyr --duration 6h` | 6 hours simulated time |
> | `simthyr --duration 3d` | 3 days simulated time |
> | `simthyr --duration 2w` | 2 weeks simulated time |

> The default setting is `--duration 24h`.

`--load`

> Simulates a disturbance beginning at the specified time. Possible loads are a TRH test and a 50% rise in TBG concentration (as observed in pregnancy or on oral contraceptive drugs). The following examples illustrate the notation:

> | | |
> |---|---|
> | `simthyr --load TRH@12h` | TRH test starting after 12 hours |
> | `simthyr --load TBG@6d` | TBG rise after 6 days |

--scenario

Uses an XML-coded scenario for the simulation run. Scenario files can be easily created with the standard GUI version of SimThyr.

Example:

```
simthyr --scenario /Users/John/Test/Thyroid/pilo.xml
```

Appendix

References

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