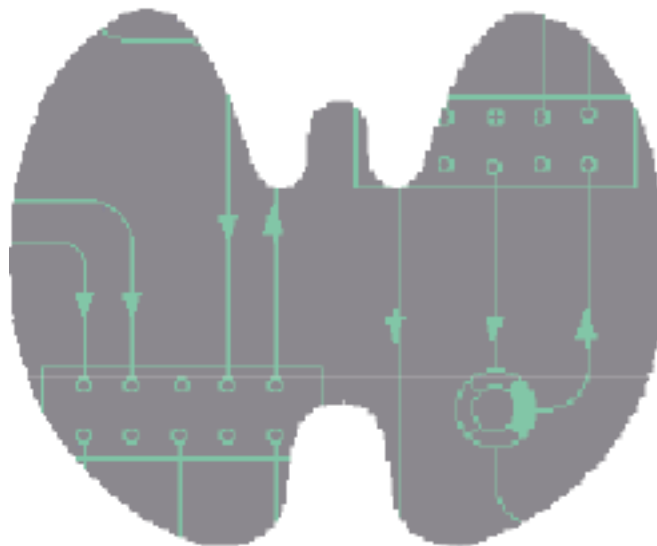


# SPINA Thyr 4.0

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## Handbook and Reference



## Preface

SPINA (structure parameter inference approach) is a cybernetic method for advanced interpretation of laboratory results. It allows for calculating constant structure parameters of endocrine feedback control systems *in vivo* from hormone levels that have been obtained from serum or plasma specimens. The method is based on mathematical and cybernetic modelling of processing structures [1, 2].

A first successful implementation applies to evaluation of thyroid function. It allows for calculating the thyroid's maximum secretory capacity ( $G_T$  or SPINA-GT) and the sum activity of peripheral 5'-deiodinases ( $G_D$  or SPINA-GD) from levels of TSH, (F)T4 and (F)T3 that have been determined once only (SPINA Thyr).

SPINA Thyr has been evaluated in clinical trials covering more than 10000 subjects with various disorders of thyroid homeostasis.  $G_T$  has been demonstrated to correlate with thyroid function [3, 4] and gland volume as obtained via ultrasonography [5]. Its retest reliability is higher than that of TSH, FT4 or FT3 [6].

$G_D$  is reduced in nonthyroidal illness syndrome (NTIS) and increased in states of hyperdeiodination [7-9], and it correlated in two large trials with TSH levels, thus mirroring intracellular cAMP levels [10, 11].

These structure parameters may therefore contribute to diagnosis of rare or at least less obvious thyroid disorders.

In addition to  $G_T$  and  $G_D$  SPINA Thyr is able to calculate TTSI and Jostel's TSH index, two static function tests for the assessment of pituitary function [12, 13].

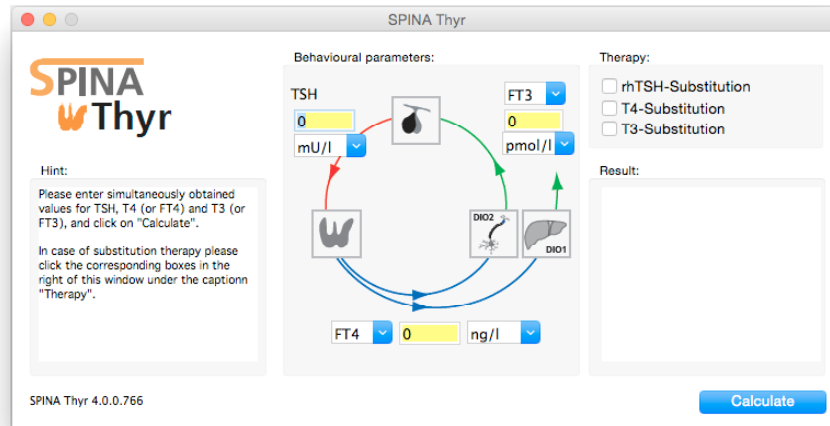
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## SPINA Guided Tour

### Starting SPINA

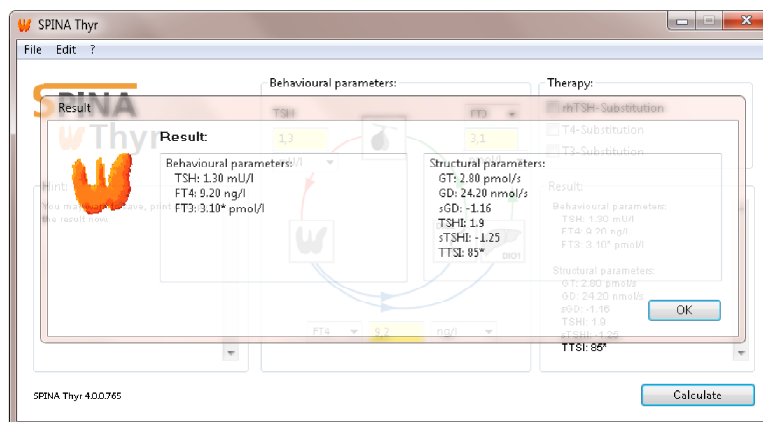
Start SPINA Thyr by double-clicking its icon. After a short while a dialog box asking for hormone values is presented:



When first run SPINA creates a set of new preferences including standard reference values for thyrotropin, thyroid hormones, structure parameters and measurement units.

### Calculating

Before using SPINA it is recommended to check and adjust laboratory methods (i.e. free or total hormones) and measurement units as required. Subsequently you may enter hormone values of your patient or proband and click the button labelled **Calculate**. This will cause SPINA to calculate structure parameters and to display the results in a dialog box.

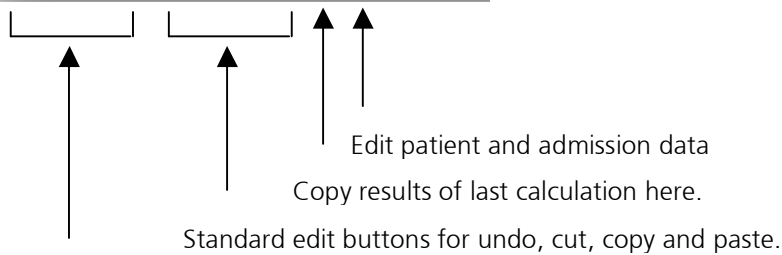


You may want to print the results via corresponding commands from the menu bar or the tool button palette. It is also possible to export results of calculation as text file or HL7 message.

## User Interface

### Toolbar

Most functions of SPINA Thyr are accessible from the toolbar. If you move the mouse cursor to a button and leave it there for a second without clicking, a small tool tip is displayed explaining its function.



File buttons: Create, save and open files, and print results here.

### Main Menu

Additional options are available from the main menu. It will look slightly different on Mac OS, Mac OS X, Windows and Linux. However, the principal functions are identical.



SPINA Thyr menu: Application-wide options, e.g. Preferences and Services (Mac OS X only)

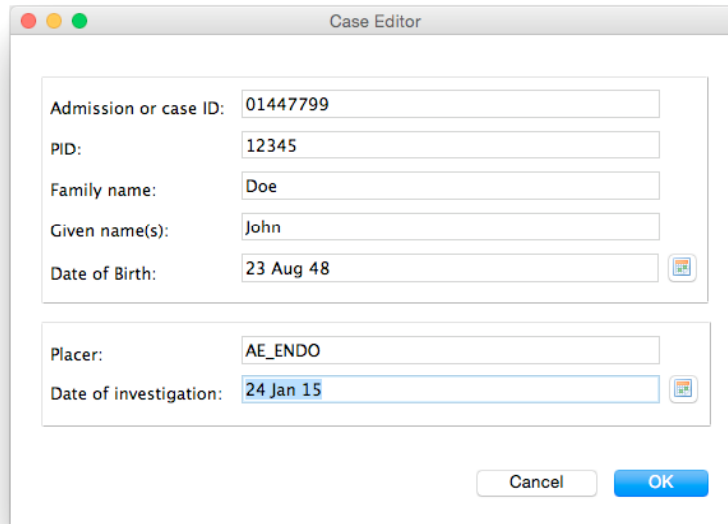
File menu: File- and scenario-wide options, e.g. for opening and saving files and editing case data.

Edit menu: Standard editing options like cut, copy and paste.

Help menu: Help and additional information.

## Case Editor

The case editor provides a user interface for entering patient and case data. Although this functionality is not necessary for basic operation, these data are valuable for printing and for import/export functions.



The screenshot shows a 'Case Editor' dialog box with the following fields and values:

Admission or case ID:	01447799
PID:	12345
Family name:	Doe
Given name(s):	John
Date of Birth:	23 Aug 48
Placer:	AE_ENDO
Date of investigation:	24 Jan 15

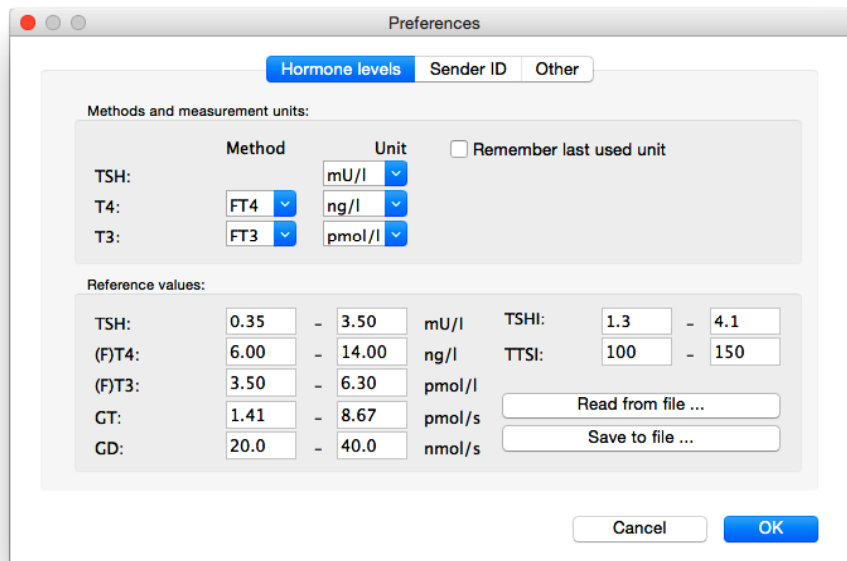
At the bottom of the dialog box, there are two buttons: 'Cancel' and 'OK'.

## Import and export functions

Hormone levels and results of calculations may be read or saved as files. SPINA Thy expects data to be provided as HL7 ORU-R01 messages and it saves data in this format per default. This allows for maximum interoperability with hospital information systems or electronic health records. In addition, it is also possible to export results as text files.

## Preferences

The preferences window (accessible via the application menu on Mac OS X or the edit menu on Windows or Linux) provides you with options to adjust global measurement units and other settings. From this window you may also import reference values from XML files according to the CDISC laboratory data model (CDISC LAB Base model version 1.0.1).



## Important hints

Hormone levels should have been obtained simultaneously in order to avoid bias by transition effects.

Calculating  $G_T$  in patients that are treated with levothyroxine (L-T<sub>4</sub>) is of little, if any, value. Likewise it is not recommended to calculate  $G_D$  in patients that receive substitution therapy with liothyronine (L-T<sub>3</sub>) or triiodothyroacetate (TRIAC). It may be interesting, however, to obtain a value for the unaffected structural parameter in affected cases, e.g. for SPINA-GD in patients on L-T<sub>4</sub> substitution. You may select the appropriate check boxes for substitution therapy in the upper right of the main window in this situation. This causes SPINA Thy<sub>r</sub> to suppress calculation of parameters that would be misleading.

Usage of SPINA implies that you agree to its license and conditions with respect of the council directive 93/42/EEC of the European Union. This information is included with the license file that comes with SPINA Thy<sub>r</sub>, and it is available online from <http://spina.sf.net>.



## References

1. Dietrich JW, Boehm BO: **Equilibrium behaviour of feedback-coupled physiological saturation kinetics.** In: *Cybernetics and Systems 2006*. Edited by Trappl R, vol. 1. Vienna: Austrian Society for Cybernetic Studies; 2006: 269-274.
2. Dietrich JW, Tesche A, Pickardt CR, Mitzdorf U: **Thyrotropic Feedback Control: Evidence for an Additional Ultrashort Feedback Loop from Fractal Analysis.** *Cybernetics and Systems* 2004, **35**(4):315-331.
3. Dietrich JW: **Thyreotoxische Krise [Thyroid storm].** *Medizinische Klinik, Intensivmedizin und Notfallmedizin* 2012, **107**(6):448-453.
4. Midgley JE, Hoermann R, Larisch R, Dietrich JW: **Physiological states and functional relation between thyrotropin and free thyroxine in thyroid health and disease: in vivo and in silico data suggest a hierarchical model.** *Journal of clinical pathology* 2013.
5. Dietrich JW: **Der Hypophysen-Schilddrüsen-Regelkreis. Entwicklung und klinische Anwendung eines nichtlinearen Modells,** vol. 2. Berlin: Logos-Verlag; 2002.
6. Dietrich JW, Landgrafe G, Fotiadou EH: **TSH and Thyrotropic Agonists: Key Actors in Thyroid Homeostasis.** *Journal of thyroid research* 2012, **2012**:351864.
7. Liu S, Ren J, Zhao Y, Han G, Hong Z, Yan D, Chen J, Gu G, Wang G, Wang X *et al*: **Nonthyroidal illness syndrome: is it far away from Crohn's disease?** *Journal of clinical gastroenterology* 2013, **47**(2):153-159.
8. Rosolowska-Huszcz D, Kozłowska L, Rydzewski A: **Influence of low protein diet on nonthyroidal illness syndrome in chronic renal failure.** *Endocrine* 2005, **27**(3):283-288.
9. Han G, Ren J, Liu S, Gu G, Ren H, Yan D, Chen J, Wang G, Zhou B, Wu X *et al*: **Nonthyroidal illness syndrome in enterocutaneous fistulas.** *American journal of surgery* 2013, **206**(3):386-392.
10. Hoermann R, Midgley JE, Larisch R, Dietrich JW: **Is pituitary TSH an adequate measure of thyroid hormone-controlled homeostasis during thyroxine treatment?** *European journal of endocrinology / European Federation of Endocrine Societies* 2013, **168**(2):271-280.
11. Hoermann R, Midgley JE, Giacobino A, Eckl WA, Wahl HG, Dietrich JW, Larisch R: **Homeostatic equilibria between free thyroid hormones and pituitary thyrotropin are modulated by various influences including age, body mass index and treatment.** *Clinical endocrinology* 2014, **81**(6):907-915.
12. Jostel A, Ryder WD, Shalet SM: **The use of thyroid function tests in the diagnosis of hypopituitarism: definition and evaluation of the TSH Index.** *Clinical endocrinology* 2009, **71**(4):529-534.
13. Pohlenz J, Weiss RE, Macchia PE, Pannain S, Lau IT, Ho H, Refetoff S: **Five new families with resistance to thyroid hormone not caused by mutations in the thyroid hormone receptor beta gene.** *The Journal of clinical endocrinology and metabolism* 1999, **84**(11):3919-3928.



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More information and a comprehensive manual are available from <http://spina.sf.net>.