



**Axel Semrau®**

## **CHRONOS 4.9**

**CHRONOS**  
Master of Time-efficient Sampling

GIVES YOU MORE TIME  
FOR ESSENTIALS

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The AS logo is located in the bottom right corner of the advertisement, identical to the one at the top left of the page.

Axel Semrau®

The advertisement features a blue background. On the left, there is a partial view of a white clock face with a red needle pointing to approximately 12:15. The numbers 11, 12, and 13 are visible on the clock face. The text 'CHRONOS Master of Time-efficient Sampling' is at the top. Below it, the slogan 'GIVES YOU MORE TIME FOR ESSENTIALS' is written in a lighter blue font. At the bottom, the copyright notice '© AXEL SEMRAU 2007-2018' and the AS logo with 'Axel Semrau®' are present.

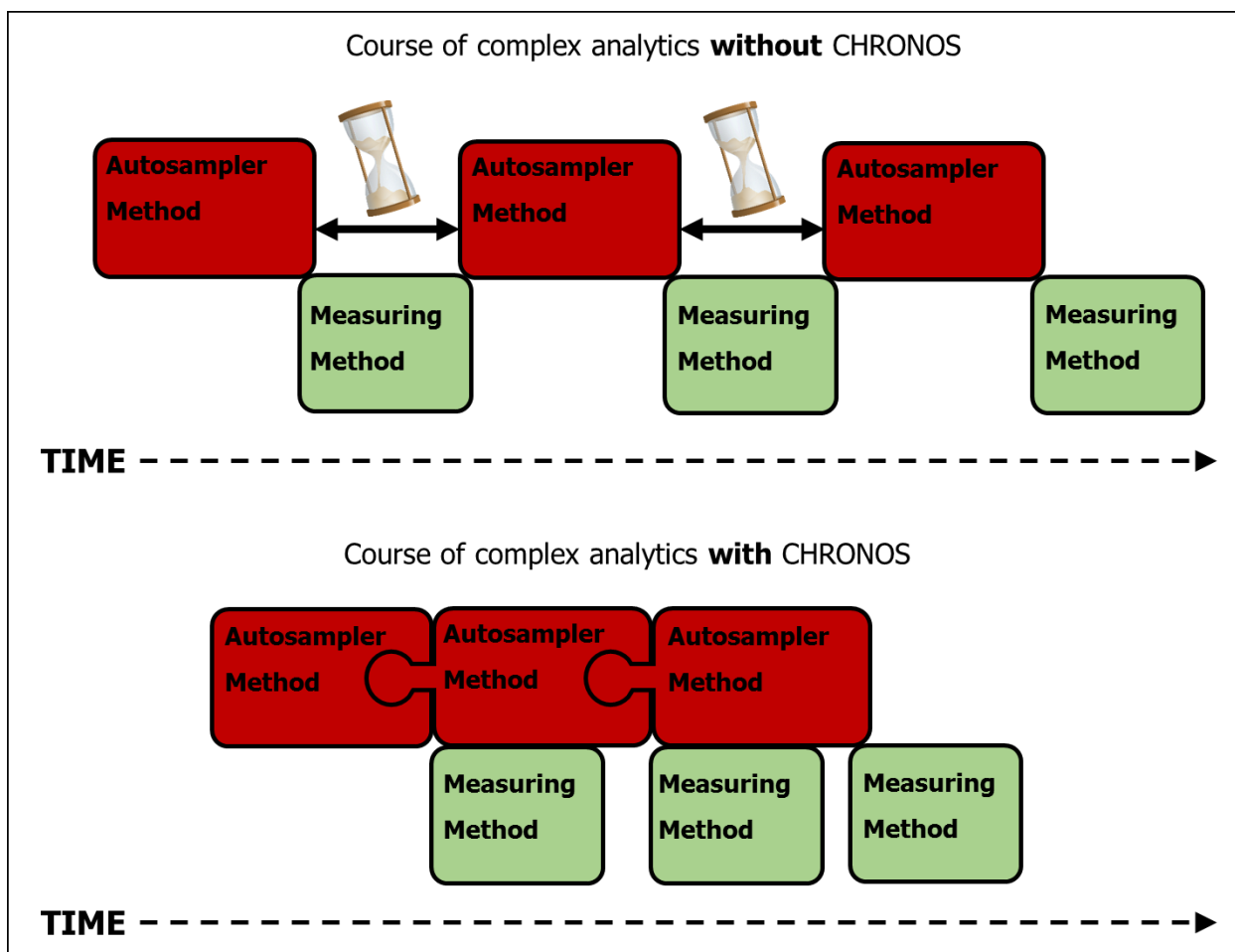
**Product Information**

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**Automation is an important topic in chromatographic laboratories. A decrease in the number of personnel and increasing requirements in parallel to that make automation necessary whenever possible. Requirements such as decreasing the turnaround time (TAT) or the introduction of lean management concepts cannot be fulfilled without high-performance automation approaches.**

Apart from considerations of efficiency, automation has the advantage that the precision of the analytics increases, since individual errors due to manual steps are reduced. CHRONOS is a software solution that offers extensive automation options and helps you to overcome the challenges of daily laboratory operations in a simpler and better way.

One of the particular strengths of CHRONOS is the automation of complex methods of analysis. This includes methods in which the automated samples preparation by the autosampler consumes considerably more time than the actual analysis.



**Figure 1:** Scheme of the saving of time during a complex analytical method without and with the use of CHRONOS for sample preparation.

One of the particular strengths of CHRONOS is the automation of complex methods of analysis. This includes methods in which the automated samples preparation by the autosampler consumes considerably more time than the actual analysis.

This results in waiting times in the analytic system; waiting times are minimized by the optimization of the temporal sequence of the sample preparation steps and the efficiency of the analytic system can be significantly increased.

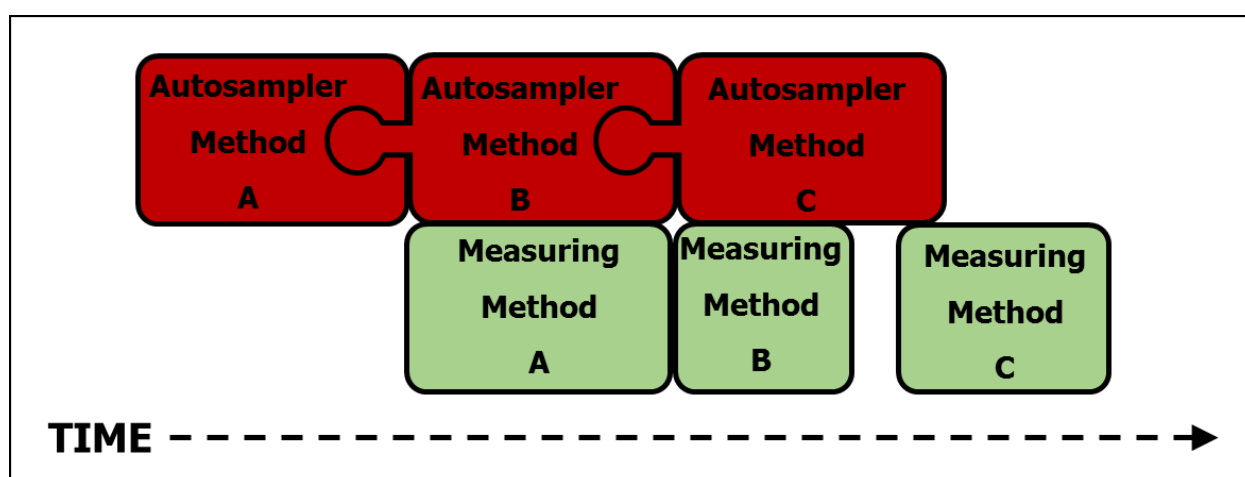
That is precisely what CHRONOS does and it accelerates the sample preparation by means of intelligent control. The time gained depends on the sample preparation time and the number of samples. The longer the sample preparation takes and the more samples there are, the greater the time gained by the use of CHRONOS.

### CHRONOS - the master software

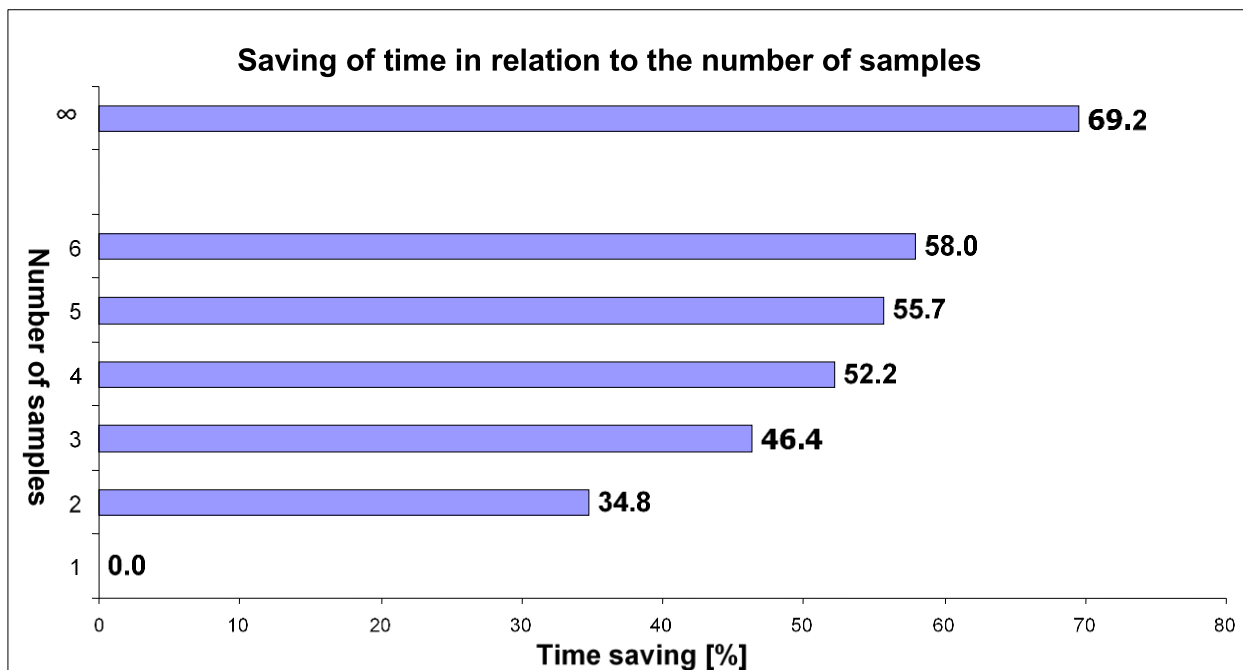
CHRONOS is a master software because it not only controls your autosampler in the most effective way possible, it also starts the data recording of your GC or LC device. Thus, with an increasing number of samples and complex analytics, a considerable saving of time can be achieved by the use of the CHRONOS software. If you look at the illustration above, you remove the superfluous hourglasses from the picture with CHRONOS.

What is unique here is that various methods with different sample preparation times by the autosampler are also nested with one another by CHRONOS in such a way that the total expenditure of time for the sequence is minimized.

Imagine you are playing the well-known Tetris game and the different blocks are time stones. CHRONOS is then that player who fits these blocks together without gaps (time gaps) and ensures that the time is optimally filled out (full utilization of your system).



**Figure 2:** CHRONOS interlaces even different autosampler methods using the same configuration, reducing unnecessary idle time.



**Figure 3:** Example of the saving of time with a headspace GC-MS analysis in relation to the number of samples (60 min incubation time and 25 min analysis time).

## The method editor

### Why does CHRONOS simplify the operation of your system with complex functions?

With CHRONOS the sample list can be arranged flexibly in the method editor.

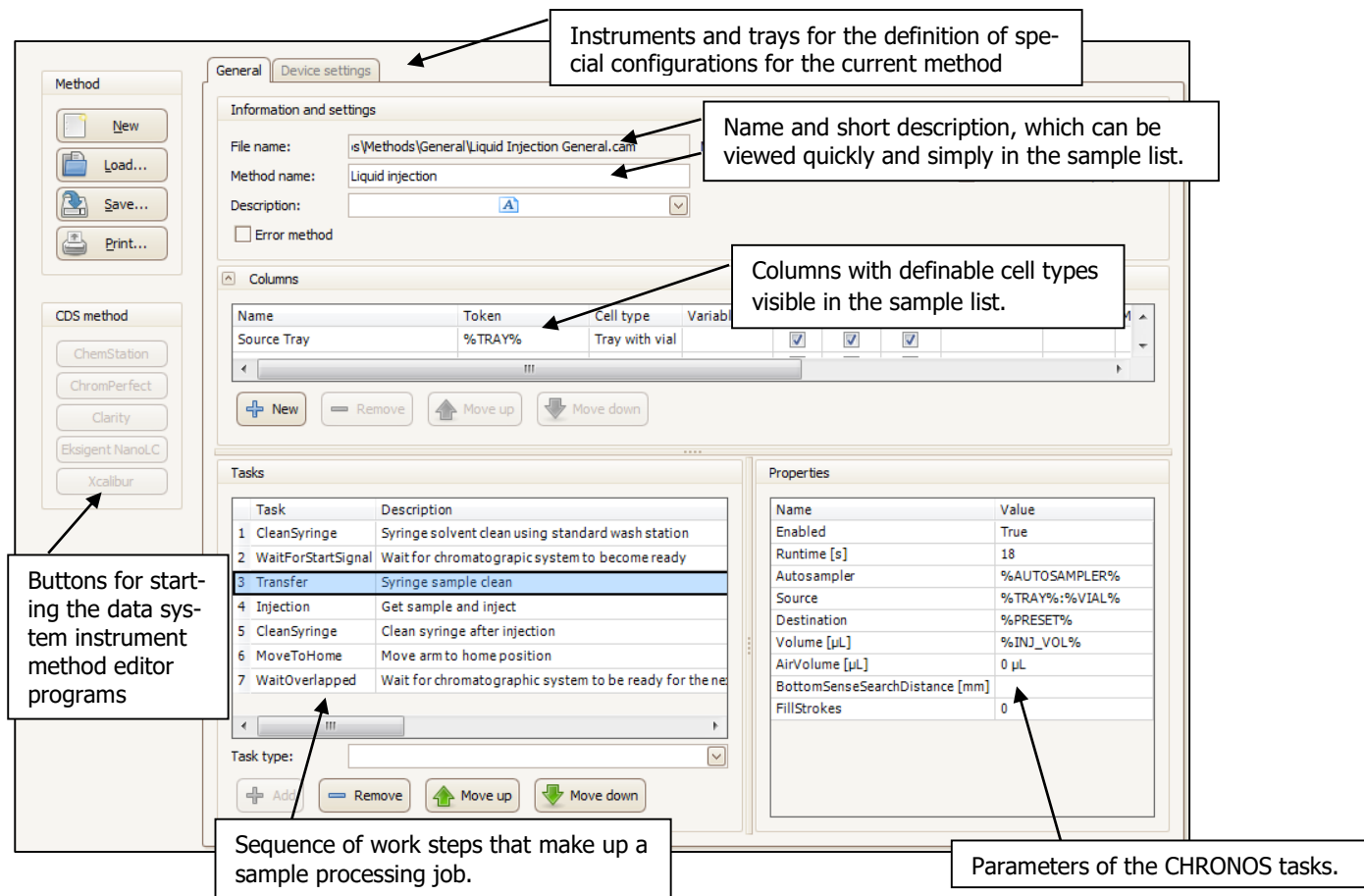
The freely definable column entries can be released for inputs, but they can also be locked or hidden. The number of changeable parameters can thus be minimized to what is absolutely necessary, e.g. the sample name, if the same method is used in routine operation and all other parameters are fixed.

However, in the case that, for example, different injection volumes or specific running times are required for each sample (e.g. different equilibration times), then a selection list for the sample list or the free input of the values in the subsequent sample list can be accomplished very simply in CHRONOS.

With CHRONOS you can devise individual methods from a list of so-called TASKS (work steps for the autosampler).

Following the choice of a task you can describe it for the purpose of clarity. Individual parameters for the task are specified or defined as variables, as shown in figure 4. CHRONOS enables the creation of complex automation methods in a simple, intuitive way. The clarity of complex methods is retained by the hiding of parameters that are not required.

Example: when pipetting liquid into a vial, which is described by the transfer task, CHRONOS performs the procedure necessary for this step automatically - for example, for a volume addition of 15 µL of liquid with a 10 µL syringe - and drives twice from the storage container to the sample.



**Figure 4:** Method editor: The individual work steps (tasks) and the sequence of the autosampler method with the specific properties and characteristic values can be found at the bottom left. The fields of the sample list, whose values can be set to 'editable' or 'not editable', are located in the top part of the method editor. The specific configuration for the method, which is stored with the method, is defined on the 'Device settings' ('Instruments' and 'Trays') tab.

### Transfer of the sample list from CHRONOS to the chromatography data system

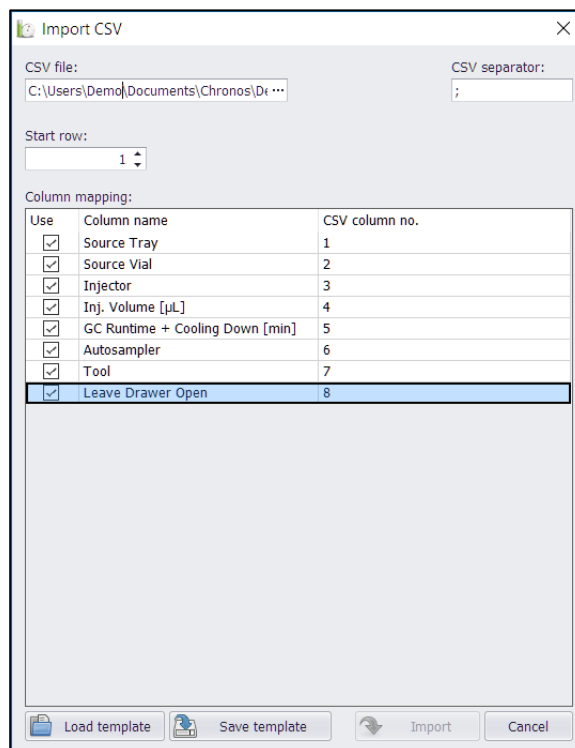
CHRONOS allows you to create your sample list very flexibly and very simply.

This sample list also includes the corresponding data recording method (e.g. MasterLAB, Clarity, Xcalibur or ChemStation method). Double entries of sample lists are superfluous with CHRONOS, because CHRONOS controls your autosampler and also transfers the measurement job to the data system.

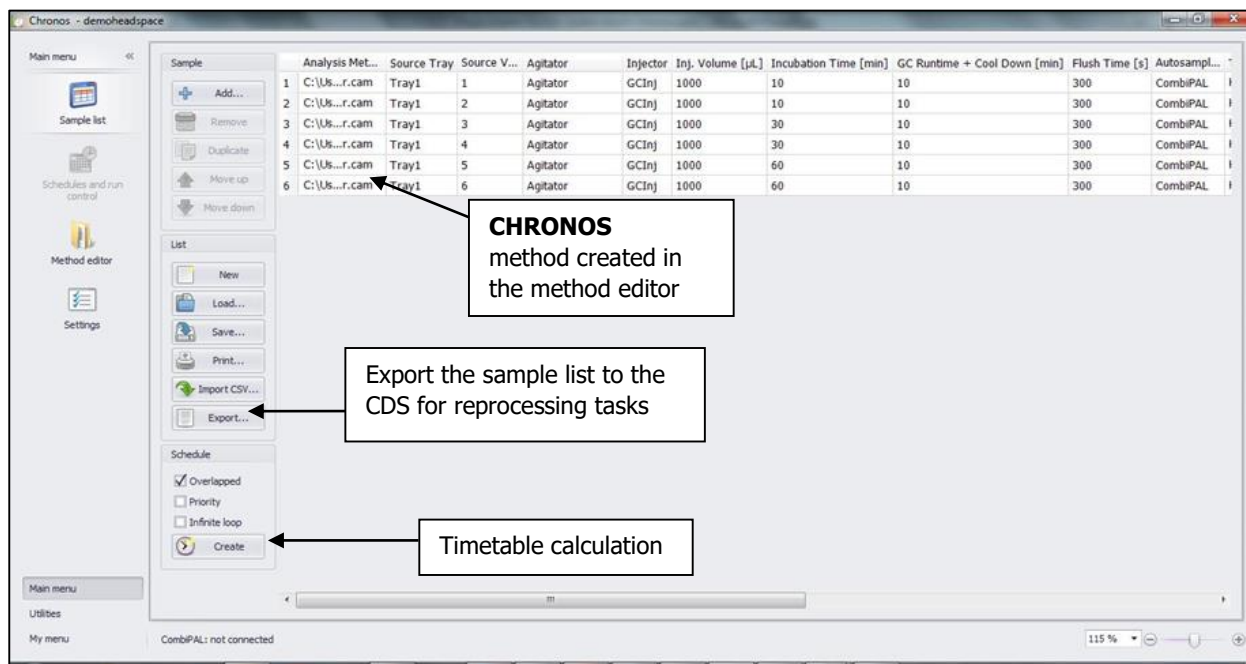
The sample list can be saved and read in Excel at a later time. Saved sample lists can also be imported back again in exactly the same way. Alternatively, CSV files may be saved and read. It is very simple to selectively adopt sample information into the sample list from CSV files provided by a LIMS.

Thus, CHRONOS becomes a universal interface between chromatography data systems and LIM systems. The seamless integration in LIM systems is shown in particular in combination with LABSQU; sample lists can be retrieved from this LIMS directly by web service. The simple tabular form permits the moving, copying, deletion, incrementing and marking of individual lines, which are then included alone as marked samples into the timetable calculation.

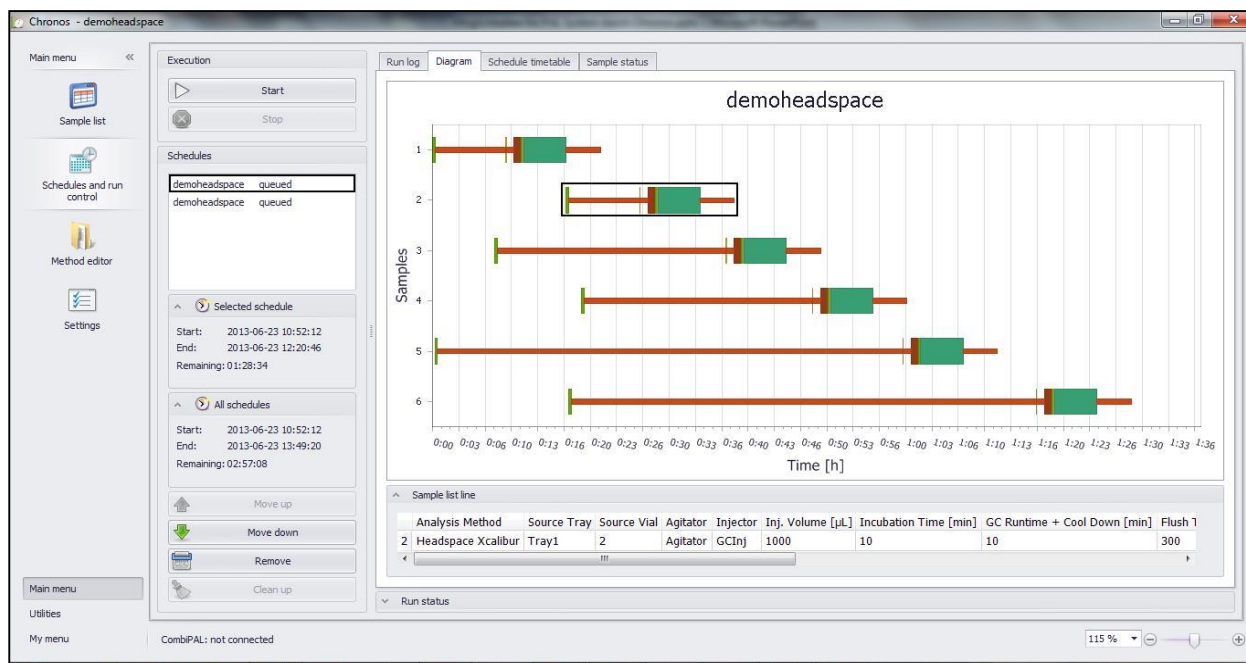
Convenient auto-fill functions enable the fast creation of the sample list. For the later editing of your measured data the sample list can then be simply exported to your chromatography or spectrum analysis system (e.g. Xcalibur, Agilent, ChemStation).



**Figure 5:** CSV import tool for the import of data from LIM systems.



**Figure 6:** Sample list with analysis method, sample name and evaluation data file. The editable values can be selected in the method editor.



**Figure 7:** Display of the timetable created by CHRONOS (nested processing of the steps where the bars overlap) for a headspace GC-MS analysis. It is easy to switch between the diagram and the timetable. The illustration shows a timetable created by CHRONOS for a headspace GC-MS analysis with different incubation periods. It can clearly be seen that first sample 1, then sample 5 and only then sample 2 is placed in the headroom oven in order to ensure optimum use of the time.

After inputting the sample list, CHRONOS calculates the optimal timetable for your analyses. The result is displayed graphically by horizontal bars. The x-axis represents time and the y-axis the individual samples. Vertical bars indicate the activities of the autosampler, e.g. moving to another position, injection, etc. These steps can be distinguished from one another by differently colored bars. The size of the bars corresponds to the necessary time for the work step. If you move the mouse pointer over the bars, the respective work step (task) becomes visible. The analysis progress is visualized by a large horizontal progress bar.

There is an option to process several timetables in succession. In this way it is possible to add further samples while an analysis is running. Timetables can be marked as priority timetables; these are then processed after the completion of the current timetable.

An intelligent termination functionality allows a running timetable to be aborted; however, samples whose processing has already started will be completely measured first. An immediate abort is alternatively possible.

For simple analysis tasks (e.g. liquid injection) it is possible to do without the time optimization and to force a classic sequential control (one step after another). Under 'Schedule timetable' you can find the exact timetable in the form of a list of all of the individual work steps with the optimized time and duration of each step.

In addition, CHRONOS creates a log file. This text file allows the individual steps to be retraced at defined times of the autosampler even after the entire sample list has been processed.

A flow diagram with the current work step (status) being processed by your autosampler and the time remaining for this step can be found under the menu option 'Sequence'.

The possibility to connect your evaluation software with CHRONOS makes it a universal interface for chromatography in general.

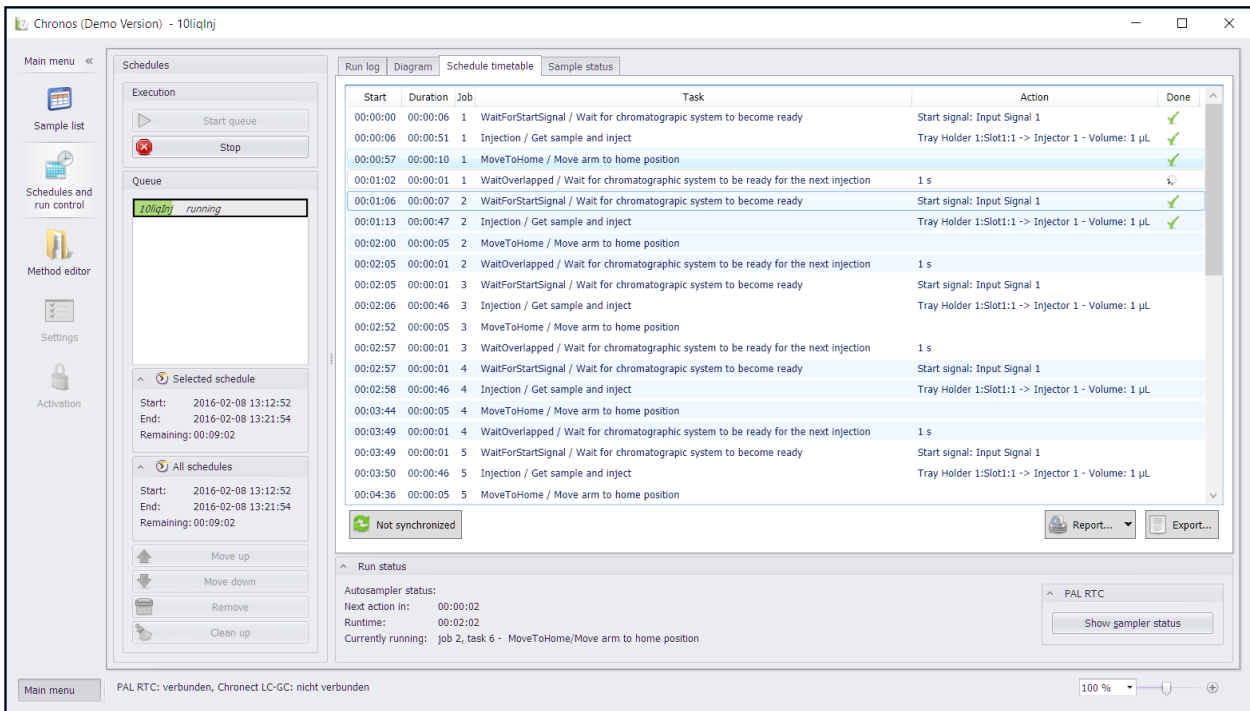


Figure 8: Schedule timetable of the CHRONOS timetable.

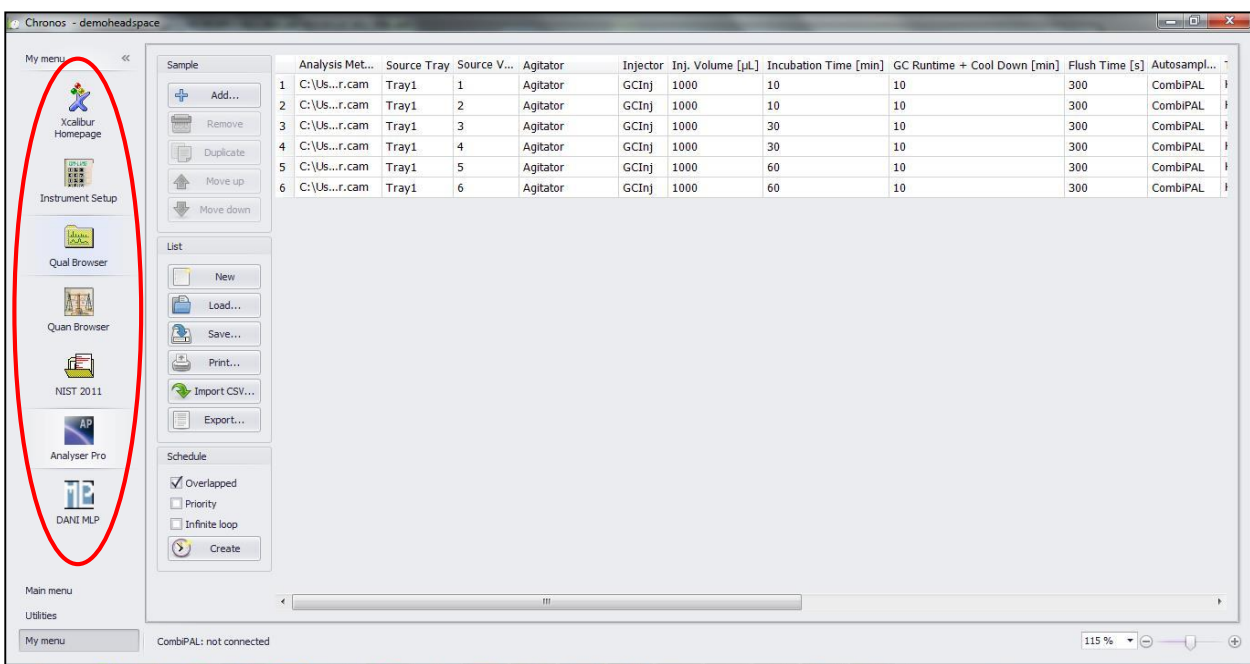


Figure 9: Access to the evaluation software via CHRONOS.



## What advantages does CHRONOS offer?

### Advantages in the control of the autosampler

CHRONOS optimizes your autosampler's complex work sequences so that your PAL does not stand idle even when the GC(-MS) or LC(-MS) system is analyzing the prepared samples. Whereas samples are otherwise processed in series, leading to waiting and idling times for the autosampler, the intelligent algorithm of CHRONOS enables these processes to be processed in parallel and thus leads to a considerable acceleration without a loss of precision or reproducibility.

The CHRONOS software thus increases the throughput of your automated systems by parallelizing the work processes of your autosampler and in this way increasing the extent of utilization.

This is comparable with the acceleration of a personal computer by installing several processors, intelligently distributing the tasks and processing them in parallel in order to significantly increase the processing power of the computer.

### General advantages of CHRONOS

The possibility of using CHRONOS to switch Valco valves, to call evaluation programs from measurement methods and to import results from balances via the serial interface gives rise to a large number of possibilities to automate cumbersome routine tasks in the laboratory. CHRONOS is more than just an intelligent autosampler controller - CHRONOS is a flexible automation tool for the analytic laboratory.

CHRONOS can contribute toward laboratory efficiency not only in the control of devices and preparation of samples; other processes in the laboratory are also supported by CHRONOS. Thus, it is possible in case of autosampler errors, for example, to inform the user by short message service or e-mail and to transmit the error message (e.g. 'vial not found') by plain text. This allows fast intervention by the laboratory employee.

CHRONOS provides a further interface to other laboratory systems such as LIM systems with a barcode reader specially developed for CHRONOS that also supports 2D barcodes. Thanks to the information density of 2D barcodes it is possible to store not only sample names, but also further information such as measurement method or sample weight in the barcode. This information can be read out by CHRONOS and can be forwarded to the data system for processing. Information read from the barcode is saved in the sample list and is therefore still available after the analysis.

A thoroughly documented open interfaces allows customized plugins in order to integrate specific in-house processes into CHRONOS. CHRONOS offers a uniform interface for the control of various data systems and can thus contribute toward the unification of the laboratory processes.

### Safety and documentation

CHRONOS has an integrated authorization system. Three different authorization levels can be selected. Starting with the simple user, who can only execute methods, to the power user, who can modify released

method parameters, to the method developer, who can use the entire range of functions. This role concept can be activated if necessary. Although they are in the universal XML format, the CHRONOS methods are protected against being modified outside of CHRONOS. Various reports and log files allow complete documentation of the analysis processes.

## Settings

CHRONOS allows you to choose between various skins and languages (English, German). In the settings you can also enter the error method, i.e. you can set the method that will be called by the program if an error message occurs. All of the devices on the autosampler, such as trays, agitators, syringes, injectors, etc., can be configured under the menu option 'Settings'. You can also simulate the analytic process in demo mode first.

**The simultaneous controlling of several PAL autosamplers or of PAL DHR / TWIN PAL autosamplers is possible with CHRONOS. CHRONOS also supports the new PAL RTC.**

**Examples of complex analytics in which CHRONOS shortens your total analysis time:**

### GC-MS

#### 1. Headspace

With a headspace analysis of volatile, organic constituents of water or aroma constituents of ethereal oils, the equilibration of the sample at a predefined temperature usually means that more time is required for the sample preparation than for the GC-MS analysis. The headspace method (see also fig. 3)

is a typical example of a method in which CHRONOS can lead to a significant increase in effectiveness. Depending on the combination of incubation and GC running time, CHRONOS processes up to six samples simultaneously and is thus at the capacity limit of the PAL agitator.

In combination with a PAL DHR or an RTC PAL, CHRONOS offers the possibility of the addition of an internal standard and calibration standard as suggested in the draft for DIN 38407-43.

## 2. H53 hydrocarbon index from water

In a H53 determination, hydrocarbons are determined as sum parameters from water. Here, too, automated sample preparation takes place with the PAL autosampler, which consists of an extraction with hexane (40 minutes), a subsequent phase separation (20 minutes), drying, purification and injection. Compared to the 75-minute sample preparation time, the analysis time of the GC-MS system is considerably shorter, supplying the results in the case of the H53 application within 20-30 minutes.

## 3. Further examples

- SPME determinations with long loading times of your fibers
- Online SPE of pesticides from water
- Protection of the chromatography system against contamination with the PMIP concept
- Determination of MOSH/MOAH in foods and packaging by means of LC-GC coupling

- Determination of the sterine content in oils by automated extraction and subsequent LC-GC analysis
- Gravimetric controlled dilutions of samples and standards

## HPLC-MS

### 1. Multidimensional chromatography

Multidimensional chromatography, e.g. with SPE for the removal of matrix constituents is useful in particular in the case of LC-MS coupling with ESI ionization. In addition to the injection, the PAL autosampler rinses syringes and valves. The actual MS analysis is much less time-consuming than the upstream multidimensional chromatography and the automated work steps of the autosampler. CHRONOS can also further increase the throughput in the case of less complex, but very fast analyses.

### 2. Ultrafast determination of active ingredients in the pharmaceutical industry

In the pharmaceutical industry active ingredients can sometimes be determined in less than a minute with only one analyte. The speed reducing factor here is the work of the autosampler: driving to the vial position, the injection and rinsing of the syringe. CHRONOS can further increase the throughput in this case as well, since the next sample can be drawn up into the syringe while the mass spectrometer is still recording data.

## HPLC-UV/fluorescence detection

### 3. Derivatization with the PAL

In order to increase the assay sensitivity, derivatizations are frequently carried out by introducing chromogen and fluorogen groups into the analytes. These derivatizations sometimes require longer reaction times, rinsing steps, etc., which exceed the time of the actual chromatographic analysis by far. CHRONOS parallelizes as many samples as possible here in order to keep step with your analyzer.

### 4. Fraction collection

CHRONOS features its own fraction collection task, with which a complete fraction collection method can be created for the HPLC with a single mouse click.

## Specifications

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| <p><b>Versions</b><br/>CHRONOS xt, CHRONOS</p>  |
| <p><b>CHRONOS xt</b><br/>CHRONOS xt enables the control of PAL-xt series and older PAL autosamplers from CTC Analytics. It does not offer support for the online SPE system SEM or the RTC PAL.</p>   |
| <p><b>CHRONOS</b><br/>CHRONOS additionally enables the control of CTC RTC PAL and xt models, all modules of the CHRONECT sample preparation series and several further hardware components of third-party providers (see below). <b>Attention:</b> PAL3 autosampler have to contain a CTC firmware. OEM sampler of the PAL3 series without a CTC firmware cannot be controlled by the standard version of CHRONOS.</p>  |
| <p><b>Controllable chromatographic systems</b><br/>Agilent GCMS MassHunter<br/>Agilent LC/GC und MS ChemStation ab Version B, also OpenLAB<br/>Agilent LCMS MassHunter<br/>Analyst since 1.5<br/>GL Sciences Evolution Software since version 2.4, also dual systems<br/>Bruker MS Workstation for LCMS und GCMS<br/>Chromcard<br/>ChromPerfect since version 6.0<br/>Clarity since 6.0<br/>Dani Masterlab<br/>Empower 2 (limited support)<br/>EZChrom min. version 3.21, Chromquest 5.0 – eingeschränkt auch OpenLAB<br/>(requires EZChrom Runtime License, which is not covered in the scope of the CHRONOS shipment)<br/>LECO ChromaTOF (using Sequence export)<br/>Open Lab Chemstation<br/>Omic Software for IR spectrometers<br/>QuanLab 2.5, 2.5.2, 3.0, 3.1<br/>Shimadzu Labsolutions<br/>Waters Masslynx ab 4.1<br/>Xcalibur versions 1.4, 2.0, 2.1, 2.2, 3.0, 4.0</p> |
| <p><b>Further supported systems</b><br/>online SPE system CHRONECT Symbiosis, Eksigent NanoLC, Gilson Dilutor 402 und 4x20, ThermoGCs via GCLink, ITSP, FlipVials, Mettler Toledo balances</p>  |
| <p><b>Controllable autosamplers to date</b><br/>HTS PAL, HTC PAL, Dual PAL, PAL DHR, TWIN PAL, CombiPAL, GC PAL, HTC-xt, HTS-xt, HTX-xt, GC-xt, COMBI-xt, COMBI-xt Extended, LSI/RSI/RTC PAL (not by CHRONOS xt).</p> <p>DLW injection (Dynamic Load and Wash injection) or the equivalent for the PAL 3 series (LCMS tool) by CTC Analytics is supported by CHRONOS.</p> <p>PAL systems can be controlled via the serial interface or by network.</p>  |

## Other Hardware

|  |  |
|--|--|
| <b>Valve control</b>                           | CHRONOS provides the control of Valco valves from the methods. Therefore, they must be equipped with a micro actuator containing a serial interface.   |
| <b>Balances</b>                                | Balances may be controlled by MT-SICS protocol via a serial interface. Thus, for example weighing results may be determined and further processed.   |
| <b>Peristaltic pumps</b>                       | CHRONOS supports the Watson Marlow 323Du pump for the pumping of liquids.  |
| <b>Magnetic stirrer</b>                        | CHRONOS supports the Thermo Variomag magnetic stirrer and IKA Shaker for the stirring or shaking of liquids.   |
| <b>Syringe exchanger</b>                       | CHRONOS supports the XChange syringe changer from SGE for the changing of liquid syringes on PAL xt systems (also possible with CHRONOS xt).   |
| <b>GL Sciences accessories</b>                 | CHRONOS supports the LINEX liner change as well as the capping/de-capping station in conjunction with the Optic Injector from ATAS GL Science.   |
| <b>Barcode reader</b>                          | Special barcode reader enable the reading of 1D and 2D barcodes containing up to ten freely definable information boxes.   |
| <b>Refractive index determination</b>          | CHRONOS supports the Abbemat refractometers by Anton Paar  |
| <b>Shaker</b>                                  | High-energy shakers by Prolab may be utilized for an efficient mixing of problematic samples.  |
| <b>Centrifuge</b>                              | During sample preparation, suspended matter from 2 mL and 10 mL vials may be separated using the small centrifuge by Prolab. Vials exchange is done by a PAL autosampler.  |
| <b>Accessibility to other software systems</b> | <p>The web service or customized plugins enable retrieval of sample lists by LABSQ from ICD.</p> <p>Sample lists generated by the method validation software Validat by ICD may be imported.</p> <p>Sample lists in the CSV format, e.g. from LIMS systems or data systems, are easy to import to CHRONOS.</p> |
| <b>System requirements</b>                     | At least a 2 GHz processor, 2 GB RAM, Windows 7 SP1 to Windows 10, serial interfaces: each PAL which is connected serially requires one interface.   |
| <b>Standard methods</b>                        | Methods are provided for the liquid injection, headspace and SPME as well as for liner change with GL Sciences systems. Registered customers can access further methods in the download section on <a href="http://www.axel-semrau.de">www.axel-semrau.de</a> .  |
| <b>License</b>                                 | Hardware dongle or activation via serial number is possible.   |

Note: CHRONOS manuals are available in English.

Subject to technical changes

### Axel Semrau GmbH & Co. KG

Stefansbecke 42  
45549 Sprockhövel  
Germany  
Tel.: +49 2339 / 12090  
Fax: +49 2339 / 6030

[www.axel-semrau.de](http://www.axel-semrau.de)  
[info@axel-semrau.de](mailto:info@axel-semrau.de)

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