

Manual for Chronos-Fit

Version 1.06

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General Information

We are giving this program away without any charge, in order to support other researchers who work in the same field of research. But in return we appreciate to be cited if you publish any results calculated with the program.

Please cite as follows:

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1. Introduction

Chronos-Fit is a program for detection of rhythmic organisation in arbitrary data, which are recorded over a period in time. Originally it was developed for the evaluation of Ambulatory Blood Pressure Monitoring (ABPM) data (Zuther P, Witte K, Lemmer B. *ABPM-FIT and CV-SORT: an easy-to-use software package for detailed analysis of data from ambulatory blood pressure monitoring. Blood Press Monit. 1996 Aug;1(4): 347-354*). However, the program has now been expanded to other fields of rhythm research: e.g. measurements of activity in humans, radiotelemetric data of blood pressure, heart rate, activity, temperature etc. in animals and data collected otherwise around the clock. Now it can process any type of data. The program performs a Linear Analysis and a Rhythm Analysis. Linear Analysis consists of conventional parameters like Mean, Standard deviation and AUC. Rhythm Analysis performs a partial Fourier analysis of the data. Moreover, modules for group analysis, power spectrum analysis and actograms are implemented.

2. Installation

Chronos-Fit is distributed in two different ways. An EXE installation file and a ZIP file. Depending on your version you need to do the following.

2.1. Installation with an EXE installation file:

Simply run the EXE file named e.g. "Chronos-Fit_1.05_Setup.exe" and follow the instructions.

2.2. Installation with a ZIP file:

Open the file with an unzipping program (e.g. UltimateZip or WinZip).

Create your desired installation directory (e.g. "C:\Program Files\Chronos-Fit").

Copy all files in the ZIP file to this installation directory.

Create a link from "Chronos-Fit.exe" to your Windows Start button (e.g. by dragging "Chronos-Fit.exe" to the desired location).

2.3. Registration

We would like to keep track of people using the program. Therefore a free registration of Chronos-Fit is mandatory. In order to register the program send an e-mail with your name, company, city, country and e-mail adress to support@chronopharmacology.de. You will receive an e-mail with the file 'abpm.cfg' attached. Copy this file to the installation directory of Chronos-Fit (e.g. 'C:\Programs\Chronos-Fit'). Then Chronos-Fit will start regularly.

3. Using Chronos-Fit

3.1. Starting the program

Click on the Chronos-Fit icon on the desktop or the Windows Start button.

3.2. Importing data

Select FILE - IMPORT. In the Open dialog, choose the appropriate File type and select the file you want to import. Subsequently, the data are imported and the evaluation is performed. There are different import filters for the most common ABPM-Devices, the Data Sciences telemetric system and a generic import format. In the following sections each format will be described. If your file extension of your data file does not correspond with the default in Chronos-Fit then type '*.*' in field for the filename and hit <enter>. This will show all available files.

Please note that Chronos-Fit can only handle up to five data sets. Exceeding data sets will be ignored (under certain conditions the program will even crash).

3.2.1. Generic Import format

If data are from a device unsupported by Chronos-Fit, the data can be converted to the generic import format in order to be imported in Chronos-Fit. This conversion can be done with a Spreadsheet program (e.g. Excel or OpenOffice) and/or text editor (e.g. Notepad). To examine the resulting file and find errors (if the data are not imported correctly) the Text Editor is preferable, since it shows the characters exactly as they are and performs no conversion as a Spreadsheet program does.

An example for the generic import format:

```
2003-12-20
SBP,DBP,MAP,HR
11.3167,194.0000,136.0000,108.0000,89.0000
11.7500,146.0000,111.0000,94.0000,92.0000
12.0000,166.0000,126.0000,107.0000,76.0000
12.2500,136.0000,110.0000,97.0000,86.0000
12.5333,149.0000,115.0000,99.0000,77.0000
12.7500,159.0000,122.0000,104.0000,81.0000
13.0000,169.0000,131.0000,113.0000,80.0000
13.2500,184.0000,134.0000,109.0000,85.0000
```

.

.

The first line contains the date of the recording (can be any string with the length of up to 25 characters). In the second line the names of the recorded parameters are given, the first parameter 'Time' is omitted, since it always stays the same. The parameters are separated by commas in this case. But space, tab and any other character which is not a letter, number, ';', '_' or '-' will be treated as separator. Therefore, beware of names for parameters, which contain spaces or special characters.

From the third line the data separated by commas (or the other separator characters) begin. One data set in each line. All values are in decimal format. The decimal separator is the point ('.'). If any error occurs in the conversion of the data e.g. if there is a character value like 'NA', the whole data set is discarded. The data are imported to the end of the file.

3.2.2. Chronos-Fit file format

The Chronos-Fit data file format has the extension '*.AFT'. In this file all the raw data and the evaluation is stored. The internal structure of the file will not be commented on, but the file can be examined with a text editor.

3.2.3. SpaceLabs

Data from the SpaceLabs devices (SpaceLabs Inc., Redmond, USA) are imported with this routine. The file is generated when with the Spacelab software when creating a Report File. These files usually have the extension '.rpt'.

3.2.4. SpaceLabs 2.0

SpaceLabs developed a new software for their ABPM devices, which now runs under Microsoft Windows. It is Version 2.0 and has changed their data format, which now has the extension '.abp'.

This is for importing SpaceLabs GSF Files with the extension '.g'.

3.2.6. DQ-Sort

This is the import routine for the DataQuest program DQ-Sort. DQ-Sort is the older program from Data Sciences International, St. Paul, USA to export data to ASCII format which are collected by the Data Sciences telemetric recording system. The exported files with the extension '*.asc' can be imported to Chronos-Fit with this import routine.

3.2.7. Dataquest A.R.T./LabPRO

The newer Software from Data Sciences LabPRO and A.R.T. has a different format. This filter imports them both. File with the extensions '*.txt', '*.xpr' and '*.xgs' will be shown in the file dialog.

The new version for data extraction from the telemetric system from Data Sciences is the Dataquest LabPRO software. Depending on export settings either '*.xpr' or '*.xgs' are created. The resulting files can subsequently be imported by Chronos-Fit. Upon request the file format from A.R.T 2.1 has been included, which obviously is the successor of LabPRO on the windows system.

3.2.8. Actigraph

Data from the Mini Motion Logger Actigraph from Ambulatory Monitoring Inc. can directly be imported in Chronos-Fit.

The data files usually have the extension '*.dat'.

3.2.9. RR-Text

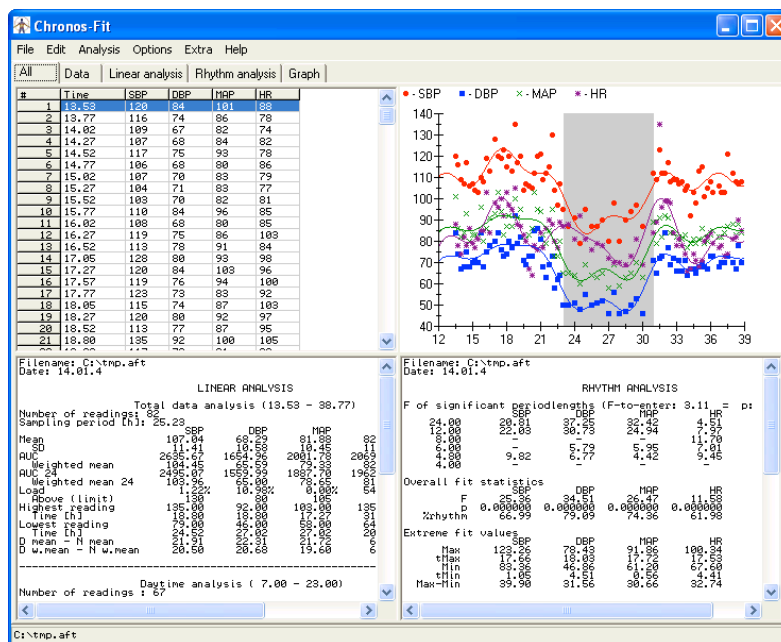
Some long-term ECG devices have the ability to export files containing every heart beat. The data usually look like the following example:

```
1316 2000 2000
1.585938 0.796875 2
2.390625 0.804688 2
3.179688 0.789063 2
3.976563 0.796875 2
4.765625 0.789063 2
5.562500 0.796875 2
6.359375 0.796875 2
```

Whereby 1316 is the starting time 13:16 and subsequently the seconds after this time for each heart beat are given, followed by the distance in seconds to the last heart beat. This way a gap between two heart beats of 0.796875s would be translated to a heart rate of $60/0.796875 = 75.29$ bpm. A file in this format can be imported in Chronos-Fit to perform a beat-to-beat analysis.

3.3. Evaluation of Data

After the data are imported they are evaluated automatically. Then (if the 'All' tab is selected) a summary of the evaluation is shown with data, graphic, Linear analysis and Rhythm analysis. It looks as follows:



Note, that there are different tabs ('All', 'Data', 'Linear analysis', 'Rhythm analysis' and 'Graph') selectable. The 'All'-tab gives a summary with four parts of the evaluation. Each part can be investigated closer by selecting the corresponding tab.

3.3.1. 'Data' tab

This tab shows the data used for the evaluation:

#	Time	SBP	DBP	MAP	HR
1	13.5333	120.0000	84.0000	101.0000	88.0000
2	13.7667	116.0000	74.0000	86.0000	78.0000
3	14.0167	109.0000	67.0000	82.0000	74.0000
4	14.2667	107.0000	68.0000	84.0000	82.0000
5	14.5167	117.0000	75.0000	93.0000	78.0000
6	14.7667	106.0000	68.0000	80.0000	86.0000
7	15.0167	107.0000	70.0000	83.0000	79.0000
8	15.2667	104.0000	71.0000	83.0000	77.0000
9	15.5167	103.0000	70.0000	82.0000	81.0000
10	15.7667	110.0000	84.0000	96.0000	85.0000
11	16.0167	108.0000	68.0000	80.0000	85.0000
12	16.2667	119.0000	75.0000	86.0000	103.0000
13	16.5167	113.0000	78.0000	91.0000	84.0000
14	17.0500	128.0000	80.0000	93.0000	98.0000
15	17.2667	120.0000	84.0000	103.0000	96.0000
16	17.5667	119.0000	76.0000	94.0000	100.0000
17	17.7667	123.0000	73.0000	83.0000	92.0000
18	18.0500	115.0000	74.0000	87.0000	103.0000
19	18.2667	120.0000	80.0000	92.0000	97.0000
20	18.5167	113.0000	77.0000	87.0000	95.0000
21	18.8000	135.0000	92.0000	100.0000	105.0000
22	19.0167	117.0000	79.0000	91.0000	88.0000
23	19.2667	120.0000	82.0000	95.0000	87.0000
24	19.5500	104.0000	71.0000	82.0000	83.0000
25	19.7667	107.0000	69.0000	81.0000	80.0000
26	20.0167	106.0000	73.0000	83.0000	67.0000
27	20.2667	105.0000	73.0000	86.0000	64.0000

Moreover, there are buttons on the right side of the window allowing to save, print and select a subgroup of data. Editing or changing the data is not supported. This was done, since Chronos-Fit is for evaluation only and the original data should not be changed with this program.

3.3.1.1. 'Save' button in data tab

Clicking this button will save the shown data to a text file. This text file will look like the table seen, including the grey fields (Numeration and 'Time', 'SBP', 'DBP',...):

```
# Time SBP DBP MAP HR
1 13.5333 120.0000 84.0000 101.0000 88.0000
2 13.7667 116.0000 74.0000 86.0000 78.0000
3 14.0167 109.0000 67.0000 82.0000 74.0000
4 14.2667 107.0000 68.0000 84.0000 82.0000
5 14.5167 117.0000 75.0000 93.0000 78.0000
.
.
.
```

The resulting file can be used to import the data to a spread sheet program. Selecting 'Open' in the spreadsheet program and then selecting the 'Text' file type will work with Microsoft Excel and OpenOffice. Other programs were not tested.

3.3.1.2. 'Print' button in data table

When you click this button the data will be printed on the printer. No window will open to ask, which printer should be used. In order to change the printer select 'File'-'Print Setup' from the main menu. Here all other printer settings can be changed, e.g. page orientation and printer resolution.

3.3.1.3. 'Fit selected values' button in data tab

When using data from telemetric recordings over several weeks or months and only data over a shorter period (for example one day) are of interest, this button can be used to cut out this period. At first, the data sets of interest must be highlighted. Highlighting works either with the mouse, dragging the mouse

while pressing the left mouse key, or with the keyboard by using the cursor keys while holding the 'Shift' key.

After clicking the 'Fit selected values' button the highlighted values are evaluated and a new window with the evaluation appears which looks like the content of the 'All' tab shown in 3.3.1.

Note that at least $2 * \text{NumberOfHarmonics} + 2$ data sets need to be selected. If 6 Harmonics (which is the pre-set) are fitted, at least 14 data sets have to be selected. Otherwise a 'division by zero' error will occur since no unique solution exists for the equation.

3.3.2. 'Linear analysis' tab

The 'Linear analysis' shown in this tab contains all values calculated from the data such as mean, standard deviation (SD) and area under curve (AUC), as opposed to the non-linear 'Rhythm analysis'. All calculated values are determined for the total recording period as well as for a user defined day- and night-period. (see Analysis options). The tab looks like this:

The screenshot shows the 'Chronos-Fit' software window with the 'Linear analysis' tab selected. The window title is 'Chronos-Fit' and it has a menu bar with 'File', 'Edit', 'Analysis', 'Options', 'Extra', and 'Help'. The 'Data' tab is active, and the 'Linear analysis' sub-tab is selected. The window displays the following information:

Filename: C:\tmp.aft
Date: 14.01.4

LINEAR ANALYSIS

Total data analysis (13.53 - 38.77)
Number of readings: 82
Sampling period [h]: 25.23

	SBP	DBP	MAP	HR
Mean	107.04	68.29	81.88	82.96
SD	11.41	10.58	10.45	11.10
AUC	2635.67	1654.96	2001.78	2069.21
Weighted mean	104.45	65.59	79.33	82.00
AUC 24	2495.07	1559.99	1887.70	1962.53
Weighted mean 24	103.96	65.00	78.65	81.77
Load	1.22%	10.98%	0.00%	54.88%
Above (limit)	130	80	105	80
Highest reading	135.00	92.00	103.00	135.00
Time [h]	18.80	18.80	17.27	31.52
Lowest reading	79.00	46.00	58.00	64.00
Time [h]	24.52	27.02	27.02	20.27
D mean - N mean	21.91	22.31	21.72	6.40
D v.mean - N v.mean	20.50	20.68	19.60	6.30

Daytime analysis (7.00 - 23.00)
Number of readings : 67
Daytime period [h]: 16.00

	SBP	DBP	MAP	HR
Mean	111.04	72.37	85.85	84.13
SD	7.91	6.55	6.62	11.50
AUC	1772.71	1150.26	1362.99	1341.94
Weighted mean	110.79	71.99	85.19	83.87
Load	0.00%	2.99%	0.00%	20.90%
Above (limit)	135.00	85.00	110.00	90.00
Highest reading	135.00	92.00	103.00	135.00
Time [h]	18.80	18.80	17.27	31.52

In this case Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP) and Heart Rate (HR) have been evaluated. The first line shows the file name of the evaluated file, followed by the date of the recording in the second line. The calculated values are explained in the following:

3.3.2.1. Mean / SD

Mean is the arithmetic mean of all values, while SD represents the Standard Deviation of all values.

3.3.2.2. AUC / Weighted mean

AUC stands for Area Under Curve and is the result of connecting all data points by a line and calculating the area between this connecting line and the x-axis. Dividing this AUC by the sampling period (e.g. 25.23 in the example above) yields the Weighted mean. This value is called weighted mean since it includes a weighting for the period in time each reading represents. If values are sampled 4 times per hour during the day and 2 times per hour during the night, the resulting arithmetic mean shows bias towards the day values since they have twice as many readings. In case of a 12h:12h day-night period this is 48 values during the day and 24 values during the night. This bias is avoided by the weighted mean.

3.3.2.3. AUC 24 / Weighted mean 24

Comparing two AUCs which represent different sampling periods e.g. 25h and 27h makes no sense. Therefore the AUC 24 is introduced representing the AUC over exactly 24 hours. It is calculated cutting of the rest of the values after 24 hours. If there is no reading exactly after 24 hours it is linearly interpolated

with the two nearest points. In case the recording is less than 24 hours, the first values is appended at the end. This means that in recordings lasting significantly less than 24 hours the first reading is severely overemphasized. So never use recordings significantly shorter than 24 hours (which is wise when fitting to 24 hour period length, anyhow).

The Weighted mean 24 results from dividing the AUC 24 by 24. Under the assumption that values differ periodically over time (e.g. high day and low night values), calculating a mean in which any of these periods are represented twice introduces a bias towards this period. This bias is circumvented by the Weighted mean 24, since it always uses exactly 24 hours.

3.3.2.4. Load / Above (limit)

The Load is a measure introduced in an attempt to estimate the 'load' the cardiovascular system has to 'carry'. The idea is, that normal blood pressure causes no harm, while elevated blood pressure is harmful. Therefore the percentage of values above a chosen (harmful) limit is calculated. The limit can be changed in Chronos-Fit by selecting Options - Analysis in the main menu.

3.3.2.5. Highest Reading / Time[h]

Here the highest reading and the time of its occurrence is given. This value is prone to error, since quite often it represents an outlier caused by faulty readings. The Maximum in the fitted curve from the 'Rhythm analysis' is preferable, since it is less error-prone.

3.3.2.6. Lowest Reading / Time[h]

Lowest Reading gives the lowest reading of all data and the time of its occurrence. This value is prone to error, since quite often it represents an outlier caused by faulty readings. The Minimum in the fitted curve from the 'Rhythm analysis' is more robust and therefore preferable.

3.3.2.7. Day mean - Night mean

The arithmetic means from the daytime analysis and the nighttime analysis are subtracted from each other (day-night) resulting in this value.

3.3.2.8. Day weighted mean - Night weighted mean

The weighted means from the 'daytime analysis' and the 'nighttime analysis' are subtracted from each other (day-night) resulting in this value.

3.3.2.9. Save button in 'Linear analysis' tab

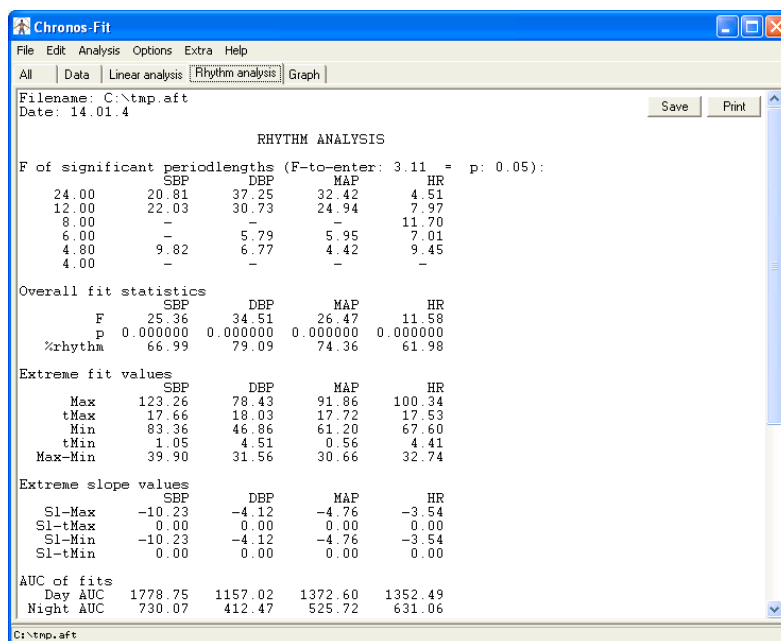
In order to save the whole evaluation page as a Text file click this button. A Pop-up menu will appear asking for the file name.

3.3.2.10. Print button in 'Linear analysis' tab

Click this button will print the evaluation page. In order to select a specific printer or to change printer settings, select File – Printer Setup from the main menu before selecting this button.

3.3.3. 'Rhythm analysis' tab

The 'Rhythm analysis' performed by Chronos-Fit is combination of a partial Fourier analysis and a stepwise regression technique. While conventional partial Fourier analysis always includes all harmonics in the fitted model, the 'Rhythm analysis' fits each harmonic separately and checks significance by F-test for each. The most significant harmonic is then included to the model if it improves the existing model significantly (in the example below at level $p < 0.05$). An example for a 'Rhythm analysis' is shown here:



The first line contains the filename, the second the date of the recording. Then follows the 'Rhythm analysis':

3.3.3.1. F of significant periodlengths

The first section shows the values of the F-statistic for each harmonic. If the F-value is higher than the F-to-enter shown on top (3.11 in this example) then this harmonic is included in the model. F-values lower than this limit result in an exclusion of the respective harmonic, which is represented by the dash sign ('-').

3.3.3.2. Overall fit statistics

The 'Overall fit statistics' are given in the second section. Here the F-statistic for the combined model (including all significant harmonics) is given. From this F-value the corresponding p-value is derived in the next line.

%rhythm is a chronobiological term for the coefficient of determination i.e. the squared coefficient of correlation times 100 ($\%rhythm = r^2 \cdot 100$). It represents the percentage of variation in the data that is explained by the fitted model.

3.3.3.3. Extreme fit values

This section contains the extreme values of the fitted curves i.e. the peak (Max) and trough (Min) with the times of their occurrence. Max-Min gives the difference between the peak and the trough.

3.3.3.4. Extreme slope values

Sometimes, not the absolute level of a measurement, but the rate of change are of interest. For example in blood pressure measurements it can be of interest to determine at which clocktime the fastest increase in blood pressure occurs and how fast the rate is. These values are given in this section. In the example above the fastest rise in systolic blood pressure (SBP) occurs at 6.53 (which is 6:32 since all values are given in decimal format) and has a rate of 10.69 mmHg/hour. The minimal slope occurs at 23.34 (23:20) with slope of -12.76 mmHg/hour.

3.3.3.5. AUC of Fits

The Area under the Curve of Fits represents the Area between the x-axis and the fitted curve. It is given for the defined day- and night-period, as well as for 24 hours. In contrast to the AUC from the 'Linear analysis' this AUC is calculated from the fitted curve and not from the line connecting the readings. The AUC over 24 hours equals the Mesor times 24 (If the fundamental periodlength is set to 24 hours).

3.3.3.6. Mean of fits

Dividing the AUC from above by the period over which the AUC was calculated (e.g. 16 h and 8 h in the case above) results in a mean over this period. The Mean over 24 hours is not given since it is the same as the Mesor given with the Parameters of Fits.

3.3.3.7. Parameters of fits

Fitting the the partial Fourier series is done with the Formula:

$$f(t) = mesor + \sum_{i=1}^S (amplitude_i \times \cos(t - acrophase_i) \times \frac{2\pi}{p_i})$$

where:

mesor = Midline estimating statistic of rhythm

i = counter for the harmonics

S = Number of included harmonics

amplitude = Amplitude of the sinewave

t = Time

acrophase = Acrophase (time of maximum) of the sinewave

p = Fundamental Periodlength (usually 24h)

The corresponding parameters (Mesor, Amplitudes and Acrophases) for the fitted curves are given for each data set.

3.3.3.8. Save button in 'Rhythm analysis' tab

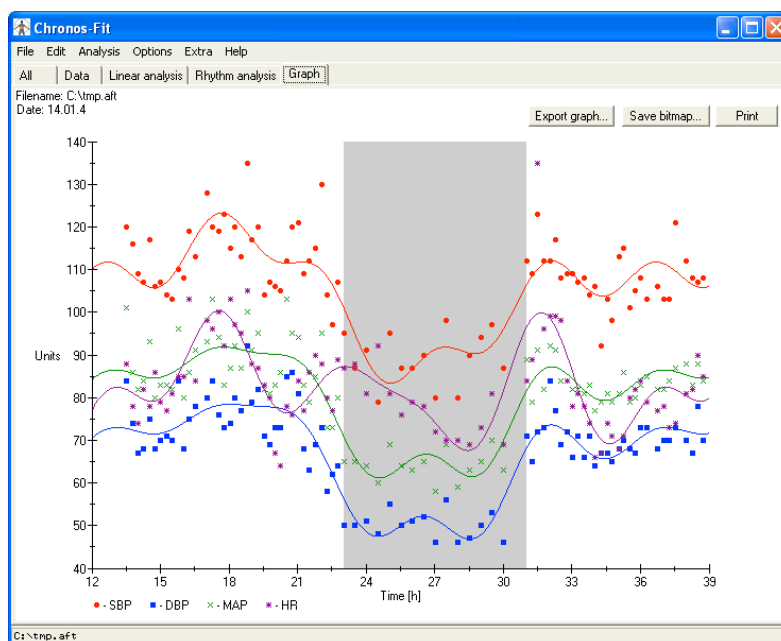
In order to save the whole evaluation page as a Text file click this button. A Pop-up menu will appear asking for the file name.

3.3.3.9. Print button in 'Linear analysis' tab

Click this button will print the evaluation page. In order to select a specific printer or to change printer settings, select File – Printer Setup from the main menu before selecting this button.

3.3.4. 'Graph' tab

In this tab a graph with the readings and the fitted curves is plotted. It is also possible to plot the slopes (first derivative) of the fitted curves, which is not shown in this example:



Settings for the graph can be changed by selecting Options – Graph in the main menu. For further processing of the graph three possibilities exist, which are explained in the following:

3.3.4.1. 'Export graph' button

For further processing in specialized graphical software, the data points can be exported to a text file. The resulting file looks this:

Data Points

Time	SYS	DIA	MAP	HRT
10.6333	146.0000	88.0000	107.0000	75.0000
11.1333	139.0000	93.0000	108.0000	73.0000
11.6333	161.0000	102.0000	121.0000	89.0000
12.1333	136.0000	105.0000	115.0000	86.0000
12.6333	146.0000	90.0000	108.0000	83.0000
13.1333	145.0000	83.0000	103.0000	83.0000

.
.

.

Fits

Time	SYS	DIA	MAP	HRT
9.0000	124.9985	78.8865	94.5314	74.0088
9.2424	124.8762	78.8832	94.2465	71.8352
9.4848	126.1151	79.2679	94.4007	69.9939
9.7273	128.5508	80.0161	94.9840	68.7971
9.9697	131.8908	81.0797	95.9591	68.4650
10.2121	135.7551	82.3905	97.2634	69.0937

.
.

.

The file is splitted in to two sections. The first section giving the data points and the second giving the fitted curve splitted in a number of segments (100 in this case). The 'Number of data points to represent curves' is selectable in Options – Graph from the main menu.

3.3.4.2. 'Save bitmap...' button in 'Graph' tab

Clicking this button allows to save the graph as a bitmap file. First the name and directory of the file has to be chosen in the dialog. Next the file type needs to be selected. Two formats are supported, Windows Bitmap format (BMP) and the Portable Network Graphics format (PNG). Since PNG uses a lossless compression technique and the resulting files are much smaller than the BMP files, it is the recommended file format.

3.3.4.3. Print button in 'Graph' tab

Click this button will print the evaluation page. In order to select a specific printer or to change printer settings, select File – Printer Setup from the main menu before selecting this button.

3.4. Changing Options

It is possible to customize the evaluation process by changing the options. All options available in Chronos-Fit are reachable under Options in the main menu. Moreover it is possible to load and save the options with Options – Load options and Options – Save options in the main menu. On start Chronos-Fit always looks for the file 'chronos-fit.cfg'. If successful, the settings from this file are loaded. This way it is possible to change the presets which Chronos-Fit uses on start-up.

It can be useful to store an options file with a group of evaluated data in order to know which settings have been used for the evaluation.

Note that in order for the changed options to take effect, the evaluation needs to be started manually with Analysis – Recalculate or <CTRL>+R.

Pressing the OK button will make the changes to take effect, the Cancel button will discard all changes made in the dialog.

3.4.1. Analysis options

In this dialogue the settings for the Rhythm as well as Linear analysis can be set. After selecting Options – Analysis the following dialogue screen will appear:

Analysis options

Rhythm Analysis:

Maximum number of Harmonics (1-6): 6

p-to-enter: 0.05

Fundamental Periodlength: 24

Time spans for evaluation of maximal and minimal slope:

Maximal slope between: 0.00 ... 0.00

Minimal slope between: 0.00 ... 0.00

Limits for determination of LOAD (Linear Analysis)

	Total	Day	Night
SBP	130	135	120
DBP	80	85	70
MAP	105	110	95
HR	80	90	70
Data 5	100	100	100

Definitions for day- and night-periods:

Day: 7.00 ... 23.00

Night: 23.00 ... 7.00

Hints:

All time values must be entered in 24h decimal format.

Examples:
 '8:30 p.m.' is entered as '20.5'.
 '7:45 a.m.' is entered as '7.75'

Cancel OK

The screen is divided into several parts. First settings for the 'Rhythm analysis' in the upper left. Settings for the 'Linear analysis' in the lower left and finally setting for the definition of day- and night-period in the upper right.

3.4.1.1. 'Rhythm analysis'

'Rhythm analysis' in the upper left contains all options available in Chronos-Fit.

3.4.1.1.1. Maximum number of Harmonics:

The number of harmonic sine waves included in the model as defined in the formula in Parameters of fits section. The pre-set is six. But under certain conditions, e.g. if only one wave with the period length of 24 hours is of interest, it is useful to change it.

Note, that at least $2 \cdot \text{NumberOfHarmonics} + 2$ data points need to be present. Otherwise no solution exists and the fitting procedure will terminate with a division by zero. A value of 6 means, that 13 parameters are fitted to the curve. Therefore at least 14 data sets must exist.

3.4.1.1.2. p-to-enter

Every single harmonic is tested before inclusion into the model. The level of significance needed to be included is given with this value. The p-to-enter must be between 0 and 1. A setting of 0 means no harmonic is included (resulting in a straight mean line fit). A setting of 1 results in all harmonics to be included.

3.4.1.1.3. Fundamental period length

The fundamental period length can be changed in Chronos-Fit. In older versions this feature was missing. It was introduced to evaluate data organized in monthly or yearly rhythms. However it is not recommended to change this setting, since some parts of the program assume the fundamental period length to be 24h (e.g. night- and day-definitions can be useless).

3.4.1.1.4. Time spans for evaluation of maximal and minimal slope

Maximal and minimal slope sometimes are only of interest within a certain time period. For example if only the maximal increase in blood pressure in the morning between 4 a.m. and 11 a.m. is of interest this time span can be entered here.

3.4.1.2. Limits for determination of LOAD (Linear analysis)

Load values as described in 3.3.2.4 have adjustable limits, which can be changed in this section.

3.4.1.3. Definitions of day- and night-periods

Day- and night-periods are used in both, 'Linear analysis' and 'Rhythm analysis'. The setting from this entry is used throughout Chronos-Fit wherever day- or night-values are used. It is possible to define overlapping periods (day 7.00-23.00, night 21.00-9.00) or periods with a gap (day 9.-21.00, night 23.00-7.00).

Note that all time values must be entered in 24 hour decimal format. Meaning that '8:30 p.m.' is entered as '20.5' and '7:45 a.m.' is entered as '7.75'.

3.4.2. Graph options

Selecting Options – Graph from the main, gives the following dialogue:

	SBP	DBP	MAP	HR	Data 5
Readings:	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Fitted curve:	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Slope:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Scaling:
 Auto scaling Highlight night Use clockhour

Manual scaling
X-Axis: 12 ... 39 Scaling: 3
Y-Axis: 40 ... 140 Scaling: 10

Export of graph to file:
Number of datapoints to represent curves: 100

This is the place where the looks of the graph from section 3.3.4 is adjusted. Three different sections are explained in the following.

3.4.2.1. 'Include in graph'

The first section labelled 'Include in graph:' enables the selection of the data plotted in the Graph tab. It is divided into the Readings (recorded data points), Fitted curve and the slope of the fitted curve. Trying out different selections and viewing the results should explain the meaning pretty well.

3.4.2.2. Scaling

3.4.2.2.1. Auto Scaling

When enabling the 'Auto scaling' function with the respective checkbox, Chronos-Fit will try to determine the best ranges for the X- and Y-Axis. After unchecking, a manual setting in the respective fields is possible.

3.4.2.2.2. Highlight night

Checking the 'Highlight night' will draw a grey shade for the night time in the graph as seen in section 3.3.4. This will simplify the visual inspection of the data with respect to day-/night-patterns.

3.4.2.2.3. Use clockhour

Usually the time on the X-axis is given in continuous hours (23, 24, 25...). Sometimes, however it is desirable to use the clocktimes (23, 0, 1...) which always are between 0-24. This checkbox will influence the x-axis labels to have the desired appearance.

3.4.2.3. Number of datapoints to represent curves

This value will influence the number of segments the fitted curves are represented by, as explained in section 3.3.4.1.

3.4.3. Group analysis options

To change the settings of the group analysis select Options – Group analysis from the main menu. The Group analysis is described in section 4. Please refer to this section for more information on the Group analysis options.

3.4.4. Periodogram options

Select Options – Periodogram to change the settings for the Periodogram as described in section 5. For further information on the options, please refer to this section.

3.4.5. Load options

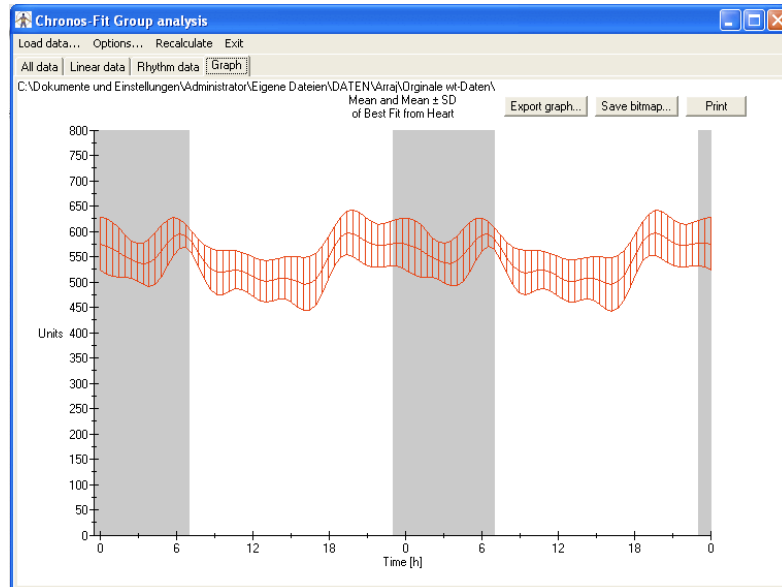
Selection of Options – Load options... allows to load a previously saved options file. Thus the options of an evaluation can be saved together with the data.

3.4.6. Save options

Selection of Options – Save options... allows to save the currently set options to a file. This is useful if the options of the evaluation of a group of data should be saved together with the data in order to be able to reproduce the calculations at a later point in time.

4. Group analysis

Chronos-Fit incorporates a module for group analysis. It can be started by selecting Extras – Group analysis from the main menu. Afterwards, a new window appears. This module works with groups of data. Therefore a group of data need to be loaded first. Here an example:



4.1. Loading data

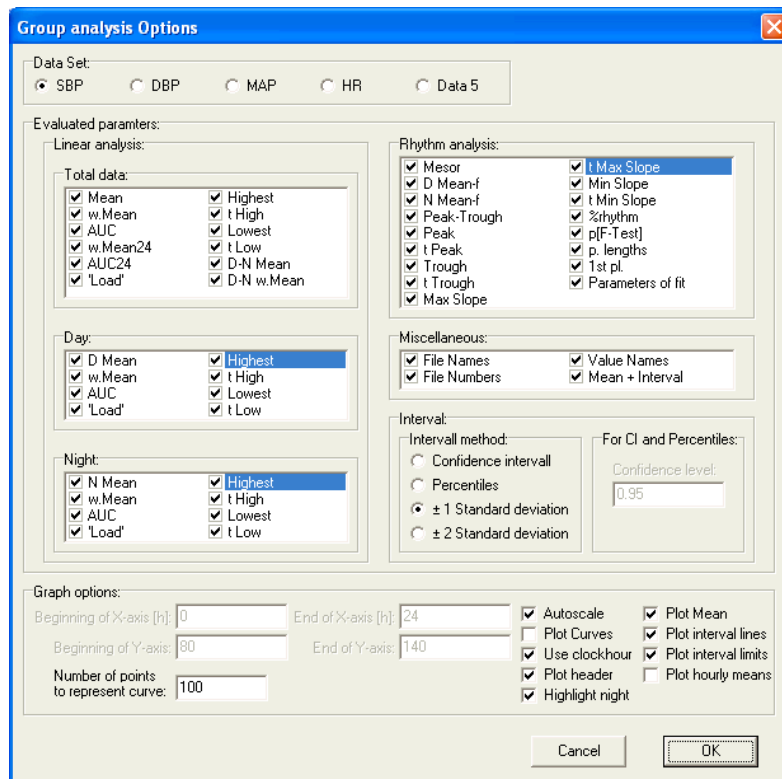
Selecting Load data... from the main menu opens a new window for the selection of a group of data. First the desired directory needs to be specified. Then, a group of file should be specified by entering the desired search mask for the file name, e.g. '*.aft' (without the quotation marks) for all files in the directory with the ending of '.aft' or 'normo??.aft' to load all files beginning with 'normo' then two arbitrary characters followed by '.aft'. Only files saved with Chronos-Fit can be loaded. If a group of data needs to imported and analysed select Analysis - Analyse complete directory... from the main menu in the main Chronos-Fit window.

4.2. Evaluation of Data

The data are evaluated automatically after loading them. If any Options have been changed select Recalculate in the main menu of the Group analysis window. Different aspects of the evaluation can be accessed by four different tabs ('All data', 'Linear data', 'Rhythm data' and 'Graph'). The 'Linear data' and 'Rhythm data' tabs show the values of Linear and Rhythm analyses of all loaded files, while the 'All data' tab shows all data combined. The 'Graph' tab shows a graph of an interval (standard deviation, Confidence interval or percentile) which describes the Rhythm analysis of the whole group. What is shown can be selected under Options... in the main menu of the Group analysis window.

4.3. Options

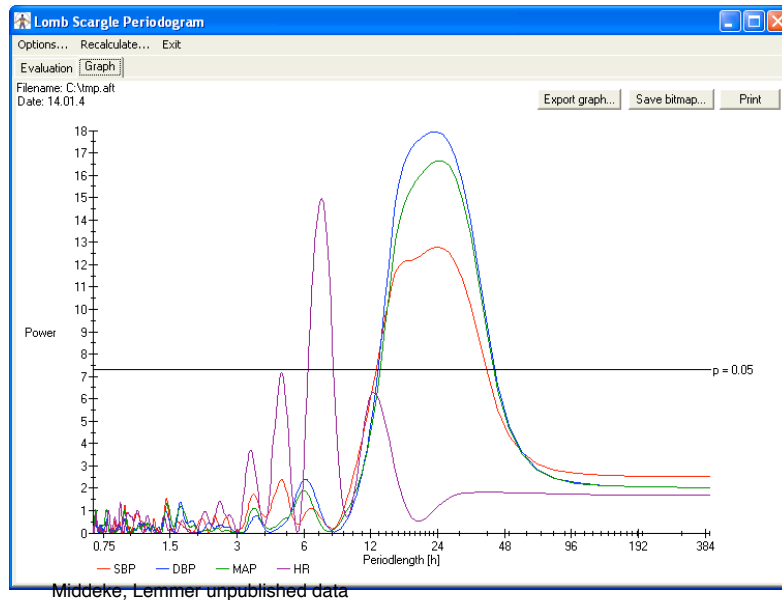
The settings of the Group analysis can be reached either by selecting Options... in the main menu of the Group analysis window or by selecting Options – Group analysis... from the main menu in the main window of Chronos-Fit. The resulting options window looks like this:



This window allow to set the options for the group analysis. The first section determines the data set which is evaluated ('SBP', 'DBP',...). In the second section, the data shown in the 'All data', 'Linear data' and 'Rhythm data' tabs are selectable. The third section refers to the 'Graph' tab.

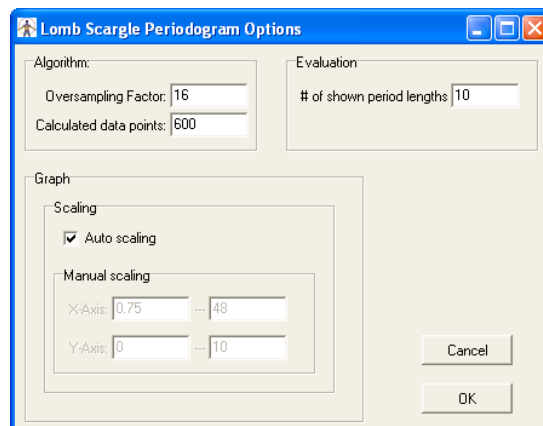
5. Periodogram

Selection of Extras – Periodogram opens a window with a Lomb-Scargle Periodogram (also called power spectrum) of the data. This Periodogram is useful for the detection of significant rhythmicity in the data. On the x-axis the period length of the tested sine wave is given, while the y-axis gives the Power. A line with the significance level of 0.05 is plotted in the graph for visual inspection of significant period lengths. The graph looks like this:



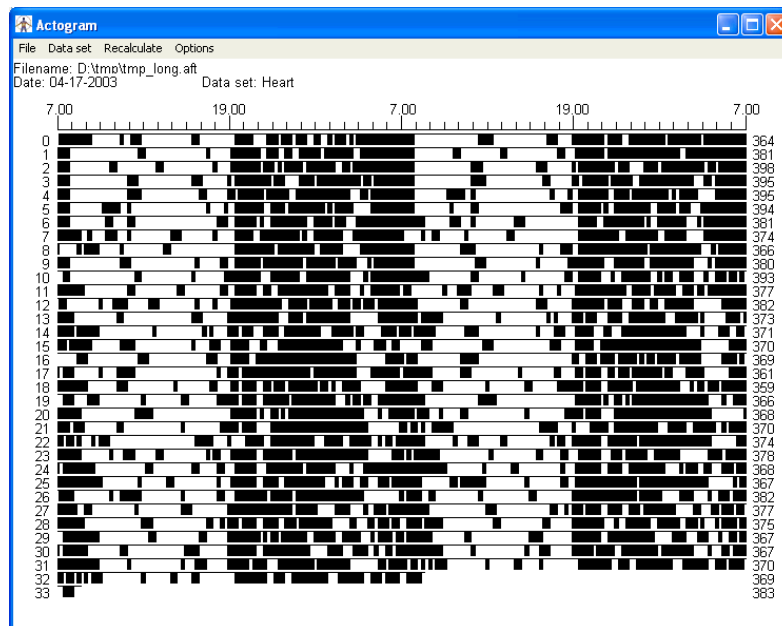
This graph shows significant period lengths of 24h in SBP, DBP and MAP while HR shows a significant period length of 6h. The Evaluation tab gives the 10 highest local maxima of each parameter with the corresponding p-values.

The settings can be change by selecting Options... in the main menu of the Periodogram window:



6. Actogram

For phase shift studies in chronobiological research an Actogram has been introduced, which looks like this:

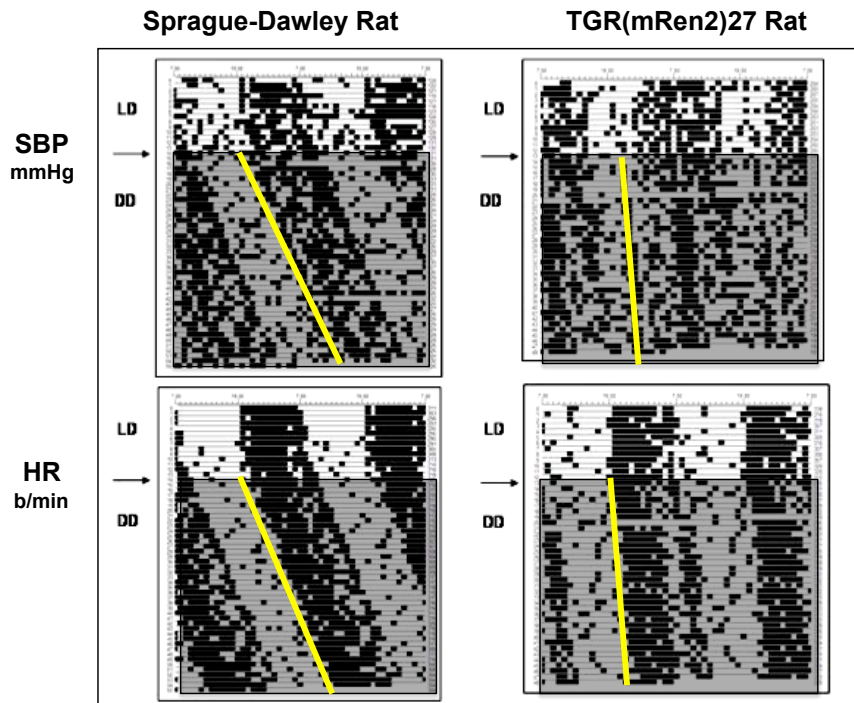


Each line represents two days. In this case numbered from day 0 to day 33 on the left side. On top is the clockhour. On the right is the mean over the day. The black section in each line represents values above the mean of the day, while white sections represent values below the mean. Options can be changed by selecting Options... from the main menu of the actogram window.

7. Examples

Rich and informative graphs can be produced using Chronos-fit and Microsoft Powerpoint:

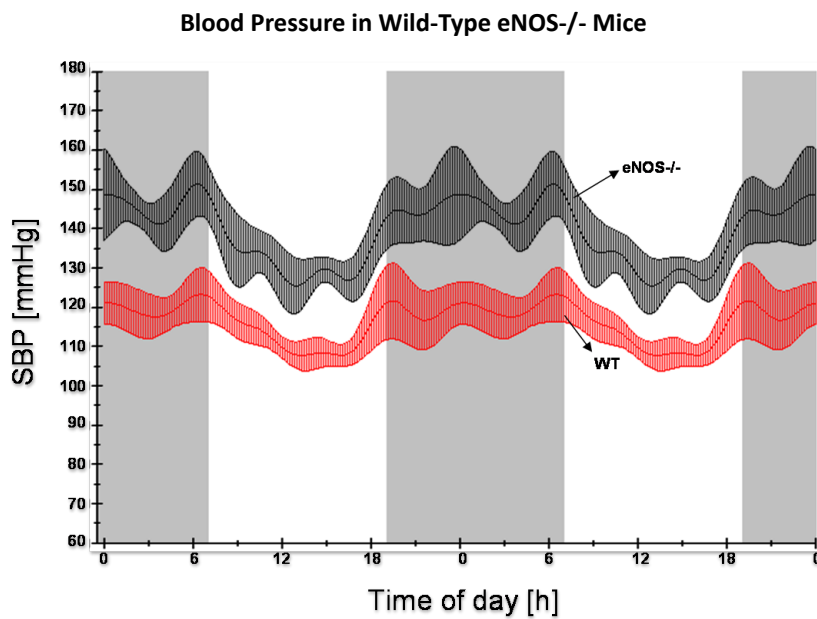
Actograms:



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Lemmer, Pharmacol Ther 111:629, 2006

Group analysis and comparison:

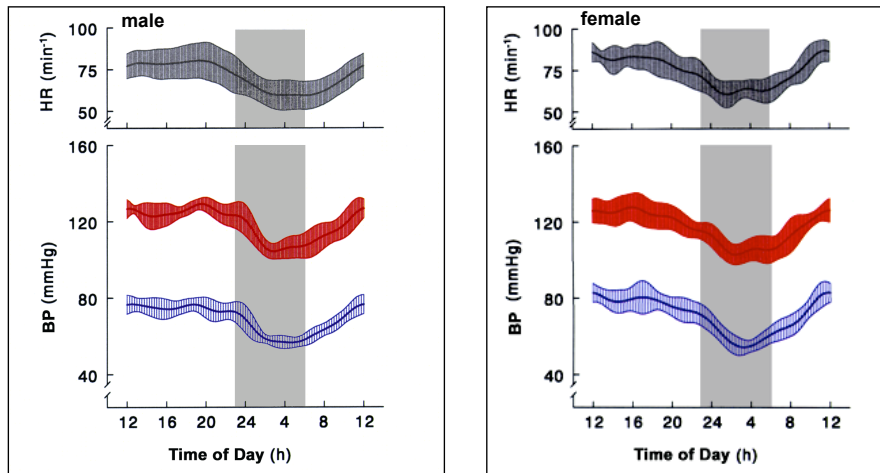


© B. Lemmer

Arraj & Lemmer, Chronobiol Int 24:1231, 2007

Group analysis:

24-Hour Profiles in Blood Pressure and Heart Rate Male and Female Healthy Subjects (21-23 y)

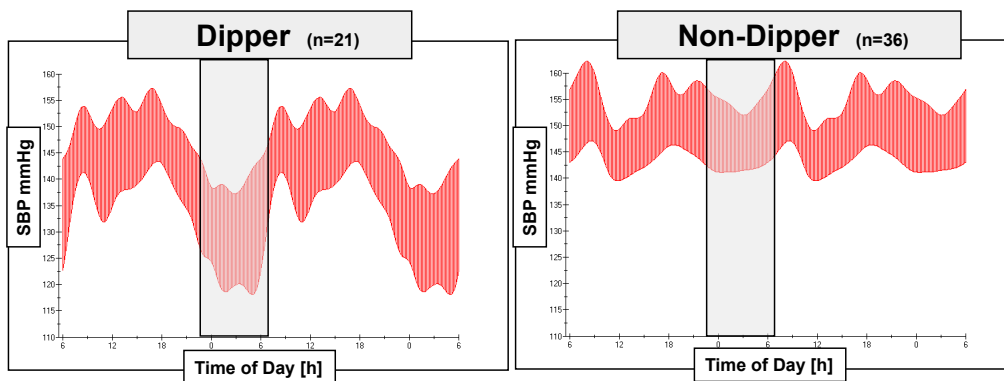


From: Hartig & Lemmer, NS's Arch Pharmacol 367(Suppl 1): R113/438, 2003

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24-Hour Blood Pressure Profiles

95% Confidence Limits from ABPM of (n) Patients

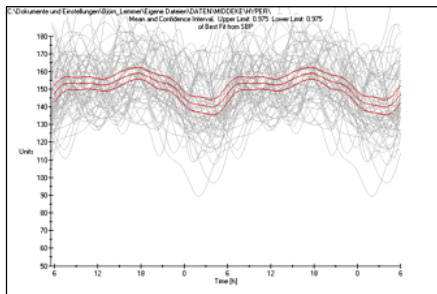


Data from: Nold et al., Blood Press Monit 3:17, 1998, Lemmer et al., AJH 15:109A, 2002

Group analysis:

In addition to the group mean with Confidence interval each single patient is shown

Hypertoniker
n = 71



Normotoniker
n = 41

