



CryMOCO

Crystallization Process Informatics System

User's Manual

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Introduction

This manual will show you how to use CryPRINS (crystallization process informatics system) for implementing simple temperature profiles to applying advanced control strategies.

The software enables users to connect and use various process analytical technology (PAT) tools simultaneously. A key feature of the software is real time display of information from different sources thus enabling easier data collection and synchronization.

CryPRINS can be easily used both in industrial and laboratory environments for routine work and investigative tasks.

The manual covers all aspects of the software and also includes some recommendations for using advanced control strategies.



Some of the conventions used in the software are as follows:

This indicates the importance of the task which must be carried out for proper functioning of the software.



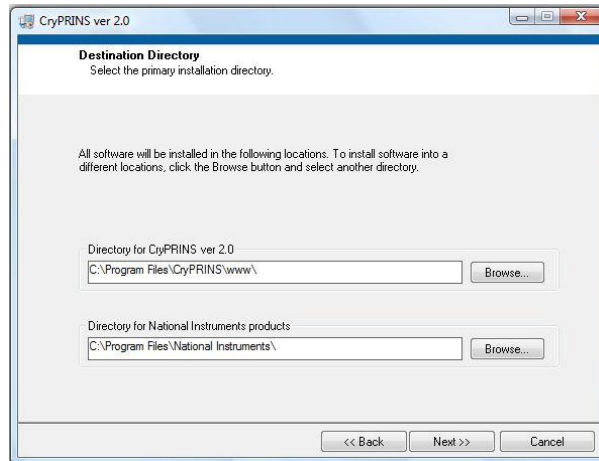
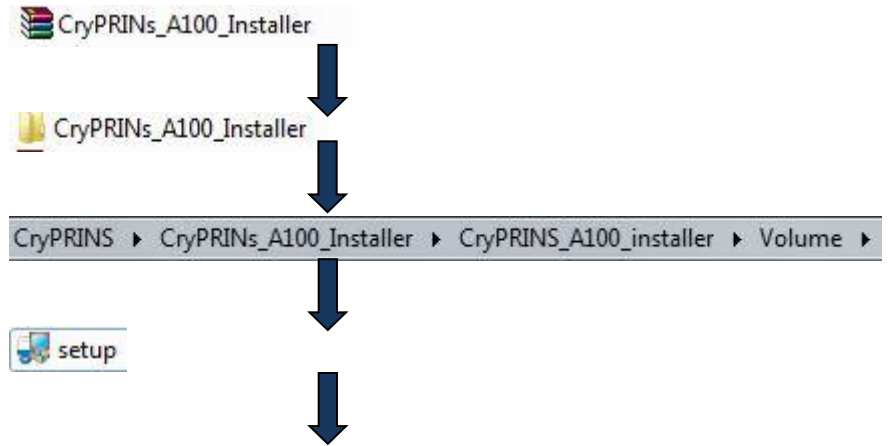
Time saving tips



Graph manipulation options

Software Installation

CryPRINS installation is quite simple, locate the zip file on the hard disk and follow the following simple steps:



Select the desired directories and click next.

Wait till the installation process is complete, you may be asked to restart the computer, after this the software is ready to use.

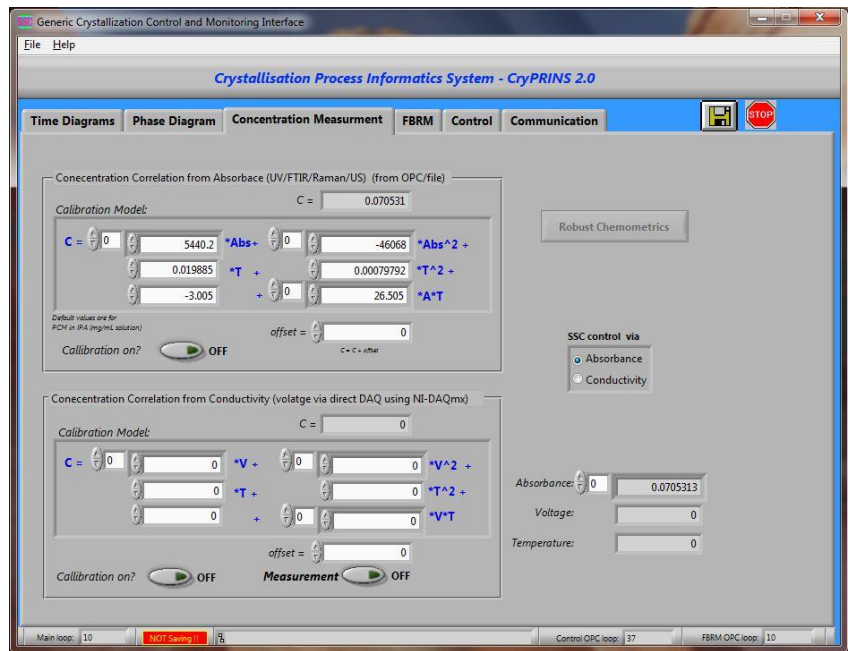
Running the Software

After the software has been installed you can start it by double clicking on the software icon:



Once open you will see the following window.

CryPRINS

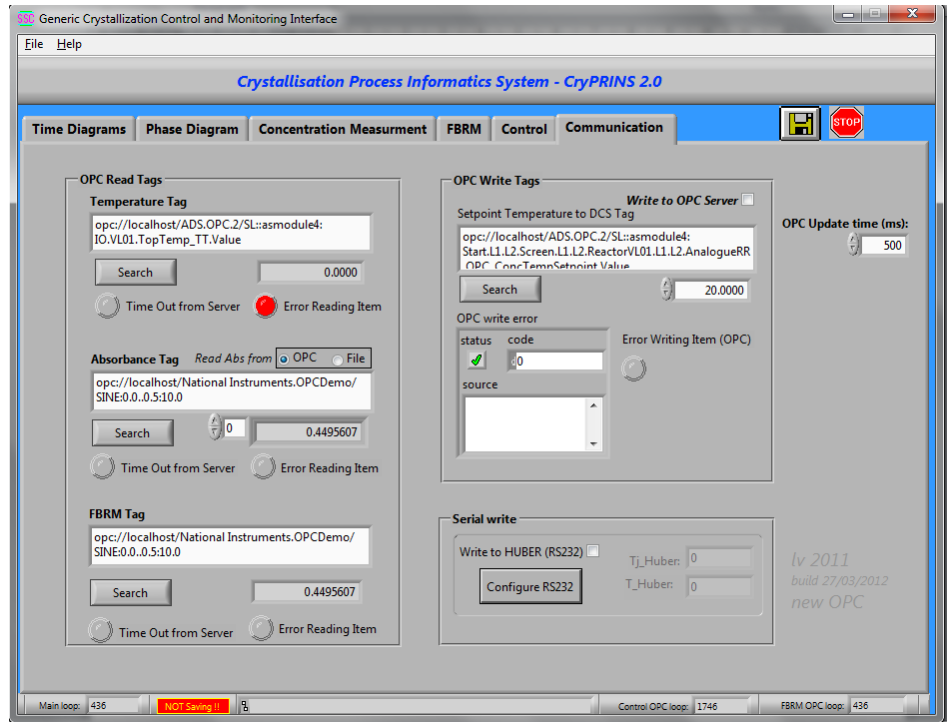


All the software menus i.e. Time diagram, Phase diagram, Communication Measurement, FBRM, Control and Communication can be accessed by clicking on the respective tab.

In the coming sections the functionalities available under each tab will be discussed in detail.

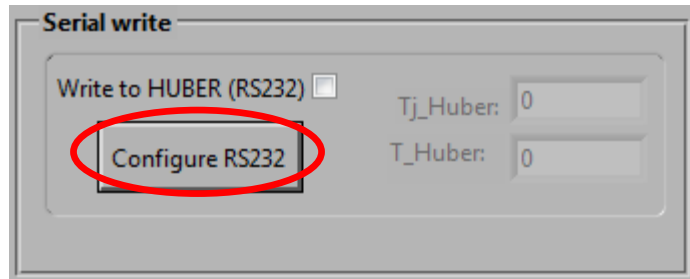
Communication

CryPRINS is versatile software and can be readily used in laboratory and industrial environments. The software offers connectivity to different equipments from simple RS232 connectivity to sophisticated OPC platform suited for industrial environments. The different options available are shown in the figure below.



RS232 Communication

The communication between the software and heating/cooling baths can be established using RS232 as shown in the following steps. Under the communications tab click on configure RS232 button in serial write box:

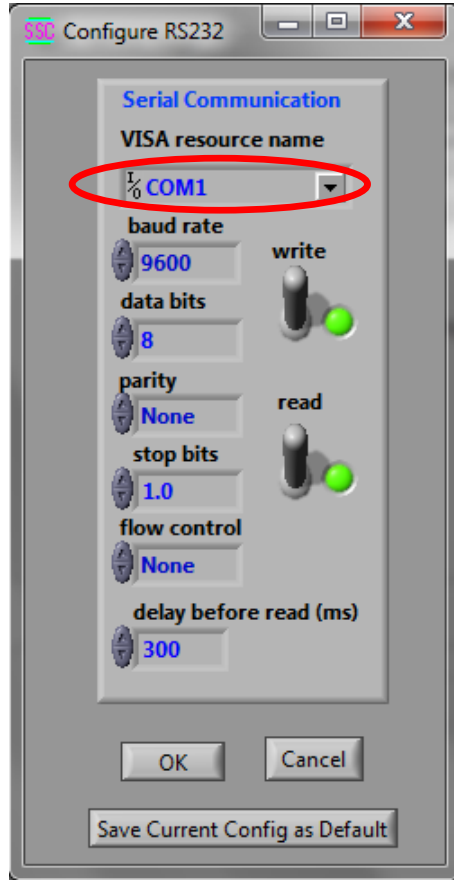


The following menu will then be presented, by selecting the dropdown menu you will be presented with all the active com ports available on your computer. From this list select the port communicating with the heating/cooling unit.

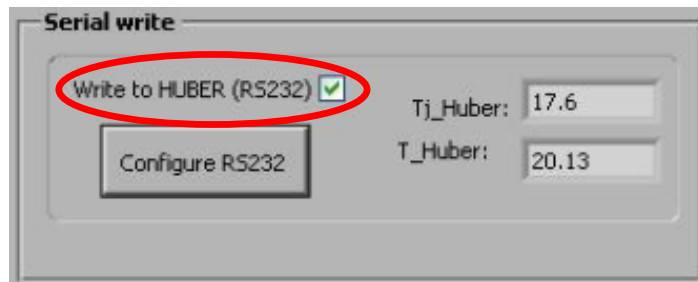
Baud rate, data bits, parity, stop bits and flow control should be set in accordance with the requirements of individual units. A reasonable value

CryPRINS

for delay before read is suggested e.g. 300 ms gives enough time to computer for exchanging reading with the heating/cooling unit. Keeping this time very short e.g. 50 ms may result in communication issues.



“Save Current Config as Default” allows the user to save settings, the software will always initialize with the saved settings every time it is restarted.



After completing the configuration process check the box “Write to HUBER (RS232)” as shown in above figure. Once the communication is established you can see the temperature values for Tj_Huber and T_Huber.

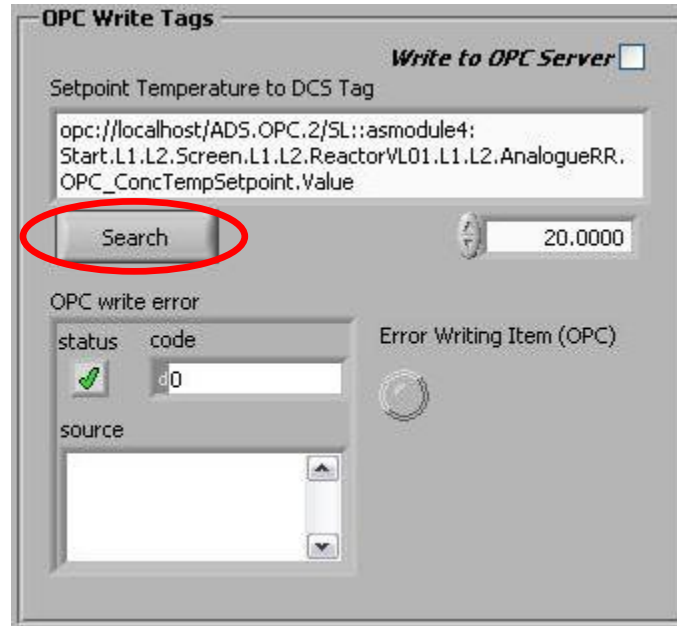


Always ensure that “Write to Huber” is checked otherwise communication with your heating/cooling unit will not be established.

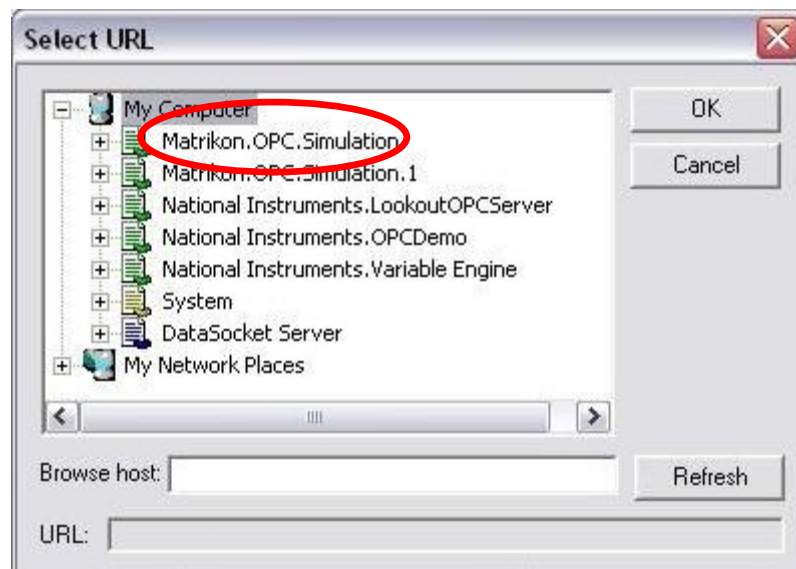
CryPRINS

The steps required for communicating with a DCS or other industrial systems are:

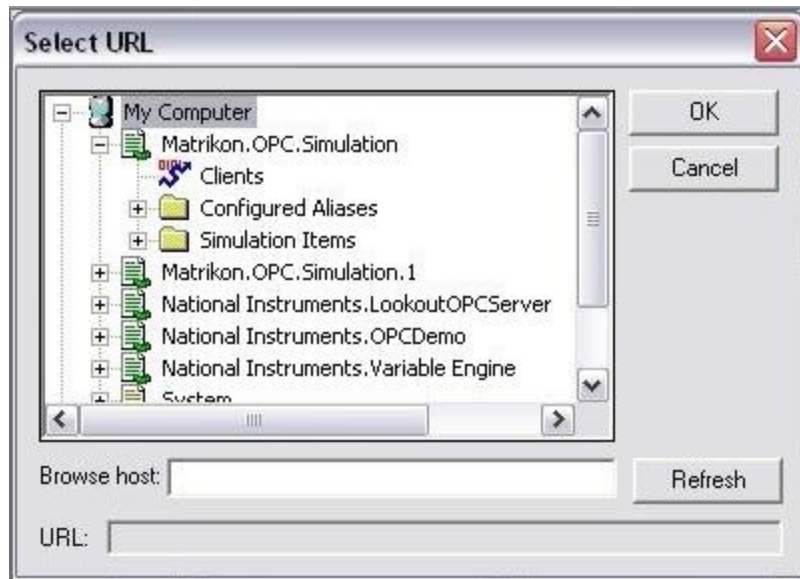
Click on search button in the OPC writing tags box.



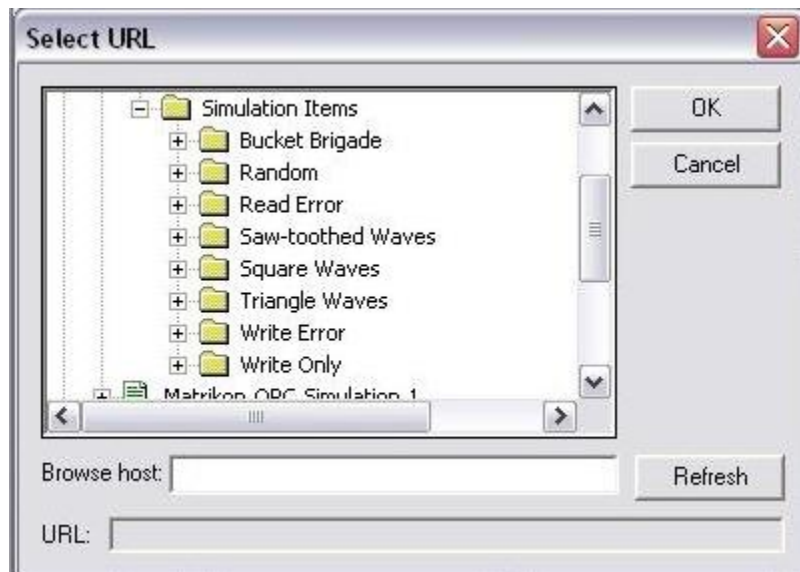
The following dialogue box will open:



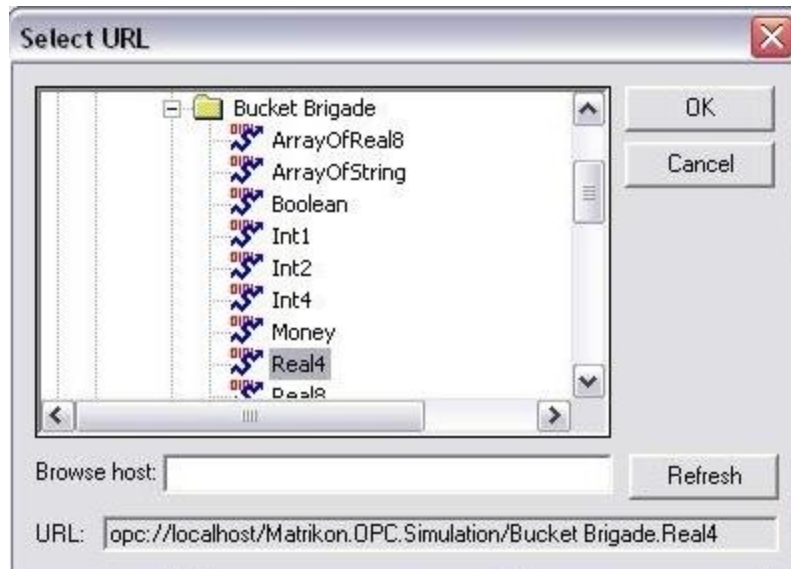
Expand the Matrikon.OPC.Simulation and select Simulation Items



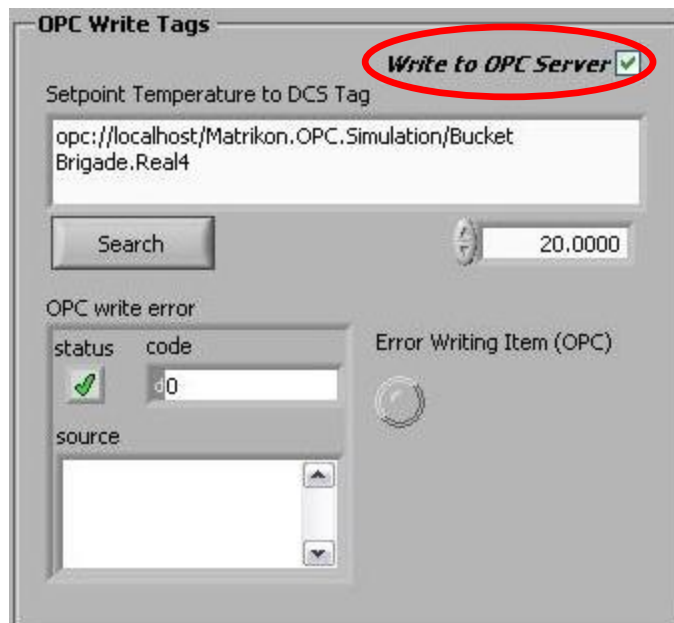
Expand Simulation Items and select Bucket Brigade.



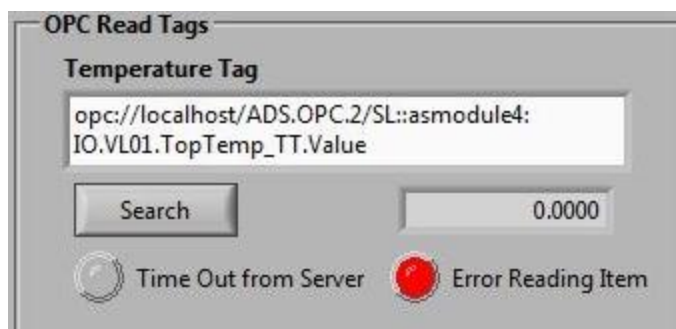
Under Bucket Brigade select Real4 and press ok.



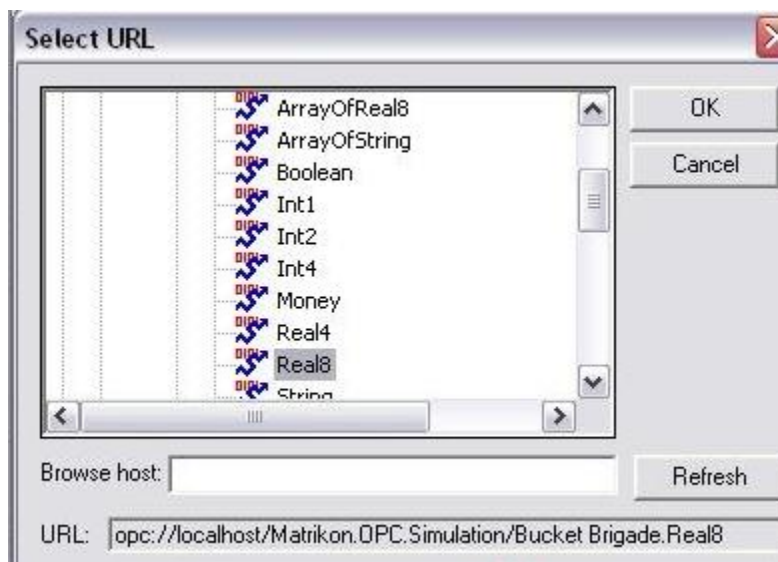
Once the configuration is complete check the box **Write to OPC Server**, if the communication is functioning properly, you will a green tick mark for status in OPC write error box.



For configuring the OPC Read Tags (for temperature) following steps have to be followed, press the Search button in OPC Read Tag box.



The remaining steps are identical to the steps shown for OPC Write Tags except for one important difference. In Bucket Brigade a different value from OPC Write Tags must be selected. For OPC Write Tags “Real4” was selected, therefore in this case Real8 is selected as shown below:



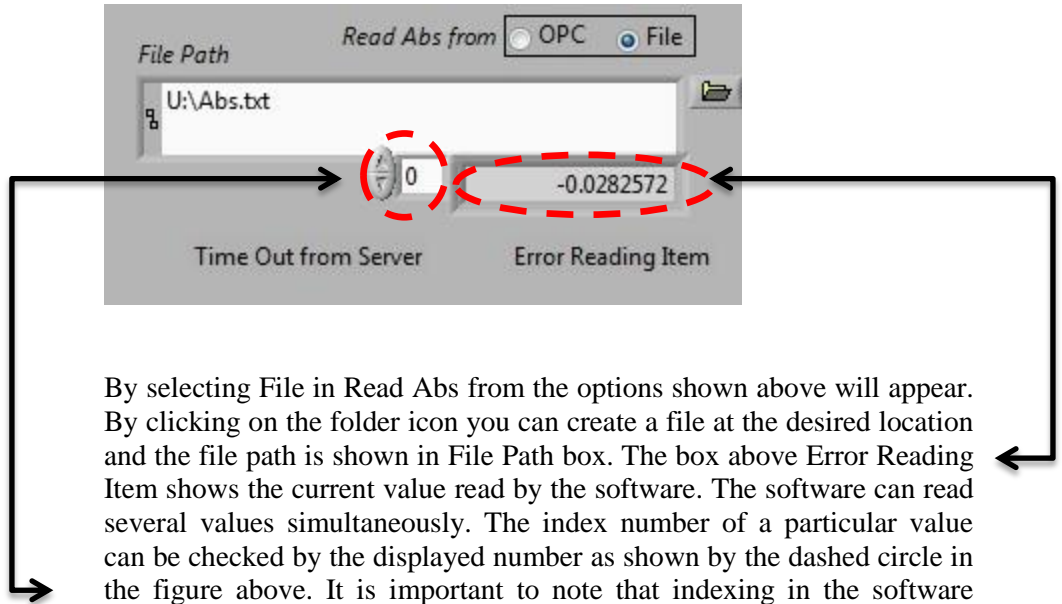
It is also worth noting that either Real4 or Real8 can be selected interchangeably for write or read modes but same values cannot be selected at the same time for both read and write.

Absorbance Tag

The software offers two different ways of reading spectroscopic data, these are:

- Reading file from a shared drive
- OPC

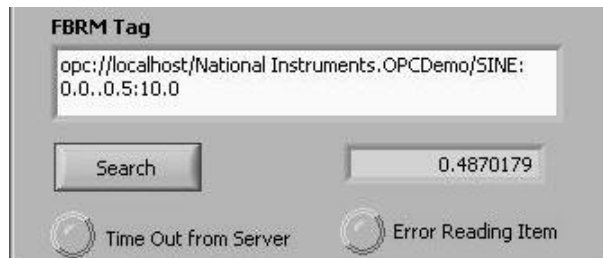
For the first option the software used for data acquisition from a spectrometer must be able to write a file with data on a shared drive. CryPRINS can read the files having a scalar or a vector inside.



By selecting File in Read Abs from the options shown above will appear. By clicking on the folder icon you can create a file at the desired location and the file path is shown in File Path box. The box above Error Reading Item shows the current value read by the software. The software can read several values simultaneously. The index number of a particular value can be checked by the displayed number as shown by the dashed circle in the figure above. It is important to note that indexing in the software starts from 0 i.e. the first value read will be indexed as 0, the second value as 1 and so on and so forth.

Different values written in the file can be checked by pressing the up and down arrows as shown in the dashed circle.

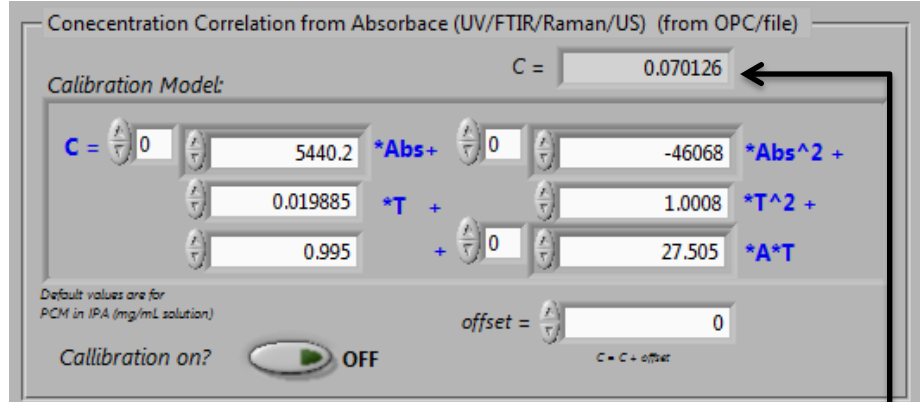
For reading data via OPC for absorbance and FBRM data, same procedure as described before for temperature reading should be followed; in this case OPC option should be selected in the Absorbance Tag box.



The appropriate OPC connectivity tags for both FBRM and absorbance should then be selected from their respective menus by clicking the Search button.

Concentration Measurement

A key feature of CryPRINS software is its ability to determine concentration in real time using spectroscopic data. The software is capable of implementing various types of models ranging from simple univariate models to more complex multivariate nonlinear models.



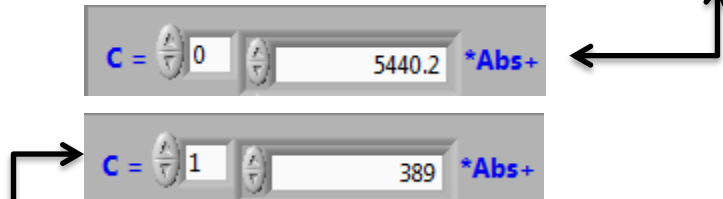
The above menu can be accessed by clicking on the Concentration Measurement tab. The concentration measured at any time is displayed in the box in the top right corner.

To show how the calibration model can be plugged in we consider the following calibration equation:

$$C = b_0 + \sum_{i=1}^n b_n A_n + \sum_{i=1}^n d_n A_n^2 + eT + gT^2 + \sum_{i=1}^n (h_n A_n) T$$

The corresponding model parameters can be inserted in the white boxes as shown in figure. Notice that each of these boxes has an up/down arrow next to it. These arrows can be used to toggle positions. The constant term as shown can be written in the box as shown above.

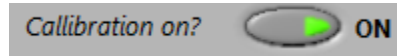
It was mentioned before that indexing in the software starts from 0 i.e. first term will be indexed as “0”, 2nd as “1” and so on and so forth. For the first absorbance term the corresponding box will look like this:



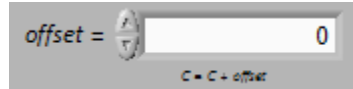
The second coefficient can be added by first clicking the arrow so that the number in the box changes from 0 to 1 and after this you can write the corresponding values. The process can be carried out for “n” number of absorbances therefore simple univariate to multivariate models can be easily implemented in CryPRINS. The same procedure can then be followed to enter the other coefficients. Once all the parameters have



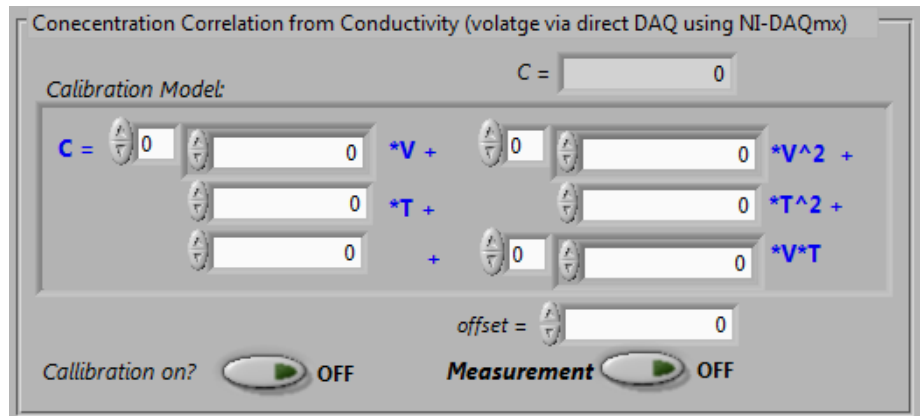
been entered press the calibration on button, the green LED shows that software is now using the calibration model.



A provision for adding a bias term to adjust the model is also provided in case it is required, this is done by writing the required values in the offset box as shown below. The concentration obtained will then be a sum of the concentration model output plus the biased or offset term.

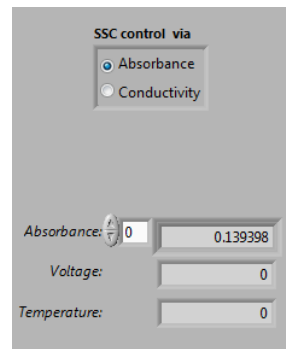


A part from implementing models using spectroscopic data, models based on conductivity or ultrasonic probe can also be implemented. A 2nd implementation box is available and the parameters can be entered in exactly the same way as shown previously for spectroscopic data. The measurement button as shown must be activated prior to the start of conductivity measurements.



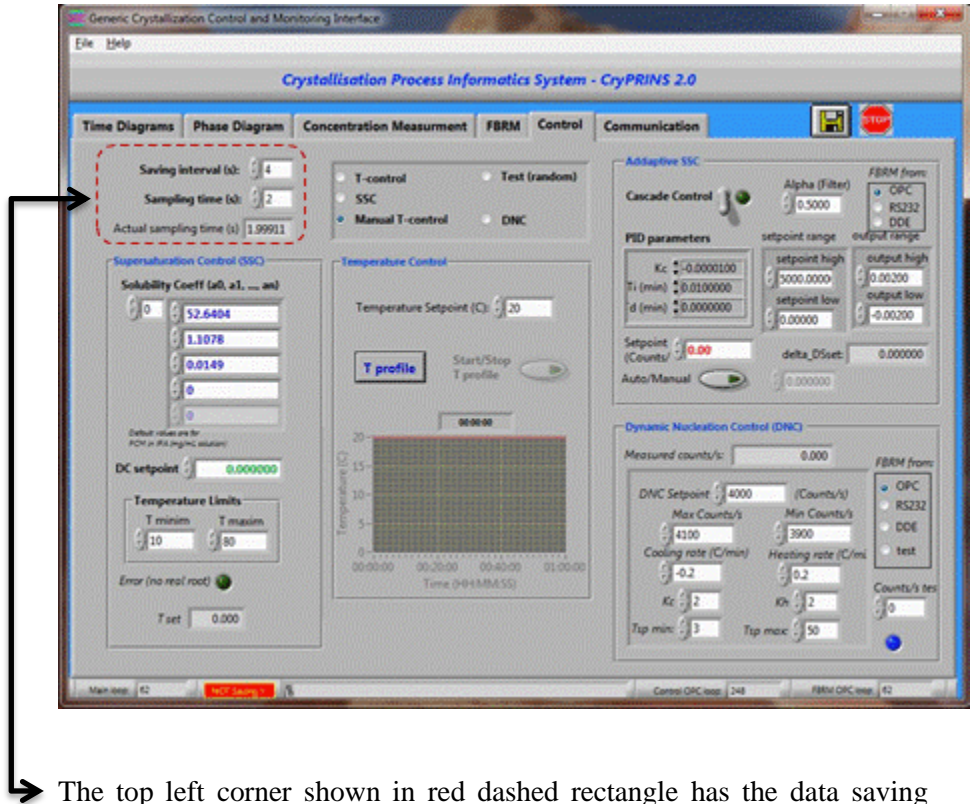
Supersaturation control can be implemented either by using spectroscopic data or conductivity measurements. The appropriate mode has to be selected as shown in the box below.

The raw absorbance(s) and conductivity data are also displayed as shown in the figure below. The temperature here corresponds to the process temperature.



Control

The following discussion will cover the software options available under Control tab. This is the main part of the software and different temperature, supersaturation control and automated direct nucleation control profiles can be configured here.



The top left corner shown in red dashed rectangle has the data saving interval and sampling time options.

A saving interval of 4 seconds means that the data will be saved by the software after every 4 seconds.

Sampling time refers to the time after which the software sends a signal to the controller to vary a setpoint. For a better control of the process it is important that this time is kept as small as possible. Having a higher sampling time may result in process not being able to follow a desired profile.

The different control policies available can be chosen by selecting the appropriate option from the following box:

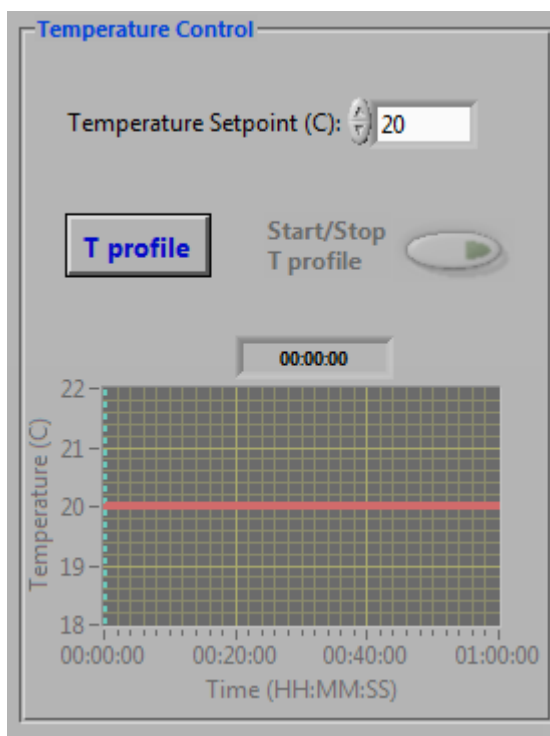


Setting up a Temperature Profile

The temperature control options will be discussed initially. One of the main features of the CryPRINS software is ease of implementing different temperature profiles.

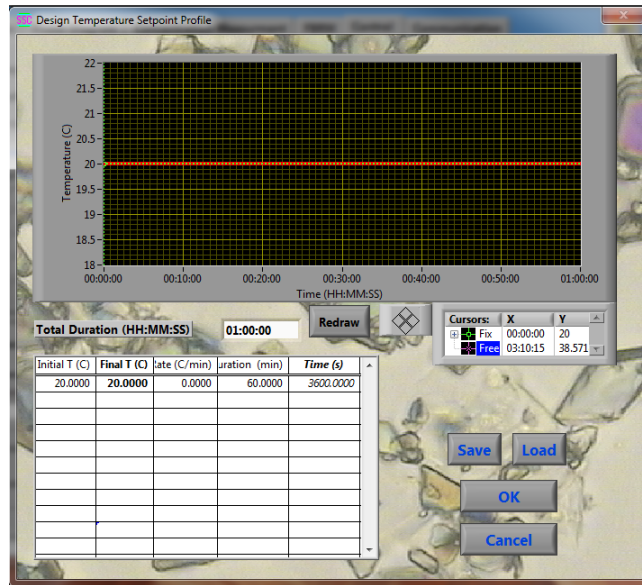
In the simplest case of Manual T-control the system will follow the temperature as specified in the temperature setpoint box.

Note that all the other options will be disabled upon selection of a particular control policy.

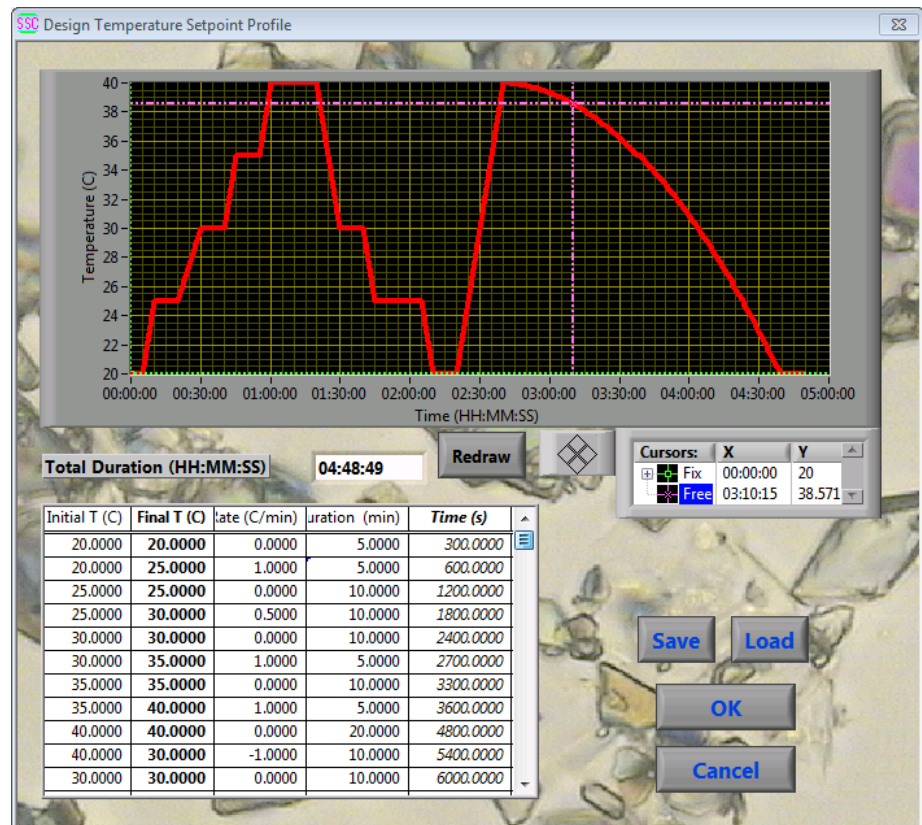


For implementing a temperature profile select T-control and then click T profile button as shown in above figure, a new window shown as follows will appear.

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This new window allows the user to load a temperature profile, setup a new profile and amend already loaded temperature profiles. A temperature profile with several heating/cooling steps with different rates is shown below:



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In this profile the system will heat up to 40°C starting from 20°C and then it will be cooled down to 20°C in several steps. To insert a temperature profile, following steps should be followed:

The first box under the heading Initial T should have the initial temperature, in this case 20°C, followed by the desired temperature in the first box of the second column titled Final T, in this case 20°C.

In the first box under Rate (°C/min) the heating/cooling rate has to be mentioned in this case the system is kept at the same temperature therefore 0 will be entered in this box.

If it is required to maintain the temperature at a certain value for a specific duration then that time should be entered in minutes in the duration column. In this example we are maintaining temperature at 20°C for 5 minutes.

To continue adding the profile click in the 2nd box of column titled Final T, you will notice that by clicking in the second box of column titled Initial T it is automatically filled with a value of 20°C. This is a time saving feature of the software that you don't have to enter values in the first column apart from entering the very first value. In the Time (s) column the cumulative time is displayed e.g. the time required to finish the first two steps is 600 seconds as shown in the figure.



To heat up the system at a specific rate, simply enter the desired rate in the rate column, the time required to carry out the step will be displayed in the duration column. In order to add a cooling step a negative sign must appear before the rate in rate column e.g. in the above example temperature is brought down from 40 to 30°C at a rate of 1°C/min. This rate must be entered with a negative sign as “-1°C” in the software.

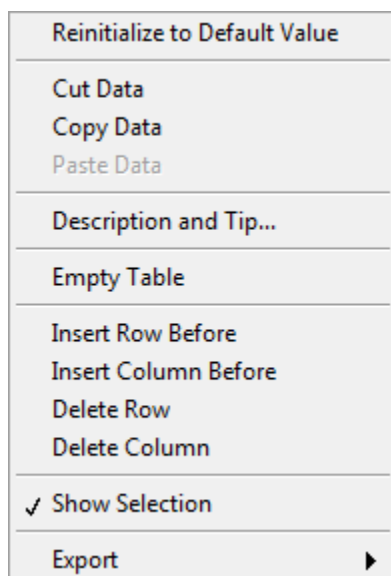
Once the last step of the profile is reached the process will be maintained at the same temperature regardless of the duration of the last step.

The temperature profile as it is entered is displayed in the graph.

Once you have finished entering the profile, press the save button, a new dialogue box will open, save the file at the desired location. If it is required to use the same profile or any other profile (provided it is written in the correct format) press the Load button and select the desired file. The temperature profile will then be loaded; the supported formats for loading a temperature profile are Microsoft Excel and Windows notepad. Please make sure that numbers are present in these files without any alphabets or text.

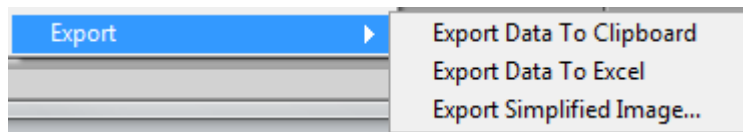
Right clicking on the profile table will show multiple options for data manipulation and export.

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Most of these options are self-explanatory e.g. data can be copied, cut, rows/columns can be inserted etc.

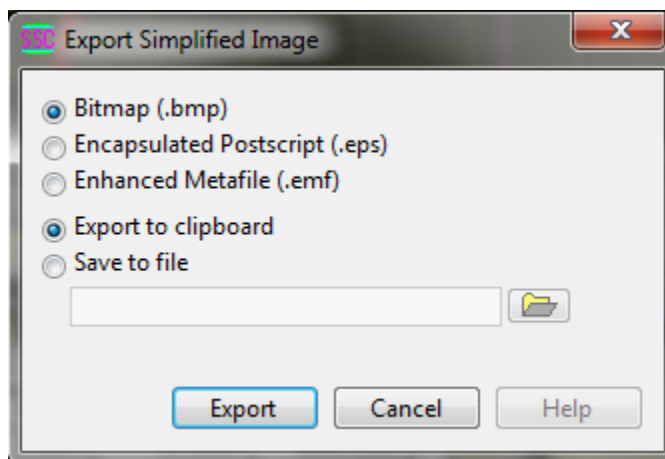
The following export options are available:



For Export Data To Clipboard, highlight the data cells, once this is done right click and go to Export submenu and select the appropriate option. Please note that only the highlighted data will be exported to clipboard.

In a similar way select the desired cells and click on Export Data To Excel option. All the data will then be copied to the currently open excel sheet. The software will open an excel sheet by itself if no sheet is open.

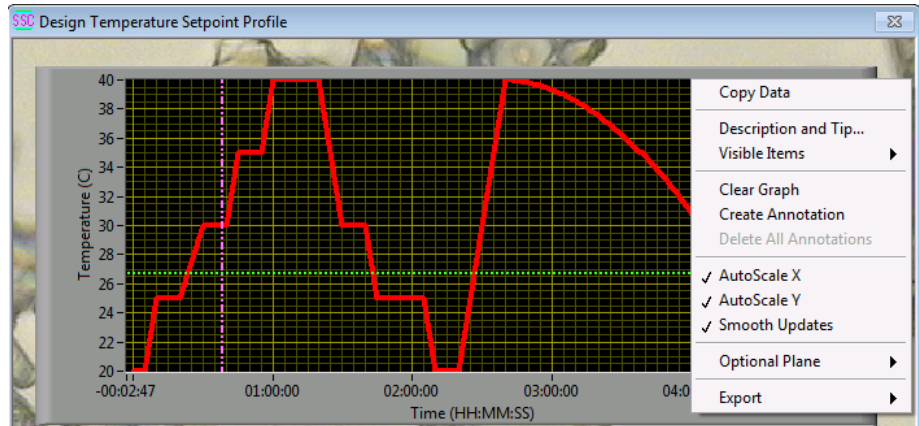
If Export Simplified Image... option is selected the following dialogue box will appear:



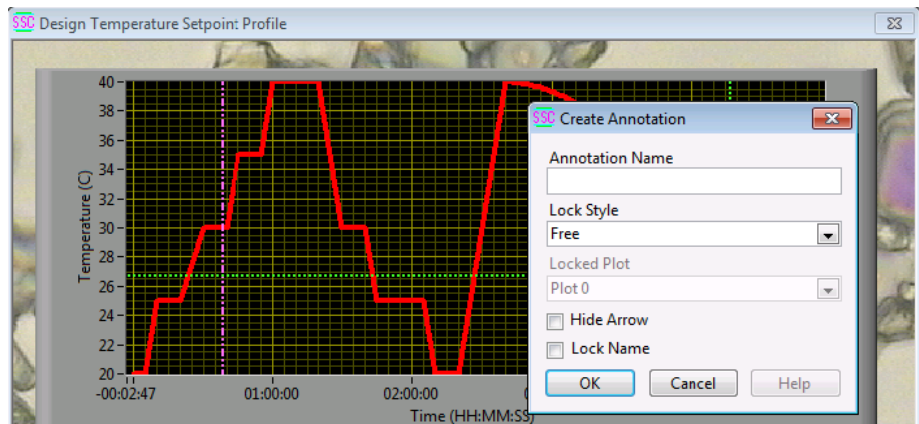
CryPRINS

Select the desired image type and file location and click export. In this case selection of cells is not required as the whole table will be exported as an image.

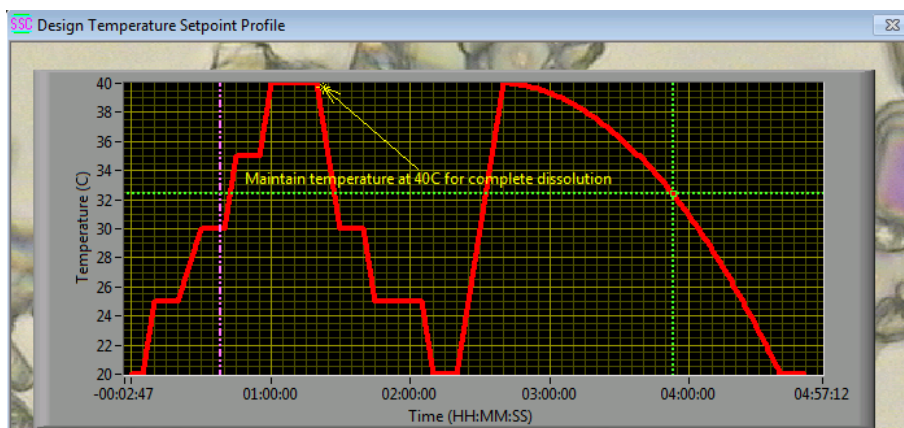
Annotation on temperature profile graph can be done for making important points or notes, this can be done by right clicking anywhere on the graph, a menu will appear as shown in the following figure.



Clicking on Create Annotation will show the following submenu:

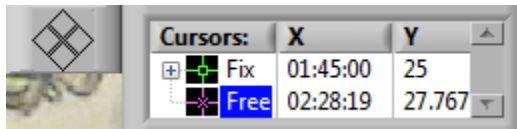


In the Annotation Name type in the notes or remarks and then select the Lock Style. Lock Style options enable you to have the menu at a fixed position or it can be moved.



Once an annotation has been added it cannot be changed, if you want to delete text that you have added, right click on the graph and click Delete All Annotations. The text will remain part of the simplified image if the annotated graph is exported. This option is particularly helpful during development of written procedures for training of personals or for personal laboratory notebooks.

In the above figure purple and green cross hairs can be seen. Purple cross hair can be moved freely across the plot, the resulting x-y coordinates are displayed in the box as shown below:



The green cross hair can be used to move step by step in accordance with the set temperature profile.

Saving Data, Starting and Stopping the Software

For saving data press the diskette symbol present in the top right corner:

The data can be saved in the same file as the one created for saving the temperature profile.

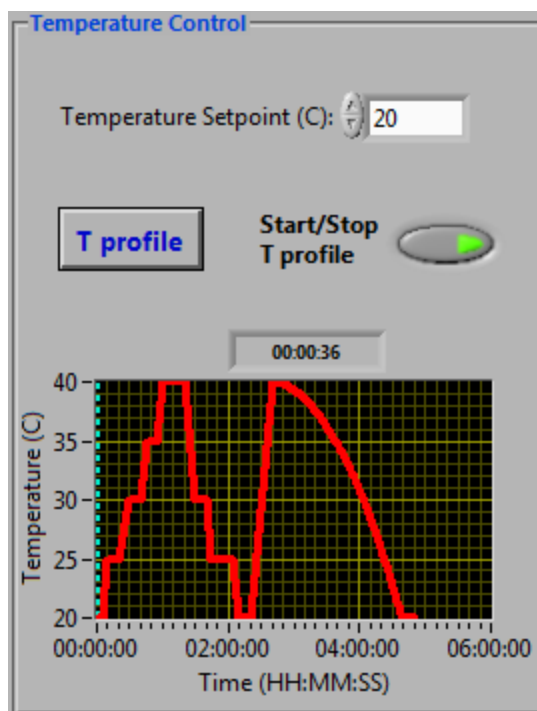



After pressing this button a dialogue box will appear asking you where to save it, select the location and press ok. Once the data saving is in progress the symbol will change as shown in the following figure.



In the control tab press Start/Stop T profile, the LED will turn on indicating that data saving has started.

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To stop the software press the  button for software integrity it is important that it must always be stopped using this button instead of simply closing it down.

The data file can be opened using note pad or excel, the file header is described in the following table:

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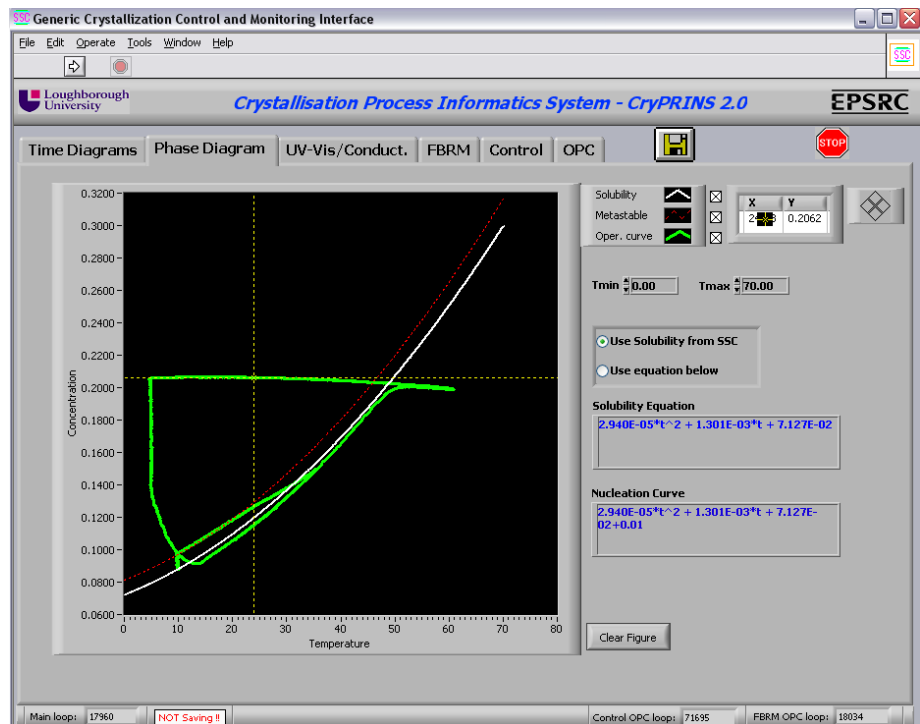
Column 1	Month	Column 24	Concentration from Conductivity
Column 2	Day	Column 25	FBRM statistic no. 1
Column 3	Hour	Column 26	FBRM statistic no. 2
Column 4	Minute	Column 27	FBRM statistic no. 3
Column 5	Seconds	Column 28	FBRM statistic no. 4
Column 6	Time from the start of software	Column 29	FBRM statistic no. 5
Column 7	Counts/s (Selected from FBRM)	Column 30	FBRM statistic no. 6
Column 8	Process Temperature	Column 31	FBRM statistic no. 7
Column 9	Concentration	Column 32	FBRM statistic no. 8
Column 10	Filtered Counts/s	Column 33	Off set used for calibration based on absorbance
Column 11	DDc	Column 34	Off set used for calibration based on conductivity
Column 12	Set Point Counts (FBRM)	Column 35	FBRM readings via OPC
Column 13	Temperature	Column 36	ADNC setpoint
Column 14	Absorbance	Column 37	Cooling rate during ADNC
Column 15	Temperature Set point (OPC)	Column 38	Heating rate during ADNC
Column 16	Jacket temperature	Column 39	Upper limit of target counts during ADNC
Column 17	Temperature	Column 40	Upper limit of target counts during ADNC
Column 18	Set point from heating/cooling unit	Column 41	Lower temperature limit for ADNC
Column 19	Set point from heating/cooling unit	Column 42	Upper temperature limit for ADNC
Column 20	Supersaturation	Column 43	K_h values
Column 21	Supersaturation setpoint	Column 44	K_c values
Column 22	Conductivity	Column 45	Absorbance
Column 23	Concentration from Absorbance	Column 46	FBRM measurements via DDE

Phase Diagram

Phase diagram can be accessed by clicking on the Phase Diagram tab. This feature gives the user another option for real time monitoring of the process. If a proper calibration model for concentration measurement is used, at any time, the process can be monitored with respect to the solubility curve. Any unusual behaviour in the process can therefore be easily detected e.g. presence of impurities etc.

The users can plug in a solubility curve and a second one called as nucleation curve. The later can be used simply as a reference point to see how far the process is from saturation point or if solubility curves are available for two polymorphs they can also be seen at the same time. This can quickly inform the user about the polymorph which is likely to be present or will disappear during the process.

Clear Figure removes all the data from the plot apart from the solubility and nucleation curves.



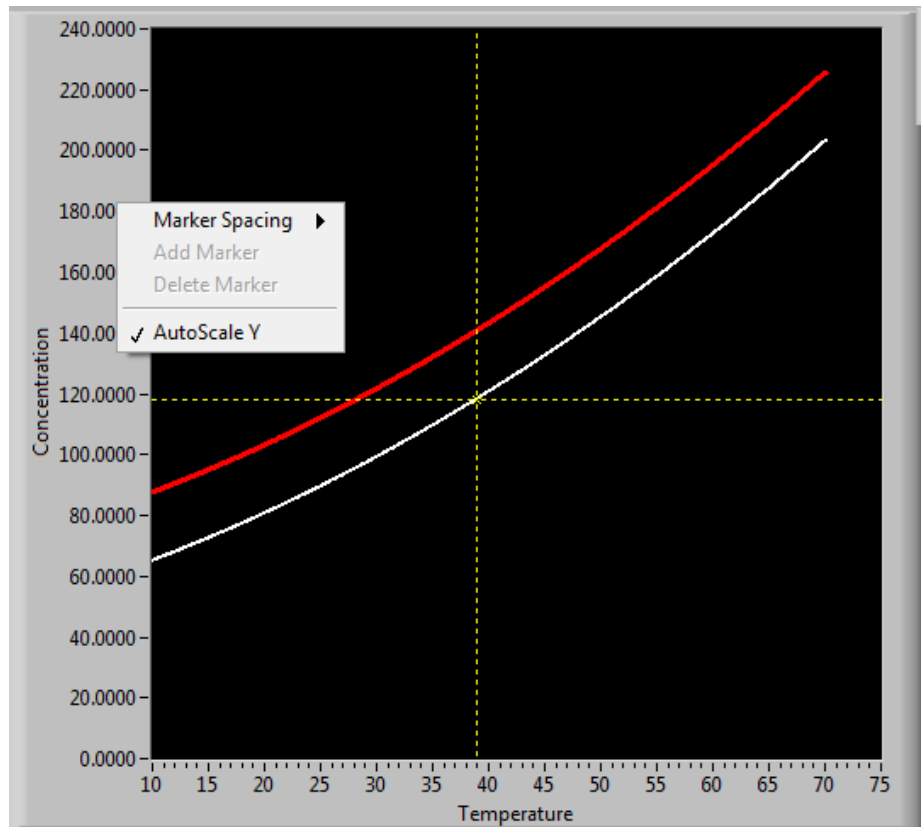
The equations for solubility and nucleation curves can be entered in their respective boxes. The equation for solubility curve can be either entered here or in SSC parameters under the Control tab.

Tmin and Tmax are used to specify temperature range while the yellow cross hair provides information about x and y coordinates.

The x and y axes can also be changed manually by right clicking on any of the axis and unchecking the AutoScale option:



CryPRINS



After this simply highlight the first or last digit of the required axis and enter the desired values.

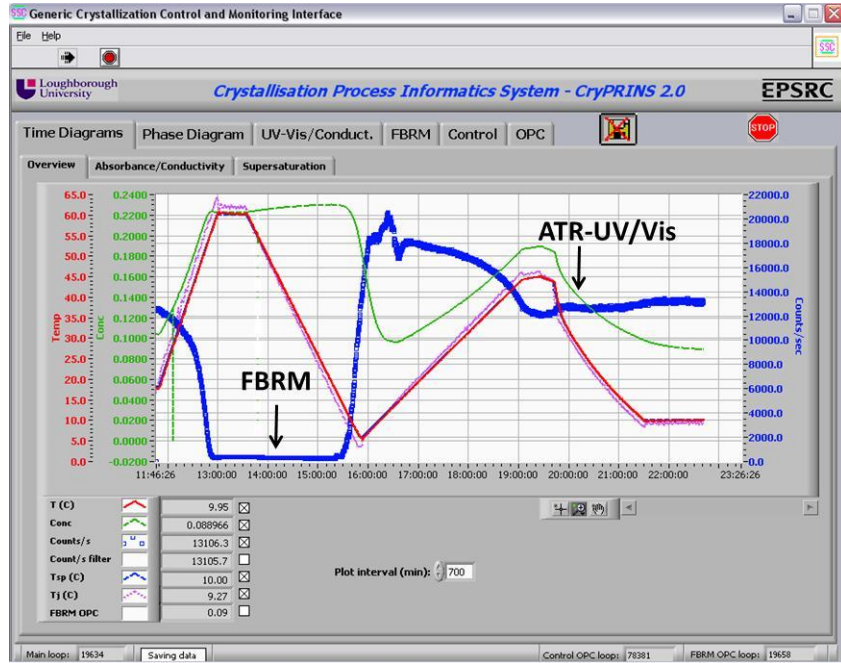
As shown previously the phase diagram can be exported as a simplified image or the whole data can be copied to excel sheet etc. This graph can also be annotated as shown previously for temperature profile.



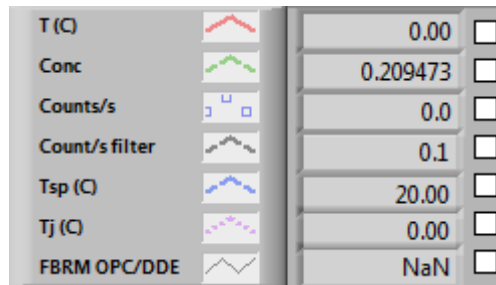
Time Diagrams

Time Diagrams provide the visual and comparative aspect of composite sensor array concept. Time diagrams features three tabs namely Overview, Absorbance/Conductivity and Supersaturation. Overview of a cooling crystallization experiment in which ATR-UV/Vis and FBRM were used as PAT tools is shown in the following figure:

Right click on the graph and select export data to excel. This will transfer all the data that can be plotted directly to the excel file along with file headers.



In this figure real time information about the process provided by FBRM and ATR-UV/Vis in the form of counts/s and concentration can be seen along with process temperature. Concentration information if provided by ATR-FTIR, NIR, Raman and conductivity probes can also be plotted here along with FBRM data. The choice of information to be displayed is selectable from the menu shown in the following figure:



The box for a particular piece of information should be selected in order for it to be displayed. Brief description of these is as follows:

- T(C) Process temperature
- Conc Concentration
- Counts/s FBRM data using RS232

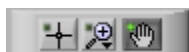
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Count/s filter	FBRM data averaged using RS232
Tsp (C)	Temperature setpoint
Tj (C)	Jacket temperature
FBRM OPC/DDE	FBRM data if obtained via OPC or DDE

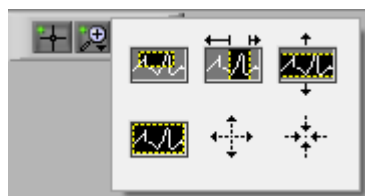
Again the data from the plot can be exported using the right click menu as shown previously. All the graph manipulation, annotation and export options previously described are equally applicable here.

Plot interval min allows you to specify time for which the information should be displayed.

A number of other advanced graph interaction options are also available, these can be accessed using the following menu:



By clicking the middle icon the following submenu will appear:



This can be used for magnifying a specific area by drawing a box.



This can be used to magnify area selected between two vertical lines. After pressing this simply drag the mouse pointer (left mouse button pressed) between two points of interest.



This option can be used if it is required to magnify area between two horizontal lines. Follow the same procedure as described in the previous step.



If it is required to zoom in at a specific point then this option should be used. After selecting this option take pointer at point of interest and press left mouse button. Pressing the button repeatedly will increase the magnification of the selected point.



This option can be used to zoom out of a specific point, operating procedure is same as described in the previous step.



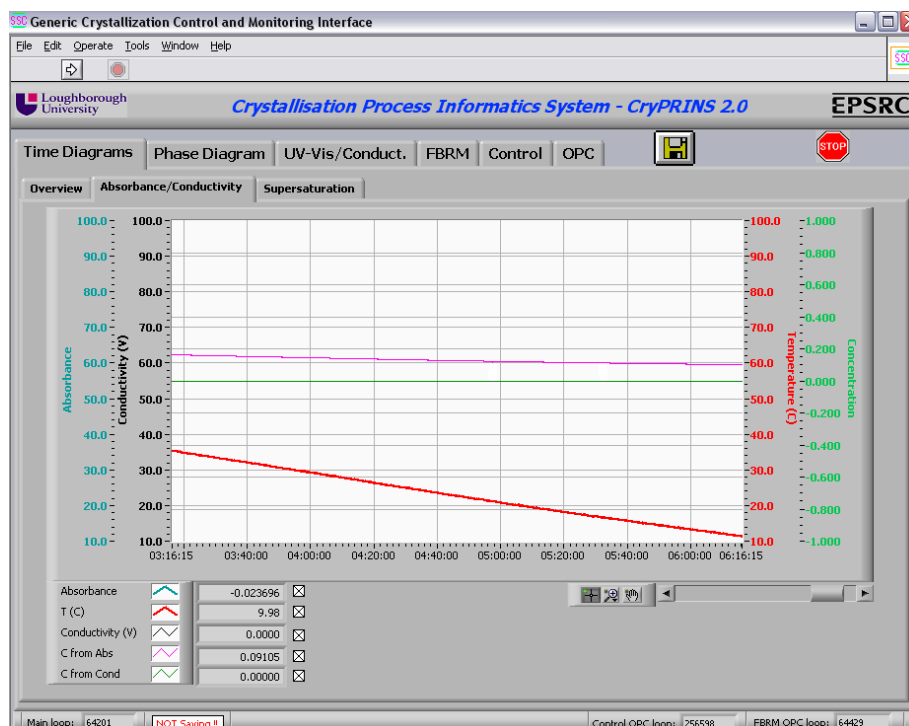
Use this option to auto scale the graph. This is particularly helpful after you have used one of the above options and would like to view the graph in the normal view.



Free hand option can be used to scroll over the plot.

Absorbance/Conductivity

Raw absorbance and conductivity are displayed alongside temperature and concentration data under absorbance/conductivity tab. One such plot with absorbance is shown in the following figure:



All the data export and graph manipulation options are applicable here as well. The submenu allows selection of data to be displayed.

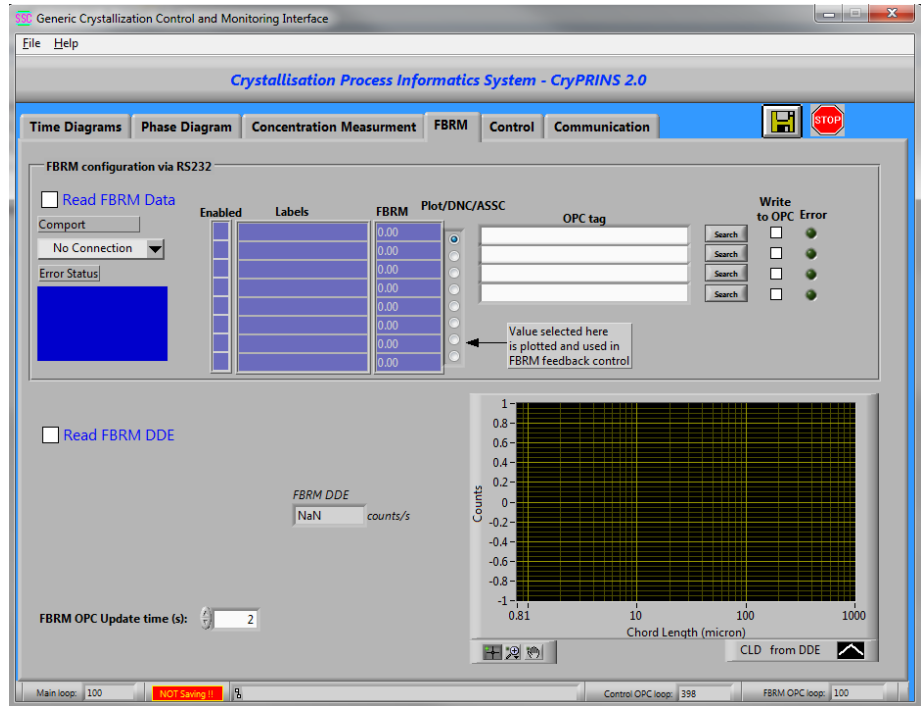
Supersaturation

The absolute supersaturation calculated by the software is plotted under the supersaturation tab along with the supersaturation setpoint. This is useful in SSC to check supersaturation level against the setpoint. All the data and graph operations can be used here as well as described before. Supersaturation plot for a SSC experiment is shown below:

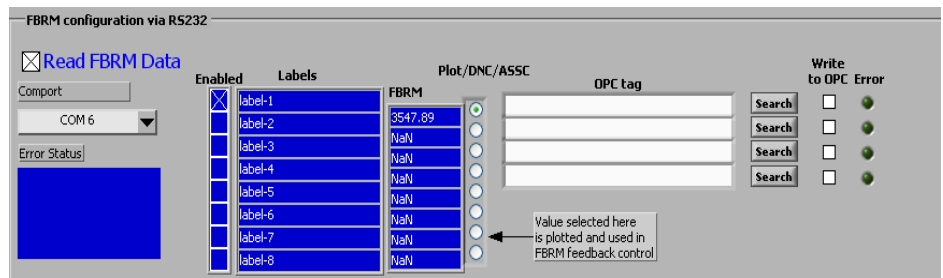
Focused Beam Reflectance Measurement (FBRM)

CryPRINS can read and display data from FBRM in real time, there are three different modes through which data can be read:

- RS232
- OPC
- DDE



All three options are available under the FBRM tab. For RS232 configuration check the box “Read FBRM Data” and then select the appropriate COM port from the dropdown menu under the Comport. Once the connection has been established the FBRM data values will be displayed in the table as shown below:



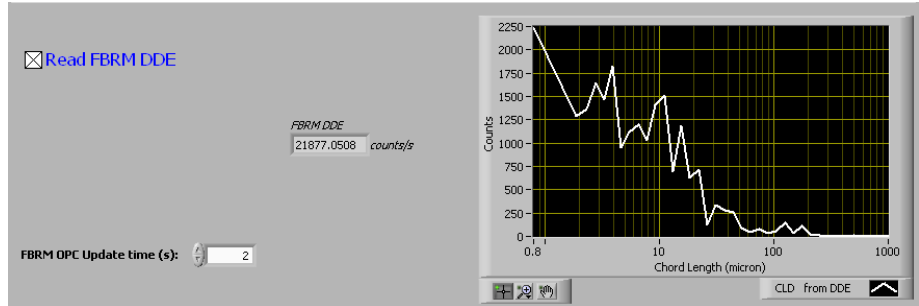
For OPC communication search for the FBRM OPC tag, once it is selected communication will be established.

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Always make sure that FBRM software has been configured properly for sending data to CryPRINS.

DDE is the third communication option available, make sure that the excel file through which transfer is taking place is open for CryPRINS to be able to read data, after this check the box Read FBRM DDE.



FBRM distribution will be displayed in the graph indicating that communication has been successfully established.

Supersaturation Control

The parameters for SSC are defined in Supersaturation Control box under control tab.

Following steps should be followed for SSC:

1. Enter the solubility coefficients in the format as shown in the above figure.
2. Specify the setpoint in DC setpoint box. Care must be taken that setpoint is defined in accordance with the units used in solubility coefficients.
3. Define upper and lower temperature limits in the Temperature Limits box.
4. Once all the parameters have been specified select SSC from the following menu.



SSC Implementation Guidelines

In SSC the system follows an operating curve which generally corresponds to constant supersaturation. For implementation of SSC a calibration model for concentration measurements is required. Following are some general guidelines for implementation of SSC. It is important to know that each system is unique and therefore all the conditions must be selected based on the individual properties of the system.

SSC starts once the seeds have been added to the system and process is in supersaturated condition. Typically 5-10% seeds based on the initial concentration can be added, the amount can however be tailored if required.

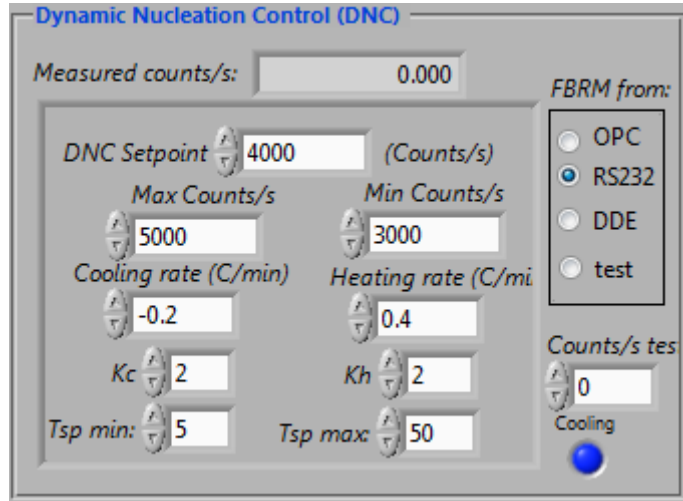
Seeds are added when the system is slightly supersaturated, adding seeds below solubility curve will result in their dissolution on the other hand there is a chance that system might nucleate if seeds additions is carried out when the system is highly supersaturated.

Selection of supersaturation setpoint is important. A high setpoint means that system will be cooled quickly generating supersaturation at a higher rate. For slow growing crystals this might result in multiple nucleation events therefore care must be taken when selecting a setpoint.

Automated Direct Nucleation Control

The parameters and conditions for implementing ADNC are specified in the Direct Nucleation Control box under Control tab. Following steps should be followed:

Always select the appropriate FBRM connectivity mode for ADNC.



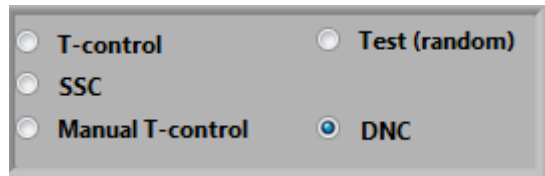
Select the FBRM communication mode that has been chosen for communication with FBRM under the FBRM tab. It is vital that same mode has been selected for ADNC as well.

Next enter the desired setpoint e.g. 4000 counts/s along with upper and lower limits under Max and Min Counts/s.

After this specify the cooling and heating rates along with k_c and k_h values. These control parameters change the heating/cooling rates once the counts are within the upper and lower limits e.g. the cooling rate will be $0.1^\circ\text{C}/\text{min}$ ($0.2/2$) when the total counts are between the lower limit and the DNC setpoint during heating up phase.

Upper and lower temperature limits are entered in Tsp min and Tsp max. The controller will only drive the process in between these temperature limits using the predefined heating/cooling rates.

Finally select DNC from the following menu:

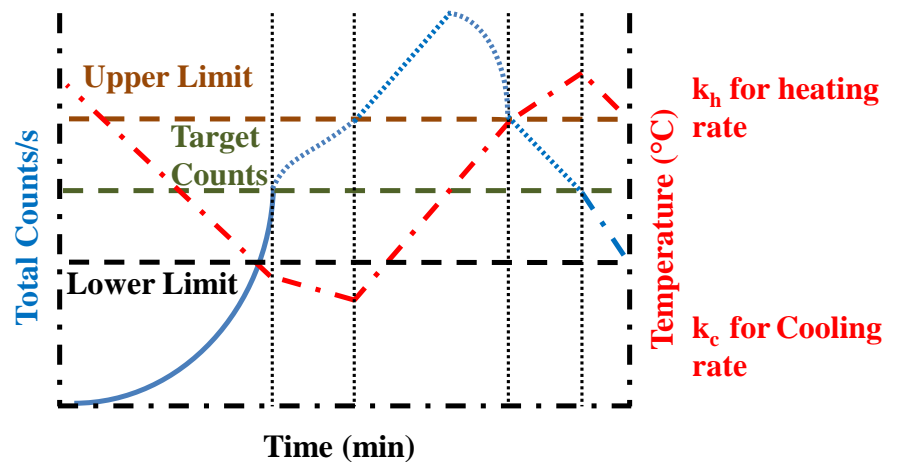


Measured counts/s box at the top displays the counts/s read by the software at any time. In the menu under “FBRM from” a test option is also available, selecting this option allows the user to check the operation of DNC in the virtual mode e.g. at what counts heating/cooling would start.

The blue LED with tag cooling tells when the process is in cooling mode, it turns red and the tag changes to heating when heating is in progress.

ADNC Implementation Guidelines

Major source of variability is crystal size distribution (CSD) comes from primary and secondary nucleation events. The issue is addressed by using ADNC which continuously preferentially dissolve fines. The resulting supersaturation is then used up by the crystal present for growth. This helps in improving the crystal size distribution but also in de-agglomeration and removal of trapped solvent. Following are some guidelines¹ for implementation of ADNC, briefly the working of ADNC is described:



Before starting ADNC target setpoint, upper and lower limits with respect to the counts and proportional gains (k_c and k_h) are specified. The upper and lower temperature limits and heating/cooling rates are also selected alongside previously mentioned parameters. After this the ADNC begins from a clear solution and continues to cool at a specific rate until nucleation takes place as shown in the above figure. Once the lower limit of counts is crossed the system switches to a different cooling rate based on k_c . The

¹ Saleemi, A.N., Rielly, C.D., Nagy, Z.K., 2012. Comparative Investigation of Supersaturation and Automated Direct Nucleation Control of Crystal Size Distributions using ATR-UV/vis Spectroscopy and FBRM. *Crystal Growth & Design*, 12, 1792-1807

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heating cycle starts once upper limit of counts is crossed and the rate changes once the counts are between the set point and lower counts limit.

Selection of target counts is important generally selecting a lower number of counts result in bigger crystals as more supersaturation is available for particles present at any time or vice versa.

This on the other hand can also lead to multiple nucleation events as less surface area would be available to consume supersaturation.

To establish a correlation between the ADNC target counts and desired CSD a simple experiment in which slurry is heated up step by step can be performed. The process temperature can be maintained at certain values for 30-60 minutes and sample should be taken and analyzed using standard measurement techniques such as laser diffraction, image analysis etc. For seeded systems this would be the number of counts after the introduction of seed.

Configuration of the Temperature setpoint output from CryPRINS/CryMOCO to iControl via iCDataShare

In addition to the RS232 interface for standard thermoregulators (Huber, Julabo) and the OPC interface the CryMOCO/CryPRINS software has the possibility to send the temperature setpoint output specified via the “Control” tab (as manual, T-control, SSC or DNC) to the Mettler-Toledo iControl software via the iCDataShare environment.

To setup the communication follow the steps below:

1. Open Excel -> Add-ins -> iCDataShare

Give a variable name for the setpoint, set the update rate and press the “Run” button

The screenshot shows the following configuration in the iCDataShare add-in:

Data Out Variable	Value	Units
Tsp_icdata	23.4	

The iCDataShare task pane shows the following settings:

- Tab: Data Out
- Update data values every: 2 seconds
- Run button: [Start]

After pressing the “Run” button the iCDataShare macro sheet in Excel should look similar to the one in the figure below. Make a note of the name of the sheet (e.g. “MTAC”) and the address of the cell with the temperature setpoint value. (e.g. “R2C2” – row 2 and column 2). These information are needed to configure the temperature setpoint output from the iControl menu of the CryMOCO software as described in Step 6.

1	Data Out Variable	Value	Units	Data In (times and values fetched from
2	Tsp_icdata	23.4		
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				
13				
14				
15				
16				
17				
18				

Cell	Tag Name	Last Value
A2	Tsp_icdata	23.4

2. Open iControl and start a new experiment.

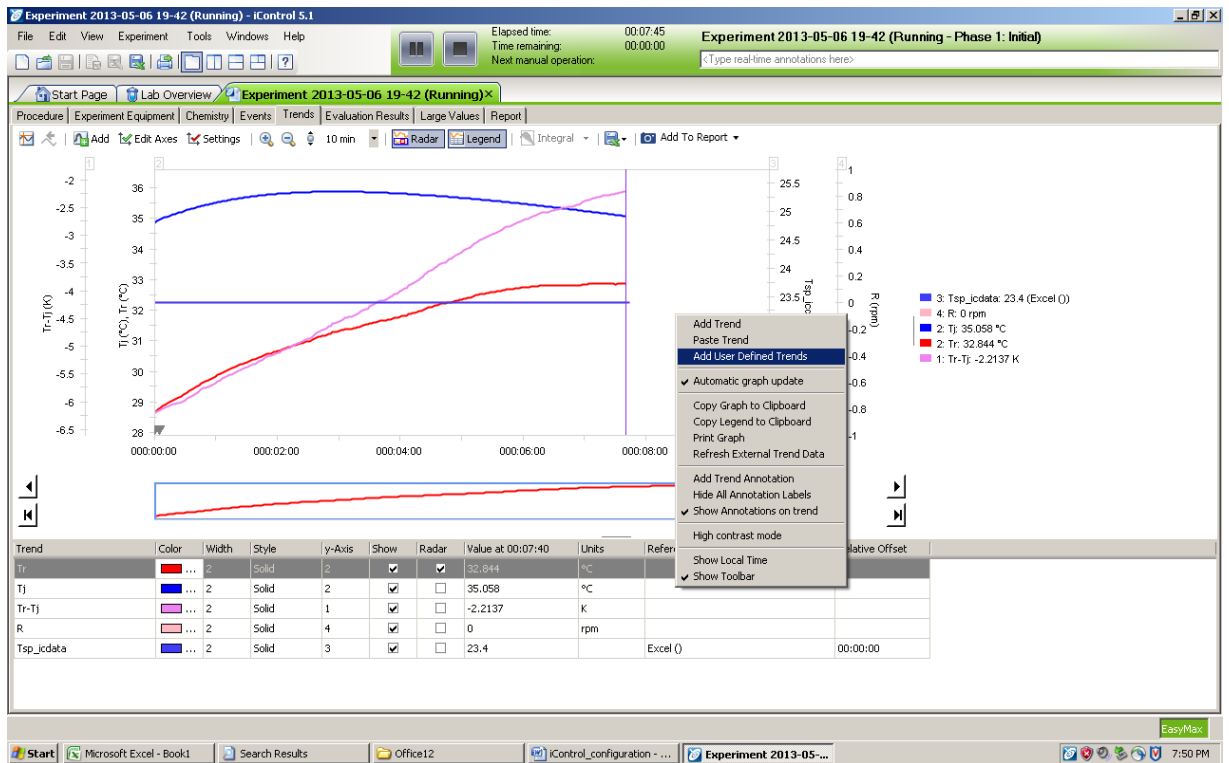
- Go to the “Trend” tab and press “Add”
- From the “Select Trend(s)” window select the variable defined in Excel in the iCDataShare window and press OK. The variable should appear in the legend of the Trend figure

Press the “Add” to add the variable defined in iCDataShare

Go to the “Trend” tab; press “Add” and select the variable define in the iC Data Share

Trend	Color	Width	Style	y-Axis	Show	Rt
Tr	Red	2	Solid	2	<input checked="" type="checkbox"/>	
Tj	Blue	2	Solid	2	<input checked="" type="checkbox"/>	
Tr-Tj	Pink	2	Solid	1	<input checked="" type="checkbox"/>	
R	Purple	2	Solid	4	<input checked="" type="checkbox"/>	

3. Right click on the trend figure and select “Add user defined trends”



4. Press “Add” in the “User defined trends for experiment ...” window.



Important: deselect the “Autoname” option and give a name for the setpoint variable that is different from the name used in the iCDataShare sheet in Excel.

The link to the iCDataShare variable should be selected in the “Trends” field and press “Add to Expression” followed by “OK”

Add name that is different from variable in iCDataShare

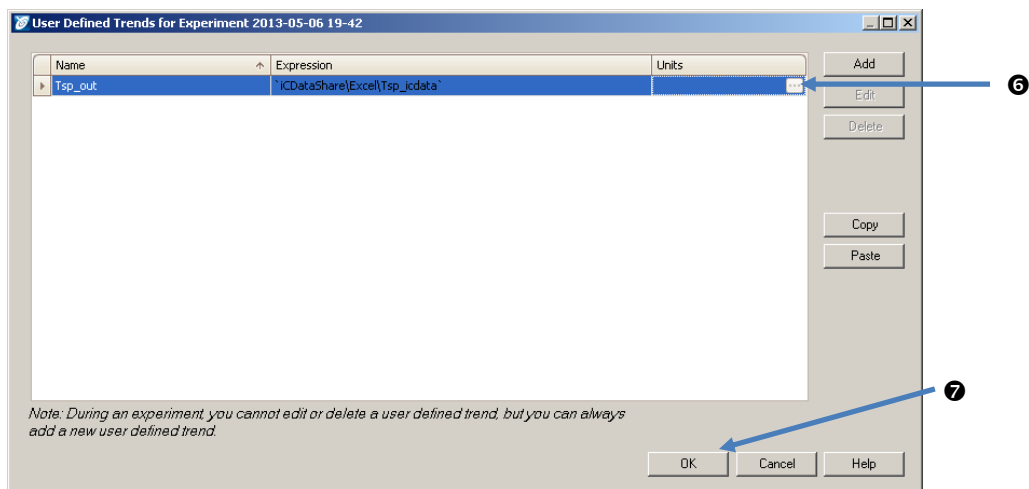
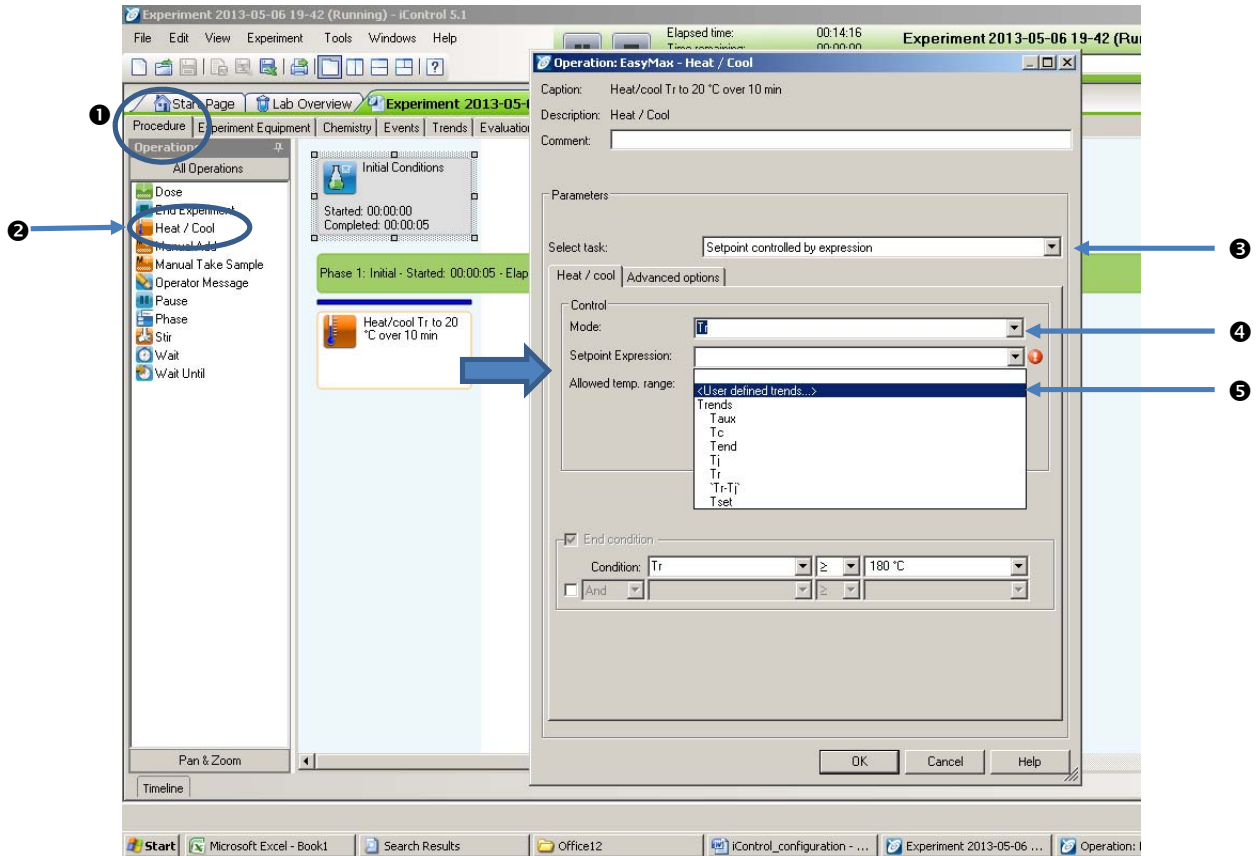
Deselect “Auto name”

Select link to the iCDataShare variable, press “Add to Expression” and “OK”

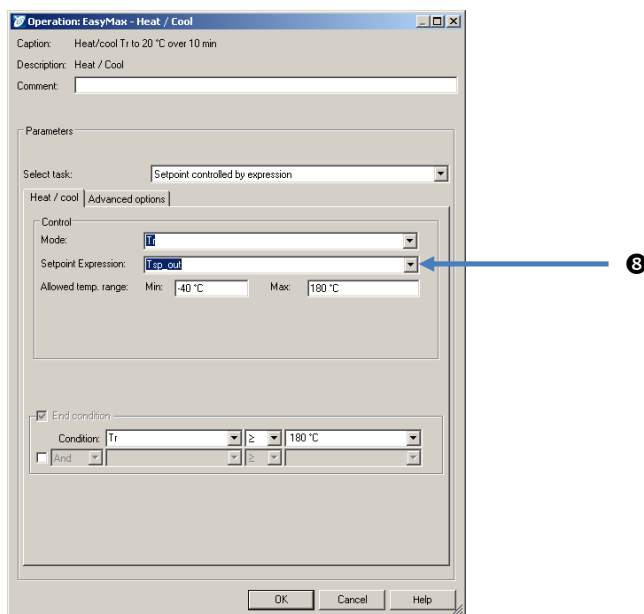
Note: During an experiment, you cannot edit or delete a user defined trend, but you can always add a new user defined trend.

Name	Expression	Units
Tsp_out	iCDataShare\Excel\Tsp_icdata	

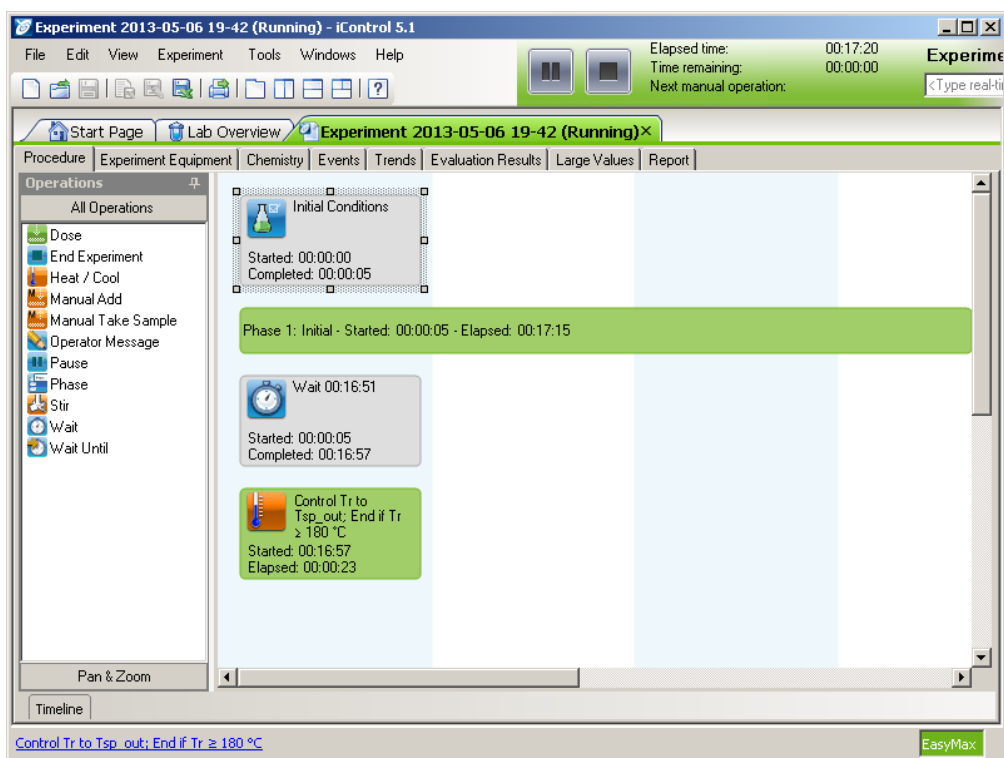
5. Go to "Procedure" tab (❶) and drag-and-drop a "Heat/Cool" element in the procedure (❷).
 - Select task: "Setpoint controlled by expression" (❸)
 - Mode: "Tr" (❹)
 - Setpoint expression "User defined trends" (❺)



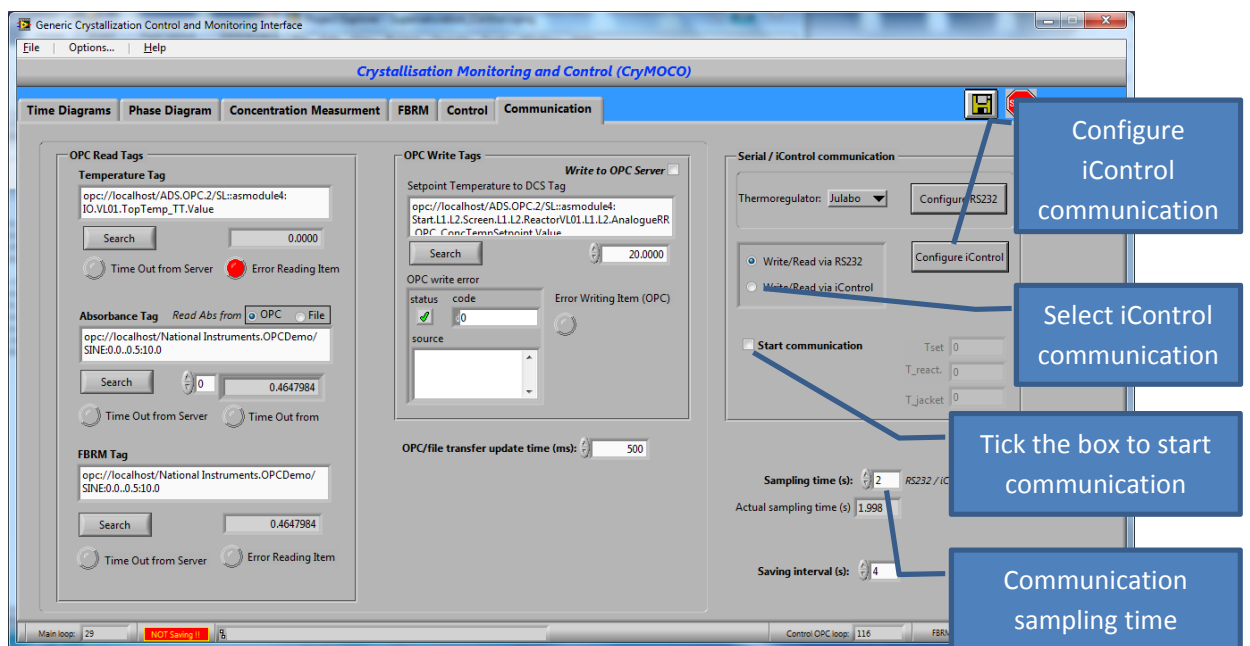
- Select the variable (6) and press OK (7). The user defined trend for the setpoint should appear in the “Setpoint Expression” field and will be used as the setpoint for the temperature controller (8).

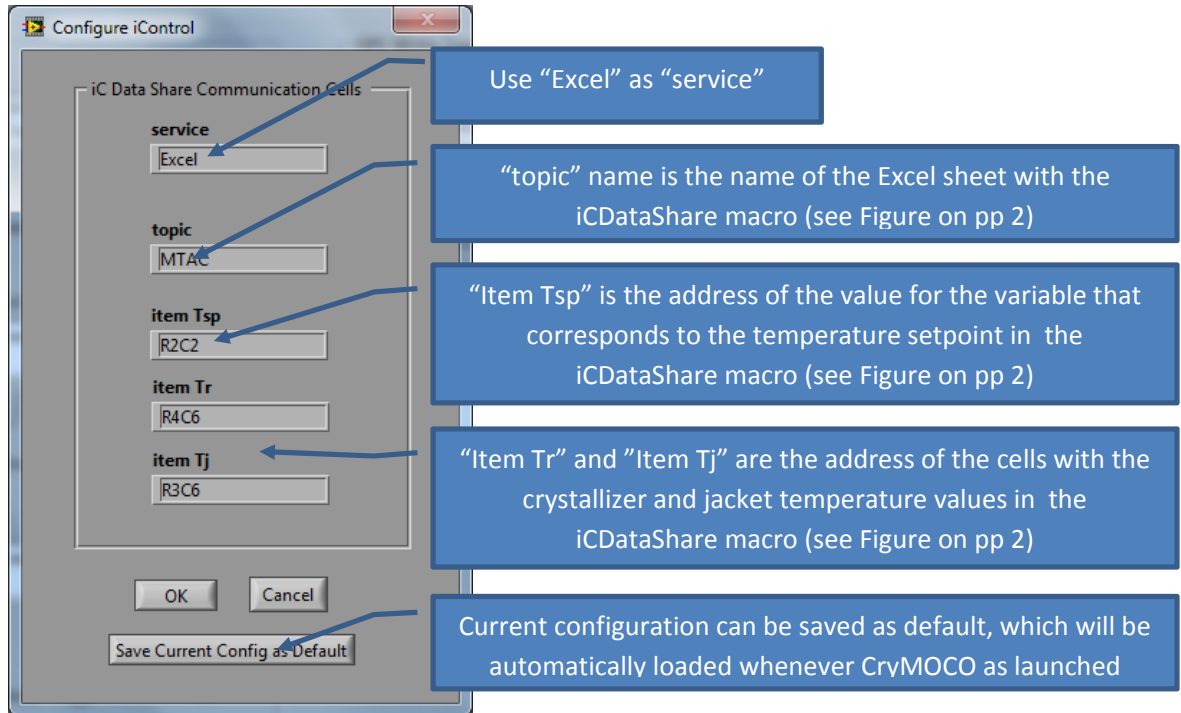


The “Procedure” window should look something similar as below:



6. After iControl is prepared for reading the temperature setpoint from iDataShare, CryMOCO can be configured to send the setpoint to the variable defined in the Excel template in iDataShare. Communication is implemented via the windows dynamic data exchange (DDE) approach through the Excel file in icDataShare used as a data transfer buffer between iControl and CryMOCO.
- Select the “Communication” tab in the CryMOCO interface and press the “Configure iControl” button the configure the communication with iControl via the excel data buffer set up in iDataShare:





After the communication parameters are defined, the "Sampling time (s)" can be set. This will determine the frequency with which the cell value in the iCDataShare will be updated by CryMOCO. It is not necessary to set the same value as set for the update time in the icDataShare excel maco.

By selecting the "Write to iControl" the temperature setpoint values obtained in the CryMOCO interface with any of the methods will be sent to iControl via the iCDataShare macro used as data transfer buffer and the crystallizer temperature and jacket temperature values from iControl will be transferred back to CryMOCO.

Appendix B - Detailed info on the use of calibration equation

Circled parts are actually coefficient **vectors**. Note that each of the three subvectors are indexed separately starting from index 0.

Put 1 for index 0 for Abs(1)

index of element in coefficient vector for the particular part of calibration model (index start with 0) put 1 for

Coefficient value corresponding to index

Concentration Correlation from Absorbance (UV/FTIR/Raman/US) (from OPC/file)

Calibration Model: C = 0.486838

$C = \frac{A}{T} 0 \frac{A}{T} 1 *Abs + \frac{A}{T} 0 \frac{A}{T} 0 *Abs^2 + \frac{A}{T} 0 *T + \frac{A}{T} 0 *T^2 + \frac{A}{T} 0 \frac{A}{T} 0 *A*T$

Put -1 for index 1 for Abs(2)

Put -1 for index 1 for Abs(2)

Concentration Correlation from Absorbance (UV/FTIR/Raman/US) (from OPC/file)

Calibration Model: C = 0.486838

$C = \frac{A}{T} 1 \frac{A}{T} -1 *Abs + \frac{A}{T} 0 \frac{A}{T} 0 *Abs^2 + \frac{A}{T} 0 *T + \frac{A}{T} 0 *T^2 + \frac{A}{T} 0 \frac{A}{T} 0 *A*T$

offset = $\frac{A}{T} 0$

Calibration on? OFF C = C + offset

In general the calibration equation implemented in CryPRINS has the form:

$$C = b_0 + \sum_{i=1}^n b_n A_n + \sum_{i=1}^n d_n A_n^2 + eT + gT^2 + \sum_{i=1}^n (h_n A_n) T$$

For example for a two absorbance model (little rearranged the terms of equation above to follow the order of the terms in the calibration equation in the cryPRINS interface):

$$C = b_1 * A_1 + b_2 * A_2 + d_1 * (A_1)^2 + d_2 * (A_2)^2 + e * T + g * T^2 + b_0 + h_1 * A_1 * T + h_2 * A_2 * T$$

The screenshot shows the 'Concentration Correlation from Absorbance (UV/FTIR/Raman/US) (from OPC/file)' window. The 'Calibration Model' section displays the equation: $C = \frac{A}{T} 1 \frac{A}{T} -1 * Abs + \frac{A}{T} 0 \frac{A}{T} 0 * Abs^2 + \frac{A}{T} 0 * T + \frac{A}{T} 0 * T^2 + \frac{A}{T} 0 * A * T$. The 'offset' is set to 0. A 'Calibration on?' toggle is currently 'OFF'. The value of C is shown as 0.486838. Callout boxes provide the following explanations:

- index 0 is b_1 , index 1 is b_2
- Here goes the value of b_1 for index 0 and for b_2 for index 1
- Similar here put d_1 for index 0 and d_2 for index 1
- This is g
- This is e
- This is b_0
- Similar here put h_1 for index 0 and h_2 for index 1

Note: Any of the coefficients can be zero, depending on the desired form of the calibration model. For example of only A_1 is to be used in second order or nonlinear $A * T$ term the other can be zero, etc.