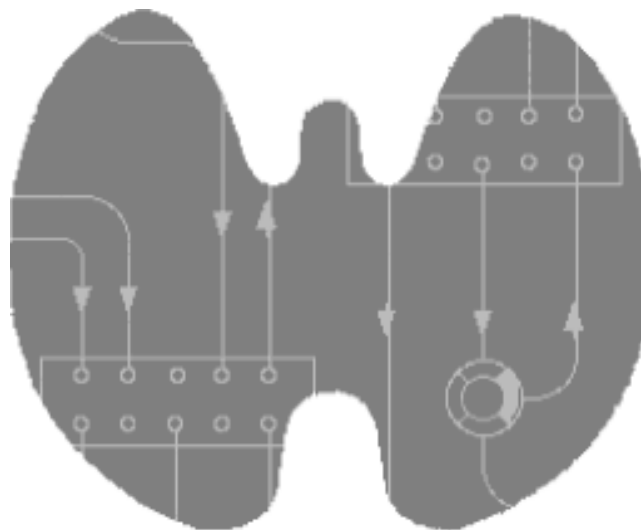


# SimThyr CLI 4.0

---

## Manual



Johannes W. Dietrich

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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 Fellingner 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.

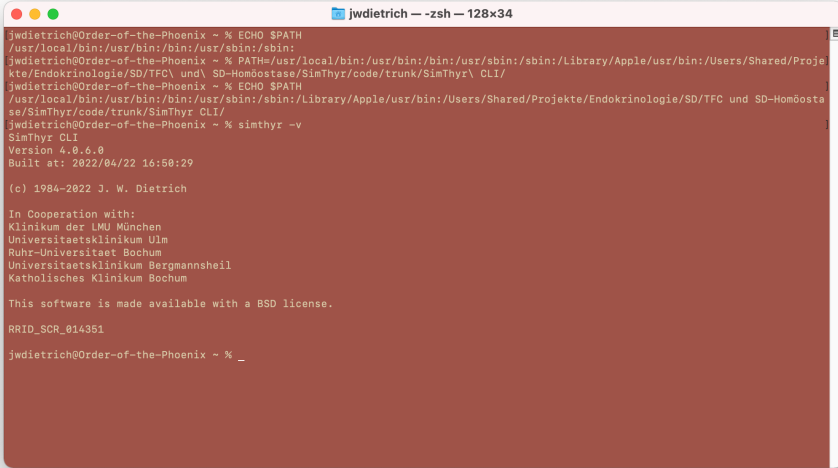
To add SimThyr's directory to the default path simply enter:

```
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/
```



```
jwdietrich@Order-of-the-Phoenix ~ % ECHO $PATH
/usr/local/bin:/usr/bin:/bin:/usr/sbin:/sbin:
jwdietrich@Order-of-the-Phoenix ~ % PATH=/usr/local/bin:/usr/bin:/bin:/usr/sbin:/sbin:/Library/Apple/usr/bin:/Users/Shared/Projekte/Endokrinologie/SD/TFC und SD-Homöostase/SimThyr/code/trunk/SimThyr\ CLI/
jwdietrich@Order-of-the-Phoenix ~ % ECHO $PATH
/usr/local/bin:/usr/bin:/bin:/usr/sbin:/sbin:/Library/Apple/usr/bin:/Users/Shared/Projekte/Endokrinologie/SD/TFC und SD-Homöostase/SimThyr/code/trunk/SimThyr CLI/
jwdietrich@Order-of-the-Phoenix ~ % simthyr -v
SimThyr CLI
Version 4.2.4-8
Built at: 2022/04/22 16:50:29

(c) 1984-2022 J. W. Dietrich

In Cooperation with:
Klinikum der LMU München
Universitätsklinikum Ulm
Ruhr-Universität Bochum
Universitätsklinikum Bergmannsheil
Katholisches Klinikum Bochum

This software is made available with a BSD license.
RRID_SCR_014351
jwdietrich@Order-of-the-Phoenix ~ % _
```

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:

```

jwdietrich --zsh --23x47
00:00:00 1,081,0075 3,4795 2,8122 121,8896 17,8884 3,2268 0,3011 11,772,9771
00:00:05 1,524,4442 3,9227 2,8492 122,8797 17,8848 3,2269 0,3092 11,773,1647
00:00:10 4,080,1972 3,3838 2,8347 122,8716 17,8889 3,2269 0,3090 11,773,1811
00:00:15 4,080,1983 3,3833 2,8347 122,8716 17,8889 3,2269 0,3092 11,773,1956
00:00:20 1,216,0773 3,2051 2,1667 122,8716 17,8855 3,2269 0,3090 11,773,4762
00:00:25 1,212,8339 3,2002 2,1584 122,8742 17,8859 3,2269 0,3090 11,773,4864
00:00:30 2,897,6323 2,3801 2,2385 122,8756 17,8885 3,2269 0,3093 11,774,4639
00:00:35 749,1413 1,4992 2,1528 122,8778 17,8897 3,2228 0,3093 11,774,7294
00:00:40 2,846,6373 1,4405 2,1432 122,8780 17,8899 3,2218 0,3093 11,774,1198
00:00:45 2,956,6887 4,4905 2,1529 122,8811 17,8864 3,2228 0,3094 11,774,9111
00:00:50 1,188,7952 1,4298 2,1627 122,8815 17,8863 3,2218 0,3094 11,774,8848
00:00:55 1,921,6487 4,4905 2,1529 122,8817 17,8864 3,2228 0,3094 11,774,9729
00:01:00 1,154,8788 4,4981 2,1243 122,8848 17,8867 3,2218 0,3094 11,775,1894
00:01:05 1,921,6487 3,4286 2,1893 122,8854 17,8899 3,2228 0,3095 11,775,9923
00:01:10 1,188,9233 3,7455 2,0855 122,8856 17,8871 3,2211 0,3095 11,775,5763
00:01:15 1,926,1243 3,4889 2,0956 122,8878 17,8872 3,2221 0,3095 11,775,7498
00:01:20 1,918,5532 1,4886 2,0857 122,8889 17,8874 3,2211 0,3096 11,775,5625
00:01:25 1,926,1243 1,4793 2,0922 122,8899 17,8876 3,2221 0,3096 11,775,7499
00:01:30 844,6184 4,6771 2,0992 122,8908 17,8877 3,2211 0,3096 11,776,1477
00:01:35 1,926,1243 1,4793 2,0922 122,8917 17,8878 3,2221 0,3096 11,776,2388
00:01:40 1,980,8828 1,4848 2,0824 122,8925 17,8879 3,2212 0,3097 11,776,7381
00:01:45 1,926,1243 1,4793 2,0922 122,8934 17,8880 3,2222 0,3097 11,776,9221
00:01:50 1,944,4586 4,674 2,0963 122,8942 17,8882 3,2212 0,3097 11,777,1152
00:01:55 1,926,1243 1,4793 2,0922 122,8951 17,8883 3,2222 0,3097 11,777,3188
00:02:00 1,778,8889 8,237 2,0976 122,8943 17,8885 3,2212 0,3098 11,777,5853
00:02:05 1,926,1243 1,4793 2,0922 122,8951 17,8886 3,2222 0,3098 11,777,7188
00:02:10 1,997,8842 1,2234 2,0834 122,8945 17,8888 3,2213 0,3098 11,777,8958
00:02:15 1,926,1243 1,4793 2,0922 122,8951 17,8889 3,2222 0,3098 11,778,0389
00:02:20 1,827,1178 1,1289 2,0642 122,8986 17,8891 3,2213 0,3099 11,778,2773
00:02:25 1,926,1243 1,4793 2,0922 122,8986 17,8892 3,2222 0,3099 11,778,4645
00:02:30 1,680,5323 4,4949 2,0895 122,9026 17,8894 3,2213 0,3099 11,778,4493
00:02:35 1,926,1243 1,4793 2,0922 122,9034 17,8895 3,2222 0,3099 11,778,6999
00:02:40 1,926,1243 1,4793 2,0922 122,9044 17,8897 3,2213 0,3098 11,779,4861
00:02:45 1,926,1243 1,4793 2,0922 122,9052 17,8898 3,2222 0,3098 11,779,7188
00:02:50 1,926,1243 1,4793 2,0922 122,9061 17,8899 3,2214 0,3098 11,779,2646
00:02:55 1,926,1243 1,4793 2,0922 122,9070 17,8901 3,2214 0,3098 11,779,2122
00:03:00 1,926,1243 1,4793 2,0922 122,9078 17,8903 3,2214 0,3098 11,779,4721
00:03:05 1,926,1243 1,4793 2,0922 122,9086 17,8904 3,2214 0,3098 11,779,5292
00:03:10 999,1219 4,7814 2,1099 122,9086 17,8903 3,2214 0,3098 11,779,7899
00:03:15 1,926,1243 1,4793 2,0922 122,9111 17,8910 3,2214 0,3098 11,779,7929
00:03:20 1,926,1243 1,4793 2,0922 122,9120 17,8909 3,2214 0,3098 11,779,8264
00:03:25 1,926,1243 1,4793 2,0922 122,9134 17,8909 3,2215 0,3098 11,780,2644
00:03:30 1,926,1243 1,4793 2,0922 122,9144 17,8909 3,2215 0,3098 11,780,2644
00:03:35 1,926,1243 1,4793 2,0922 122,9154 17,8911 3,2215 0,3098 11,780,5353
00:03:40 1,926,1243 1,4793 2,0922 122,9164 17,8911 3,2215 0,3098 11,780,5353
00:03:45 1,926,1243 1,4793 2,0922 122,9174 17,8911 3,2215 0,3098 11,780,8099
00:03:50 1,926,1243 1,4793 2,0922 122,9184 17,8911 3,2215 0,3098 11,780,8099
00:03:55 1,926,1243 1,4793 2,0922 122,9194 17,8911 3,2215 0,3098 11,780,8099
00:04:00 1,926,1243 1,4793 2,0922 122,9204 17,8911 3,2215 0,3098 11,780,8099
    
```

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`

```

jwdietrichOrder-of-the-Phoenix - % simthyr | more
SimThyr CLI
Version 4.0.0.0

Duration of simulated time not set.
Running for 24 hours per default settings.
Iterations: 60.
Simulation started.

i      t      TRH      pTRH      TSH      TT4      FT4      TT3      pncf/L      FT3      cT3
00:00:00 2,580,0000 4,0000 1,8138 121,9379 17,6696 3,2188 0,3087 11,693,7498
00:00:05 1,207,1874 4,0000 1,8138 121,9379 17,6696 3,2188 0,3087 11,693,7498
00:00:10 3,971,3774 4,0000 1,7859 121,9379 17,6696 3,2188 0,3087 11,693,7498
00:00:15 3,289,1551 4,0000 1,7758 121,9379 17,6696 3,2188 0,3087 11,693,7498
00:00:20 4,746,7498 4,0000 1,7628 121,9379 17,6696 3,2188 0,3087 11,693,7498
00:00:25 1,331,1763 4,0000 1,7013 121,9378 17,6696 3,2188 0,3087 11,693,7498
00:00:30 1,626,3897 4,0000 1,7056 121,9376 17,6696 3,2188 0,3087 11,693,7498
00:00:35 2,827,1159 4,0000 1,7812 121,9376 17,6696 3,2188 0,3087 11,693,7498
00:00:40 1,846,7482 4,0000 1,6838 121,9371 17,6696 3,2188 0,3087 11,693,7498
00:00:45 2,451,7488 4,0000 1,6712 121,9367 17,6696 3,2188 0,3087 11,693,7498
00:00:50 786,2589 4,0000 1,6668 121,9362 17,6696 3,2188 0,3087 11,693,7498
00:00:55 2,821,2883 4,0000 1,6283 121,9356 17,6693 3,2188 0,3087 11,693,7498
00:01:00 1,186,2285 4,0000 1,6151 121,9349 17,6692 3,2188 0,3087 11,693,7498
00:01:05 1,444,9936 4,0000 1,6894 121,9342 17,6691 3,2188 0,3087 11,693,7498
00:01:10 2,752,8779 4,0000 1,5674 121,9333 17,6689 3,2188 0,3087 11,693,7498
00:01:15 999,5389 4,0000 1,5571 121,9326 17,6688 3,2188 0,3087 11,693,7498
00:01:20 821,2449 4,0000 1,5218 121,9315 17,6687 3,2188 0,3087 11,693,7498
00:01:25 138,1141 4,0000 1,5865 121,9382 17,6689 3,2188 0,3087 11,693,7498
00:01:30 3,229,3462 4,0000 1,9728 121,9378 17,6683 3,2188 0,3087 11,693,7498
00:01:35 1,862,8351 4,0000 1,4482 121,9277 17,6681 3,2188 0,3087 11,693,7498
00:01:40 2,924,8314 4,0000 1,6020 121,9292 17,6679 3,2188 0,3087 11,693,7498
00:01:45 2,242,6769 4,0000 1,4549 121,9245 17,6677 3,2188 0,3087 11,693,7498
00:01:50 742,1043 4,0000 1,4688 121,9222 17,6676 3,2188 0,3087 11,693,7498
00:01:55 958,3818 4,0000 1,4344 121,9212 17,6672 3,2188 0,3087 11,693,7498
00:02:00 1,921,7078 4,0000 1,4326 121,9210 17,6672 3,2188 0,3087 11,693,7498
00:02:05 2,826,1121 4,0000 1,4813 121,9177 17,6667 3,2188 0,3087 11,693,7498
00:02:10 1,472,2852 4,0000 1,4329 121,9166 17,6667 3,2188 0,3087 11,693,7498
00:02:15 183,8223 4,0000 1,3716 121,9139 17,6663 3,2188 0,3087 11,693,7498
00:02:20 1,926,1243 4,0000 1,3149 121,9119 17,6659 3,2187 0,3087 11,693,7498
00:02:25 1,926,1243 4,0000 1,3344 121,9095 17,6659 3,2187 0,3087 11,693,7498
00:02:30 1,926,1243 4,0000 1,3259 121,9076 17,6659 3,2187 0,3087 11,693,7498
00:02:35 1,926,1243 4,0000 1,3142 121,9053 17,6649 3,2187 0,3087 11,693,7498
    
```

## 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:  
  

<code>simthyr --duration 6h</code>	6 hours simulated time
<code>simthyr --duration 3d</code>	3 days simulated time
<code>simthyr --duration 2w</code>	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:  
  

<code>simthyr --load TRH@12h</code>	TRH test starting after 12 hours
<code>simthyr --load TBG@6d</code>	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
```

```

juedetrich -- ssh -- 23&47
juedetrich@Order-of-the-Pheonix: ~ % simthyr --
simthyr CLI
version v.4.0.0

Prediction:
Predicted concentrations:
TSH:
TPO:
FTI:
FTI:
FTI:
FTI:
Negative values represent virtual solutions delivered by equilibrium polynomials.
Small deviations between predictions and simulated values may result from temporal dynamics including circadian and ultradian rhythms, transition effects and rounding.

juedetrich@Order-of-the-Pheonix: ~ % simthyr --scenario /Users/Shared/Projekte/Endokrinologie/SD/Dejontierung/Simulationen/Thyroida.xml --
simthyr CLI
version v.4.0.0
Using scenario: /Users/Shared/Projekte/Endokrinologie/SD/Dejontierung/Simulationen/Thyroida.xml

Prediction:
Predicted concentrations:
TSH:
TPO:
FTI:
FTI:
FTI:
FTI:
Negative values represent virtual solutions delivered by equilibrium polynomials.
Small deviations between predictions and simulated values may result from temporal dynamics including circadian and ultradian rhythms, transition effects and rounding.

juedetrich@Order-of-the-Pheonix: ~ %

```

## Appendix

### References

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<http://simthyr.sf.net>