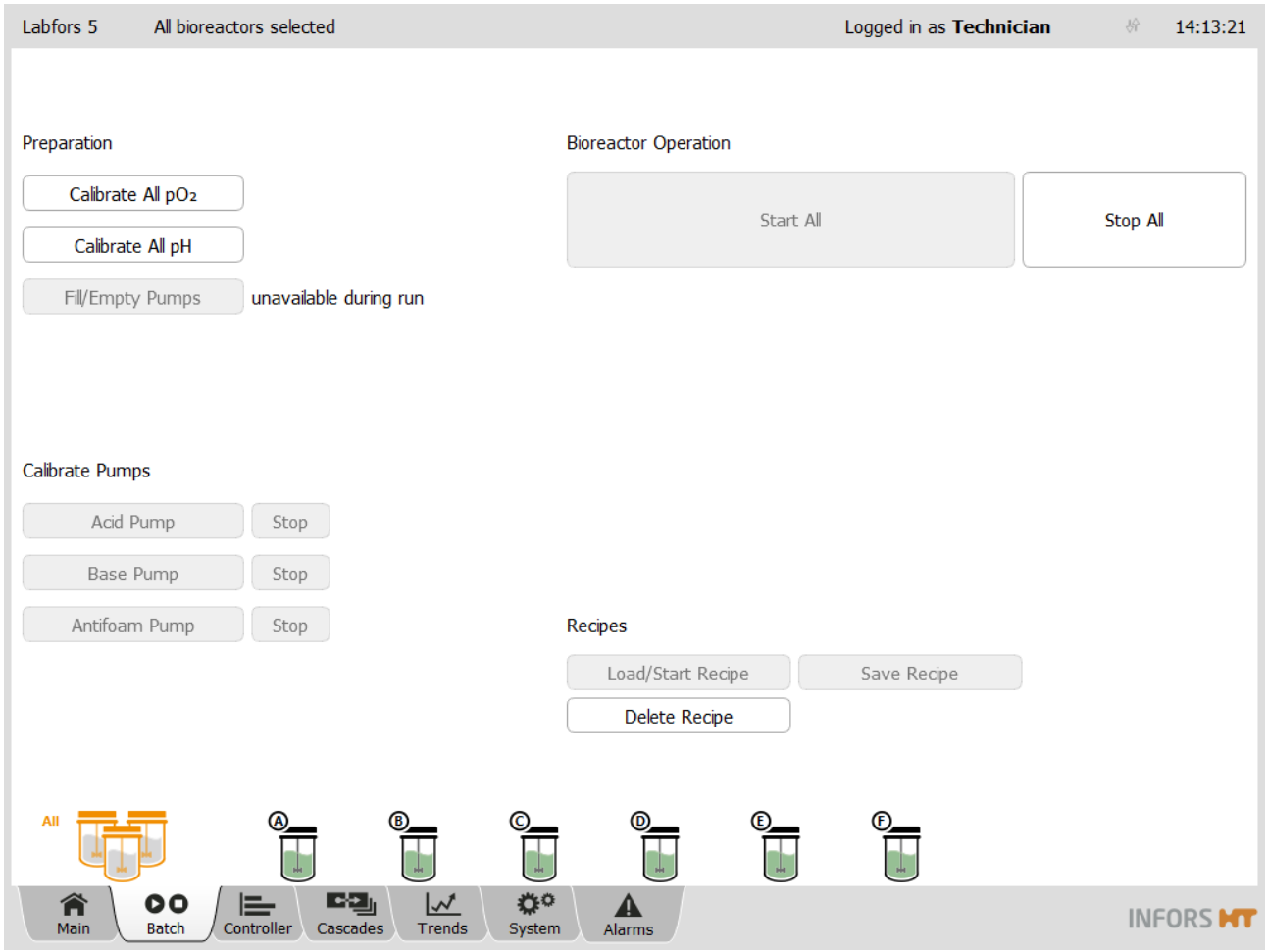
Operating Manual

Touch Screen Software V 3.3

for Bench-Top Bioreactors Labfors 5 and Multifors 2



CE Dok-ID: 77085 - Original - V.02.01

INFORS HT

Infors AG
Headoffice, Schweiz
Rittergasse 27
CH-4103 Bottmingen
T +41 (0)61 425 77 00
F +41 (0)61 425 77 01
info@infors-ht.com
service@infors-ht.com

Infors GmbH
Dachauer Str. 6
D-85254 Einsbach
T +49 (0)8135 8333
F +49 (0)8135 8320
infors.de@infors-ht.com

Infors UK Ltd
The Courtyard Business Centre
Dovers Farm, Lonesome Lane,
Reigate
Surrey, RH2 7QT, UK
T +44 (0)1737 22 31 00
F +44 (0)1737 24 72 13
infors.uk@infors-ht.com

Infors Sarl
2, rue du Buisson aux Fraises
Bâtiment D13
F-91300 Massy
T +33 (0)1 69 30 95 04
F +33 (0)1 69 30 95 05
infors.fr@infors-ht.com

Infors Benelux BV
Markweg 9-A, NL-6883 JL
Velp (GLD)
P.O. Box 125, NL-6880 AC
Velp (GLD)
T +31 (0)26 369 31 00
F +31 (0)26 369 31 09
infors.bnl@infors-ht.com

Infors USA Inc.
9070 Junction Drive, Suite D
Annapolis Junction, MD20701
T +1 301 362 3710 /
T +1 855 520 7277 (toll-free USA)
F +1 301 362 3570
infors.usa@infors-ht.com

Infors Canada
8350 rue Bombardier
Anjou, Quebec
Canada H1J 1A6
T +1 514 352 5095
F +1 514 352 5610
infors.ca@infors-ht.com

Infors Bio-Technology (Beijing) Co., Ltd.
Room 505C, Building 106
Lize Zhongyuan
Wangjing New Industrial Zone
Chaoyang District, Beijing
100102 P.R. of China
T +86 10 51652068
F +86 10 64390585
info@infors-ht.com.cn

Infors South East Asia
16, 1st Floor, Taman City
MY-51200 Kuala Lumpur
Malaysia
T +603 625 771 81
F +603 625 067 48
info@infors-ht.com.my

Infors LATAM Ltda.
Rua Dr. Alceu de Campos
Conjunto 205
CEP: 04544-000
São Paulo – SP
Brasil
T +55 (11) 95304-0201
F +55 (11) 98585-5334
Infors.br@infors-ht.com

Contact details of our local dealers worldwide can be found on our website.

www.infors-ht.com

QUALITY
MADE IN SWITZERLAND

Engineering and production in Switzerland

Table of Contents

Table of Contents

Table of Contents

1 Screen, Menu Navigation and Control Elements

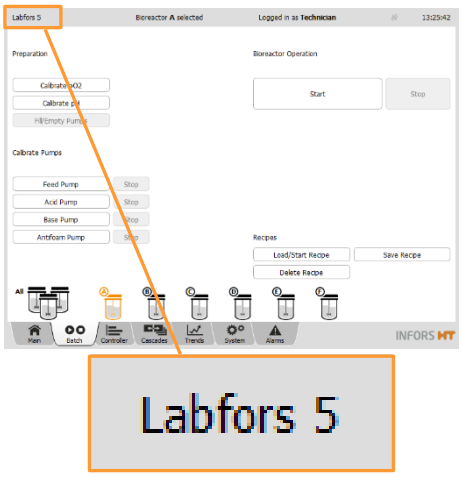
Most of the figures in this manual showing the various menus, dialogue boxes and tab pages of the touch screen software reflect the view of a user with the user authorisation level of *Technician*.

ATTENTION

Changing settings in the touch screen software by unqualified personnel or personnel with insufficient training may lead to loss of property.

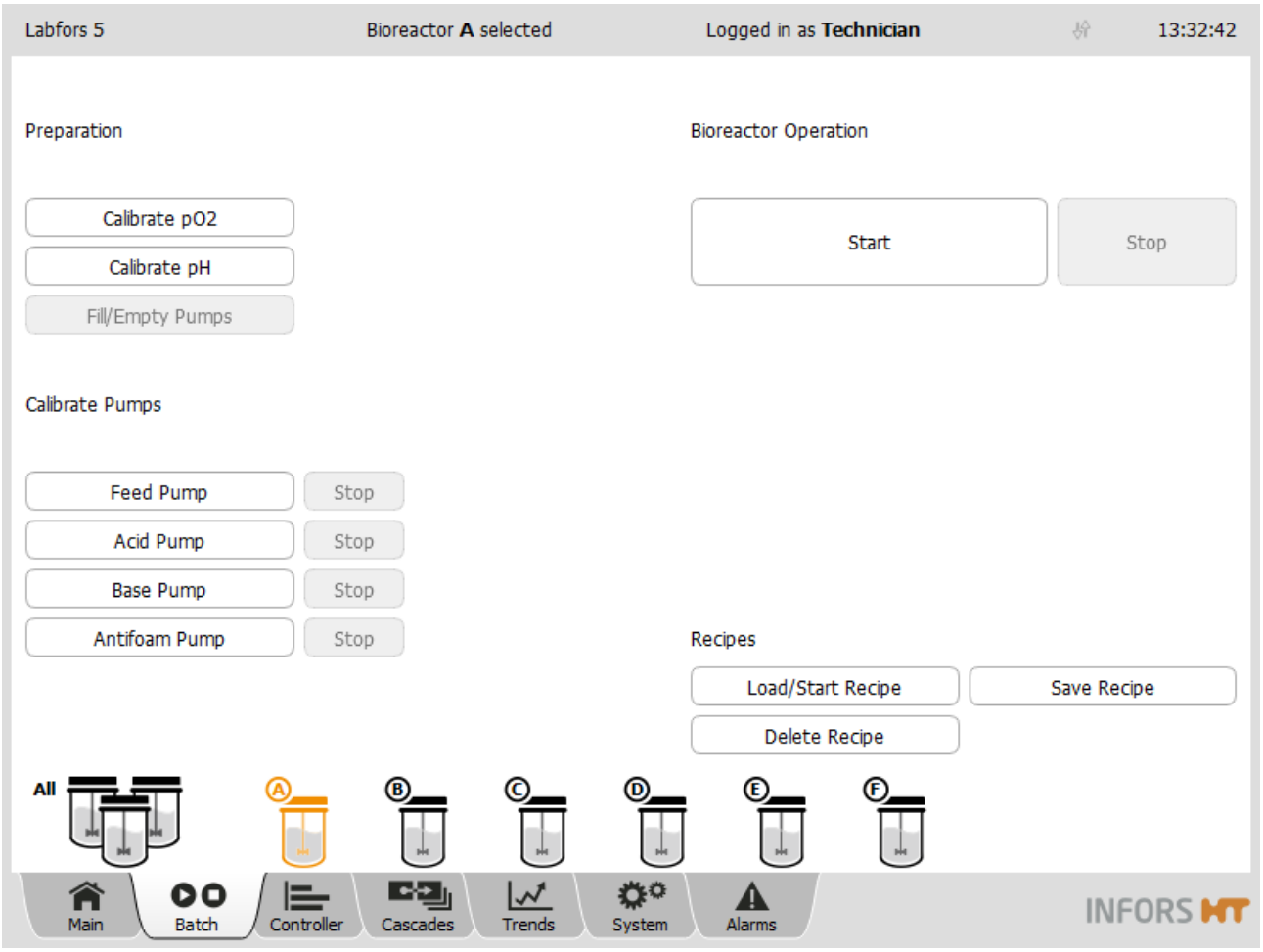
For further information about user levels and access authorisation see chapter “Security – User Management”, “User Levels”.

The figures in this manual showing main menus always show the maximum possible number of controllable bioreactors (= 6) and are from the touch screen software for Labfors 5.



The touch screen software for Labfors 5 and Multifors 2 is identical except for the different names of the equipment displayed in the upper left corner of the screen.

1.1 Screen Areas



The screen is divided into the three sections:

Header

shows (from left to right): name of the device, selected bioreactor e.g. *Bioreactor A selected*, login-status, e.g. *Logged in as Technician* and the time.

Two opposing vertical arrows in the header signalise that an external software like e.g. eve® has access to the OPC XML DA server of the touch screen software. They are flashing while data is transmitted

Main area

shows main menus, e.g. Batch (figure), and submenus. Inputs are made exclusively in the main area. I.e. you press buttons or input fields to select bioreactors or to call up menus and dialogue boxes.

Screen, Menu Navigation and Control Elements

The lowest part of the main area shows a selection bar of the individually selectable bioreactors. The bioreactors are displayed symbolically as culture vessels.

Depending on the configuration of the system, up to six bioreactors (= culture vessels) may be connected. This equates to six Labfors 5 basic units with one culture vessel or max. three Multifors 2 basic units with two culture vessels each.

One operating unit with touch screen software can be used to control up to six bioreactors. I.e. one basic unit serves as the master unit and can control up to five more basic units of the Labfors 5 bioreactor and up to two more basic units of the Multifors 2 bioreactor. These basic units are referred to as satellite units.

Bioreactors 1 to 6 correspond to the bioreactors **A** to **F** in the selection bar. They can be operated independently of each other.
Available bioreactors are shown in dark grey colour with grey content, non-available bioreactors are in light grey colour without content.
A selected bioreactor is shown in orange colour with grey content.

A running bioreactor (operating status *running*) is shown with green content.
ALL can be used to select all available bioreactors simultaneously.

Footer

comprises 7 tabs which provide access to the 7 main menus.

The tabs are displayed with a grey background. A selected tab is shown light grey.

The following main menus are available (from left to right):

- *Main*: shows parameters and values for the available bioreactors. If a single bioreactor is selected, its available pumps are also visible here.
- *Batch*: this is where bioreactors (cultivation processes) are started and stopped, and where sensors and pumps are calibrated. Depending on the access authorisations, it may also be possible to store, upload or delete recipes.
- *Controller*: shows parameters for the selected bioreactor and offers the option of changing values.
- *Cascade*: allows to set up a serial, parallel or parallel serial (mixed) cascade control of one or several parameters.

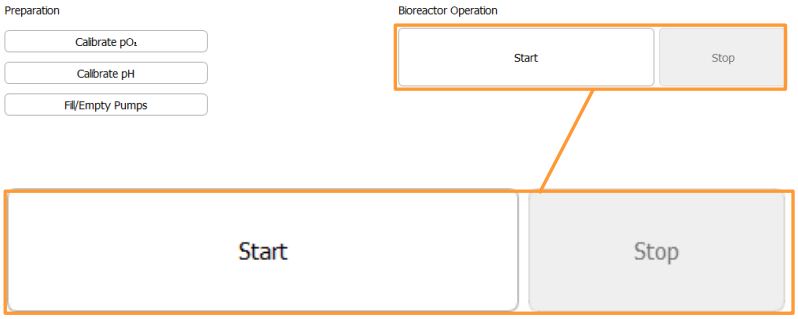
- *Trends*: shows trends in the parameters, time span between 15 min. and 2 days.
- *System*: provides access to the submenus *Valves*, *Security, Settings, Wipe Screen* and *Shutdown*
- *Alarms*: shows parameter alarms, user alarms and system alarms

1.2 Control Elements

Buttons

Depending on the selected main menu or submenu and access authorisations, various buttons may be visible and available. Pressing a button either opens a sub menu, or a dialogue box or a tab page.

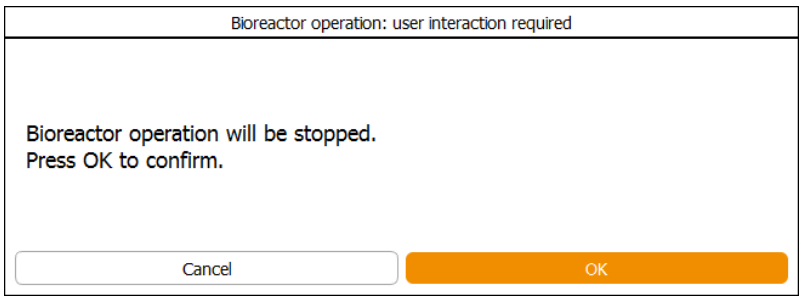
Enabled buttons are white in colour, disabled buttons are grey in colour.



Buttons, which are intended as the next logical step in the procedure, are shown in orange colour, see example in next section.

Dialogue boxes and tab pages

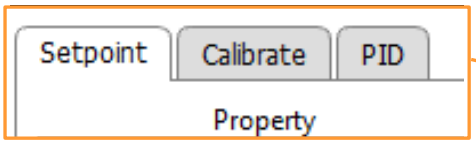
A dialogue box may contain instructions, notes, warnings or general information.

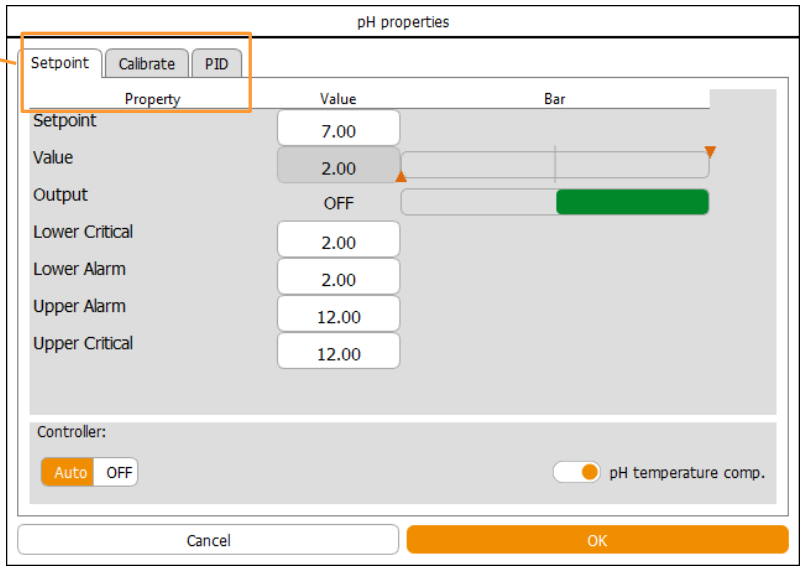


A dialogue box may also contain further buttons, input fields or view boxes and tabs.

Example: *pH properties* dialogue box with tabs which lead to the different parameter options.

Pressing a tab leads to access of the respective option for the selected tab page. The tab for a selected tab page is displayed with a white background.





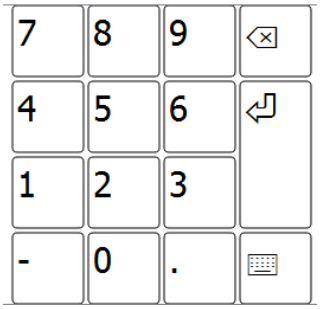
Depending on the parameter and the access authorisations there may be more or less available options for a parameter.

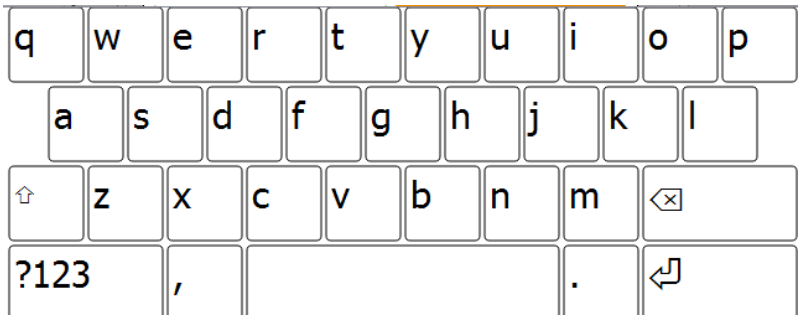
Input fields and view boxes

They are included in various menus, dialogue boxes and tab pages. They either require the inputting of a numerical or an alpha-numerical value or show these values.

Numeric keypad and alphanumeric keyboard

Numerical values are entered using a numeric keypad. Alphanumerical values are entered using an alphanumeric keyboard. After pressing an input field, the appropriate pad/board appears.





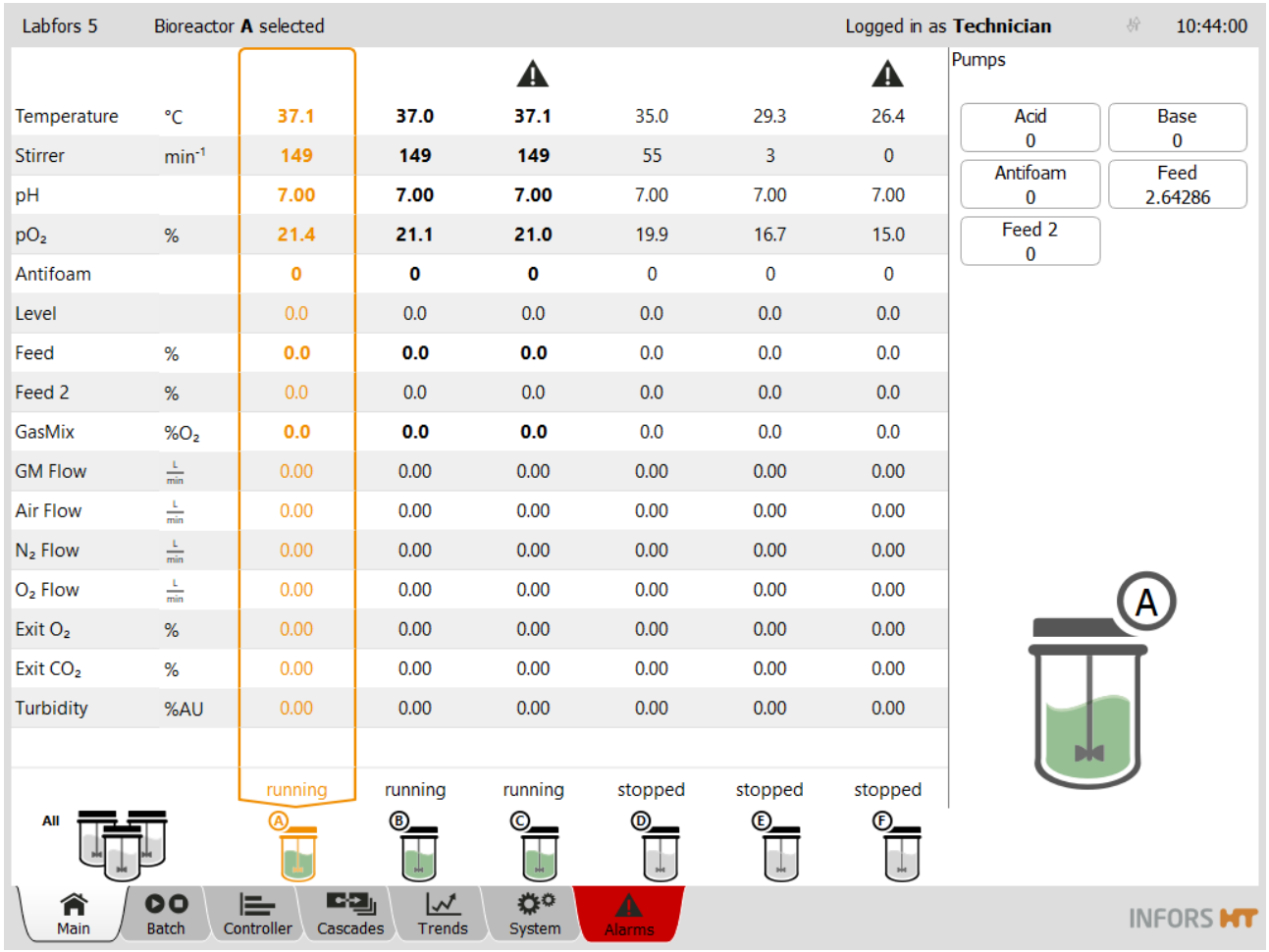
ON / OFF switch

The ON / OFF switch is used in order to switch a function on or off.

- **ON**: the switch is in orange colour
- **OFF**: the switch is in white colour

2 Main Menus

2.1 Main – Parameter Display All Bioreactors



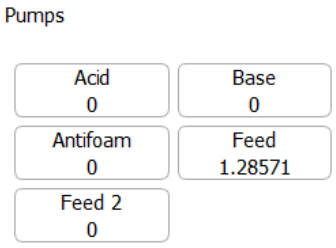
The main menu *Main* opens automatically after system start. Here all parameters are listed with current values of the available bioreactors. The operating states (running / stopped) of the bioreactors are also visible here, and parameter alarms are signalled.

The quantity and type of parameters differ depending on the system configuration but remain the same for each individual available bioreactor.

Value display and alarms

Parameter values and the symbol of a selected bioreactor are displayed in orange. Current values of switched-on parameters of running bioreactors are in bold letters.

Parameter alarms which have not been confirmed are signalled in the corresponding bioreactor column with a warning symbol above the actual values. A detailed list of parameter alarms can be found in the main menu *Alarms.*



Pumps

A large illustration of the bioreactor which has been selected via the selection bar is displayed on the right-hand section of the screen. All pumps of the selected bioreactor are displayed above it as buttons.

The following four pumps are available by default:

- *Acid*
- *Base*
- *Antifoam*
- *Feed*

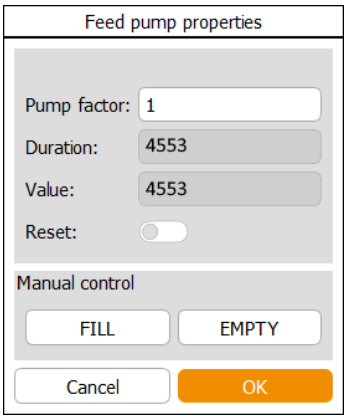
The *Feed 2* pump is optional

INFORMATION

If all bioreactors (*ALL*) are selected, the message *Please select the bioreactor to view the pumps* appears instead.

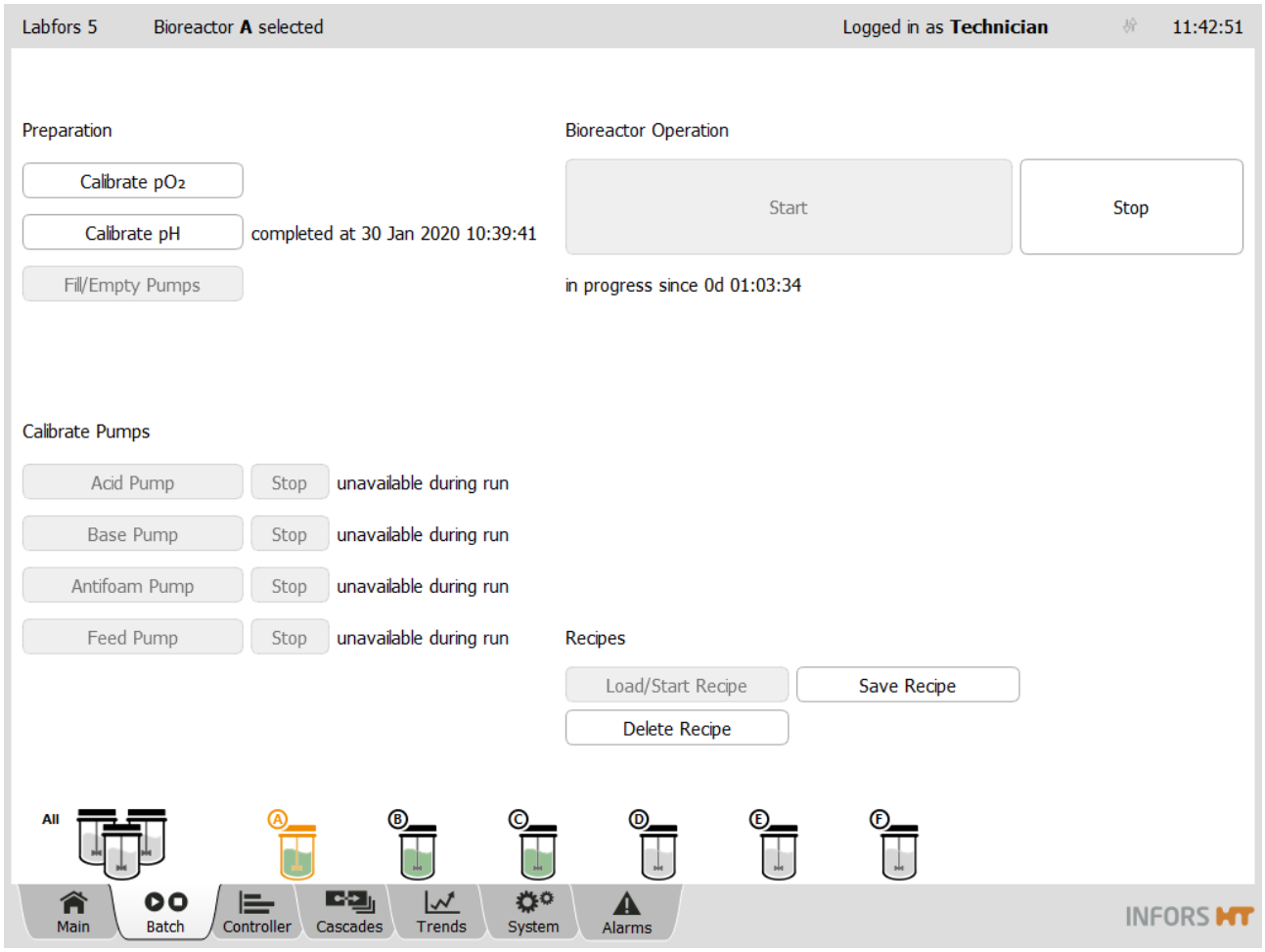
The delivered volume (in mL) of a calibrated pump is continuously shown during a cultivation. This numerical value is displayed on the corresponding pump button.
If the pump is not calibrated, the number of revolutions is displayed.

Main Menus



After pressing one of the four buttons a dialogue box, e.g. *Feed pump properties* appears where the number of rotations of the selected pump can be reset to zero. The pump factor calculated during pump calibration is also visible and can be changed manually here.
In addition, the two buttons **FILL** / **EMPTY** on the standard pumps allow the manual filling or emptying of the hoses.

2.2 Batch – Start Menu



The main *Batch* menu is divided up into groups with various buttons which correspond to the function of the group:

- *Preparation*: to calibrate individual or all pH and pO_2 sensors and automatic and to simultaneously fill or empty all pump hoses.
- *Calibrate Pumps*: to start and stop pump calibration. Pumps can only be calibrated individually for each bioreactor.
- *Bioreactor Operation*: to start and stop one bioreactor (cultivation), several bioreactors or all bioreactors
- *Recipes*: to load, save and delete recipes.

Depending on access rights of the operator, selection of the bioreactor(s) and operating status of an individual or several bioreactors more or less functions are available. Detailed descriptions of each

function can be found in the appropriately named chapters in this manual.

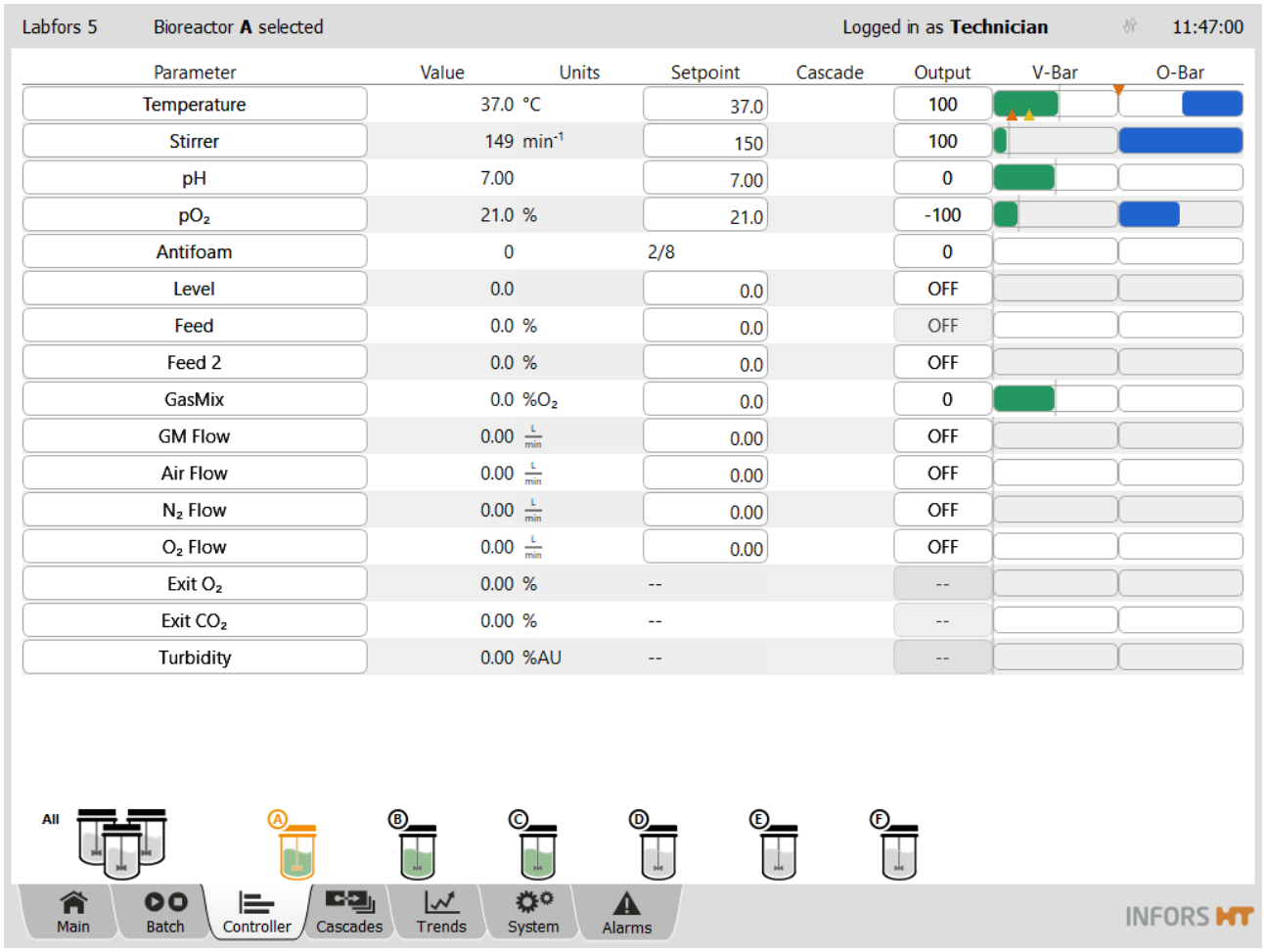
The following additional functions are available for certain device versions of the bioreactor Labfors 5:

- Version for microorganisms with option LabCIP: **Perform CIP/SIP** (starting/stopping the CIP/SIP).

  The CIP/SIP process and its configuration are described in detail in the separate operating manual of the device (LabCIP).
- Version for solid substrates and enzymatic bioprocesses: **Set Stirrer Max.** (activating/deactivating rotation speed limit).

  This function is shortly described in the main chapter “Parameters” chapter “Stirrer”, section “Set Stirrer Max. - rotation speed limit”.

2.3 Controller – Value Display



The main menu *Controller* shows current values, setpoint values and controller outputs for the parameters of a selected bioreactor. This menu is not available when all bioreactors (*ALL*) are selected.

Settings for parameters can be changed here.

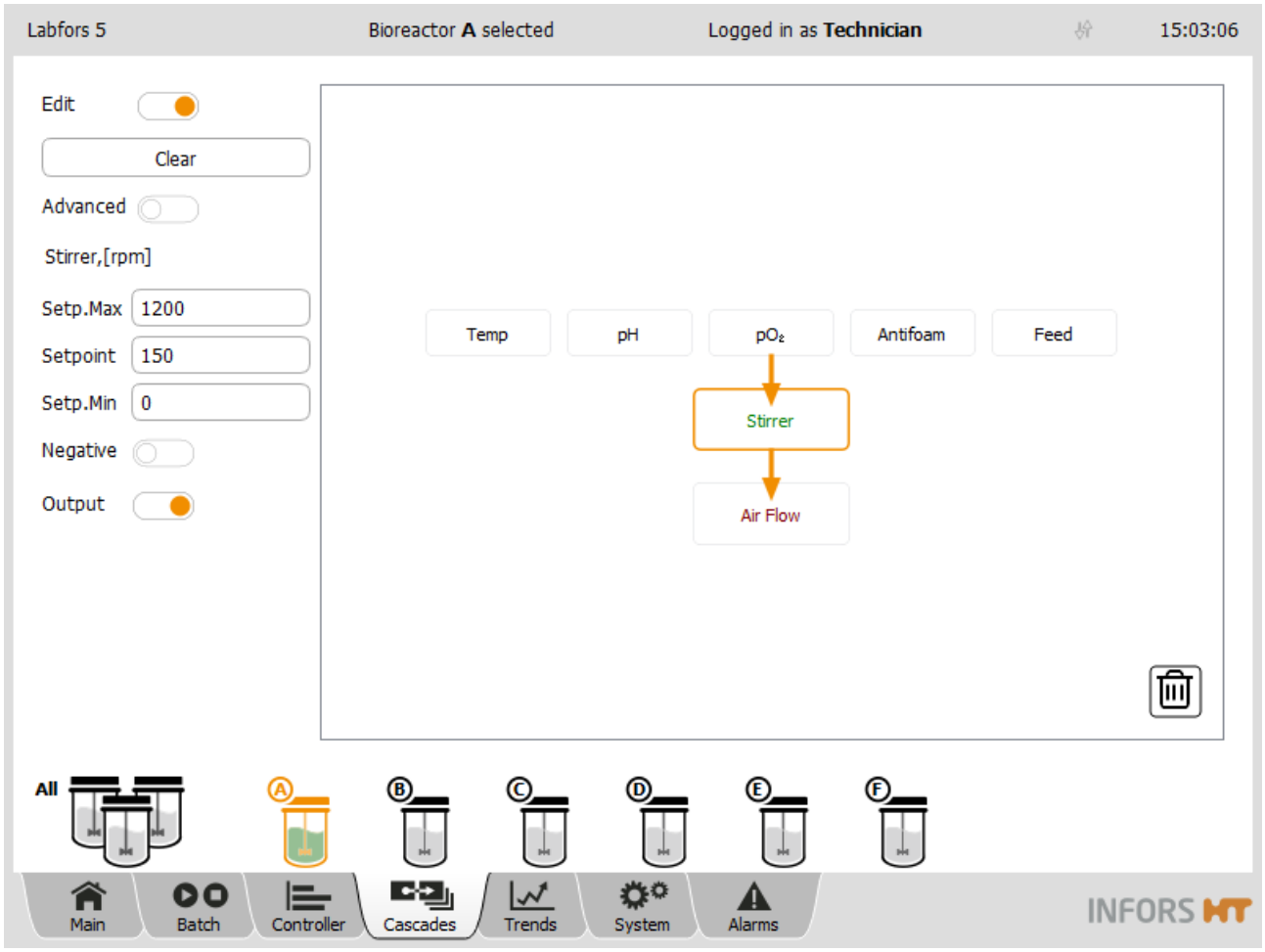
- *Parameter*: lists the available parameters. Touching the desired parameter button opens its setting menu, see chapter “Parameter Options”.
- *Value*: displays the actual parameter values
- *Units*: displays the units of the parameters
- *Setpoint*: to enter/change setpoint values of parameters

INFORMATION

When the bioreactor has been stopped, setpoint values in the Controller menu are overwritten with the setpoint values set in the start dialogue. See the chapters “Setpoint” and “Setting Setpoint Values, Switching Parameters ON / OFF” for details.

- *Cascade*: indicates, whether and how cascade control is active and which process parameters are used. Settings for a cascade are made in the main menu Cascade. A detailed description about cascade control can be found in the chapter “Cascade Control”.
- *Output*: displays the controller output for a parameter in % when a bioreactor is running. A switched off parameter is displayed as *OFF*. When the bioreactor has been stopped, all its parameters are automatically switched off. Parameters can be switched on or off here whilst a bioreactor is running by touching the controller output (displayed value *OFF* or %). This is only possible, if the automatic mode is set in the *Setpoint* option of the parameter concerned.
- *V-Bar* (vertical bar): shows a graph comparing the current value, set value and alarm limits:
  - Grey continuous marking: set setpoint value
  - Yellow marking: set alarm value (lower alarm / upper alarm).
  - Red marking: set critical values (lower critical / upper critical).
  - Green bar: current value is within the alarm limits.
  - Yellow bar: current value has exceeded the upper alarm value or dropped below the lower alarm value.
  - Red bar: current value has exceeded the upper critical value or dropped below the lower critical value.
- *O-Bar* (controller output bar): shows a graph of the current controller output (%). Parameters which are controlled on two sides (e.g. pH and temperature) are shown as a two-part bar.

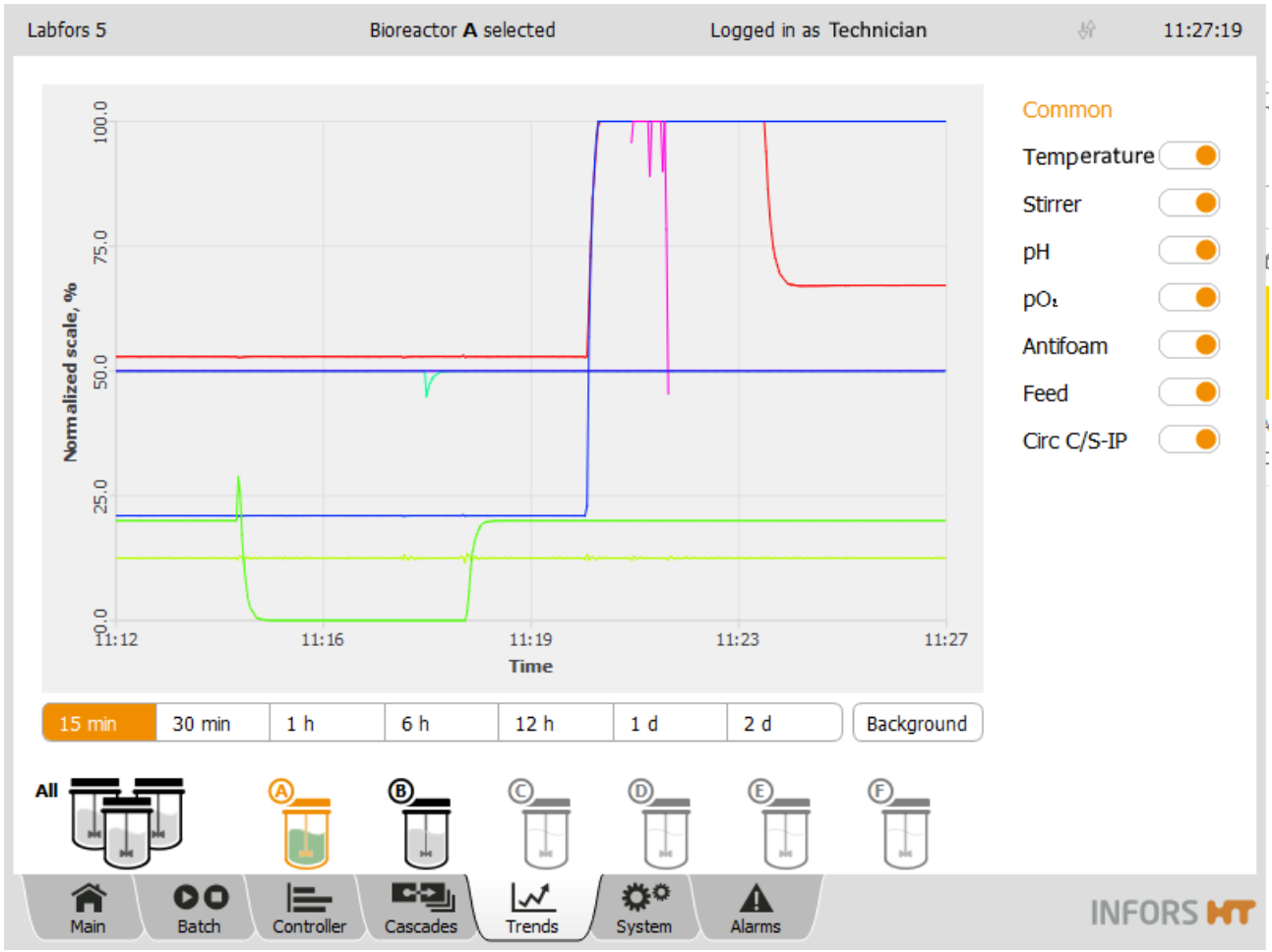
2.4 Cascade



The main menu *Cascade* provides the option of setting up a serial, parallel or mixed cascade control of a parameter. This function is mainly used for pO_2 regulation.

The cascade settings are made in the left-hand section of the screen and the main section presents these schematically. The individual process parameters can be added to a cascade by dragging & dropping them.

2.5 Trends – Trend Lines



The touch screen operating unit keeps the current parameter values in a buffer and continuously charts them in the main menu *Trends*. This data can neither be archived nor edited or exported. The main menu *Trends* serves to provide quick information on the progress of the cultivation only. This menu is not available when all bioreactors (*ALL*) are selected.

However, the data can be archived on computer connected via network using eve®.

The parameters for the selected bioreactors are listed on the right-hand side of the screen. The **ON/OFF** switch next to each parameter allows to activate/deactivate the display of its trend line in the main area of the screen.

All trend lines are normalised to the value range of the respective parameter. The maximum value (= 100 % of the normalised scale) is located on the top of the diagram, the minimum value (= 0 % of the normalised scale) on the bottom. When a parameter is selected from the list, the labels on the Y axis will switch to the value range

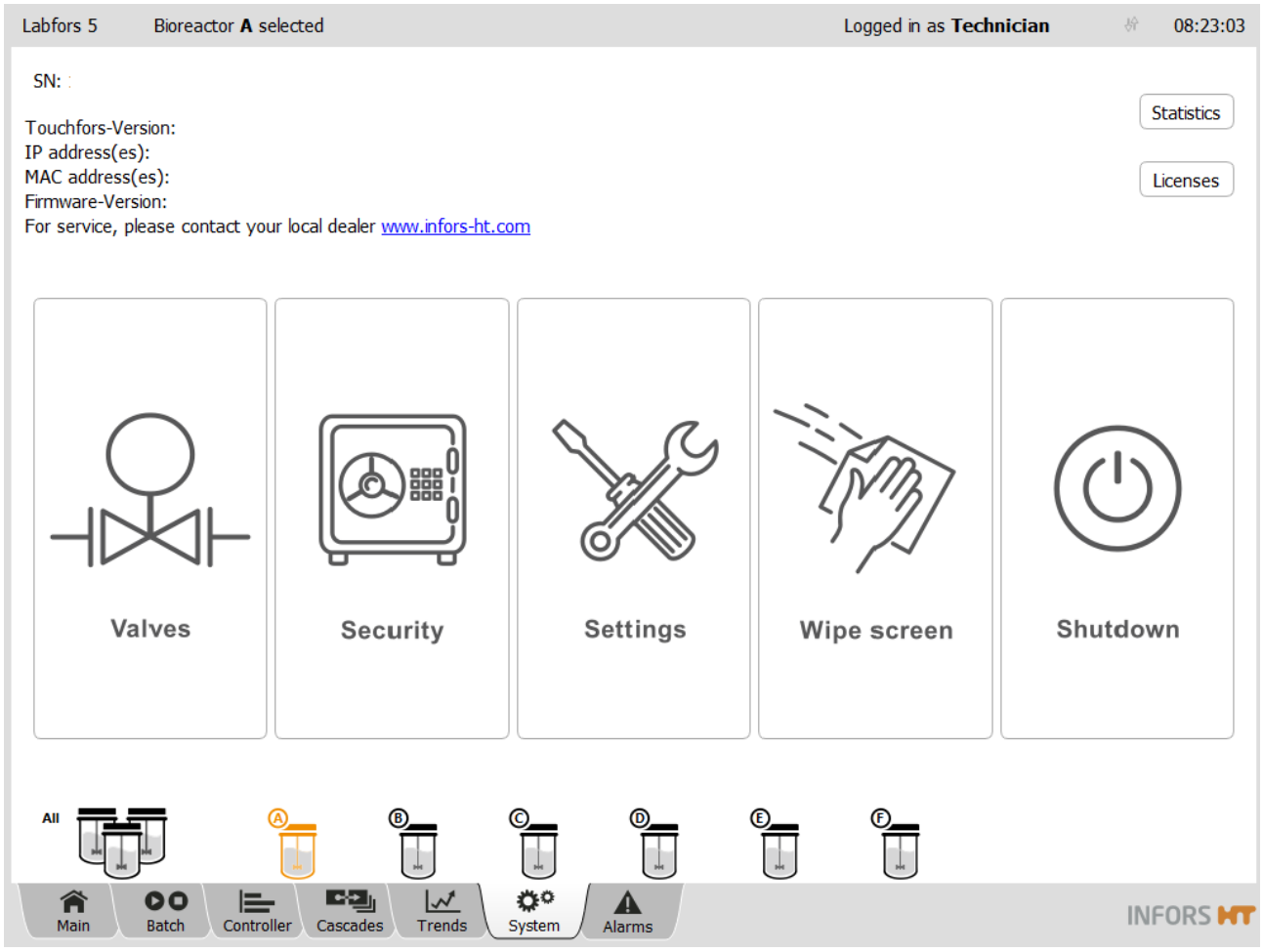
of the selected parameter. When *Common* is selected, the labels on the Y axis are reverted to the normalised scale.

The sideways spread of the diagram can be selected via the buttons below the diagram:

- **15 min** and **30 min**: 15 and 30 minutes
- **1 h**, **6 h** and **12 h**: 1, 6 and 12 hour(s)
- **1 d** and **2 d**: 1 and 2 day(s)

The **Background** button allows to change the background colour of the diagram display (white, grey and black).

2.6 System – System Settings



The main menu *System* shows the following:

- Serial number (SN)
- Software version
- IP address of the system(s)
- MAC (hardware) address(es)
- Firmware version
- Manufacturer's internet address (Domain)

Two buttons are situated in the upper right side of the screen:

- **Statistics**: enables viewing some statistics of the software communication with the controller, i.e. the hardware of the bio-reactor(s). The function is only used for fault diagnosis for the technical support from the manufacturer.

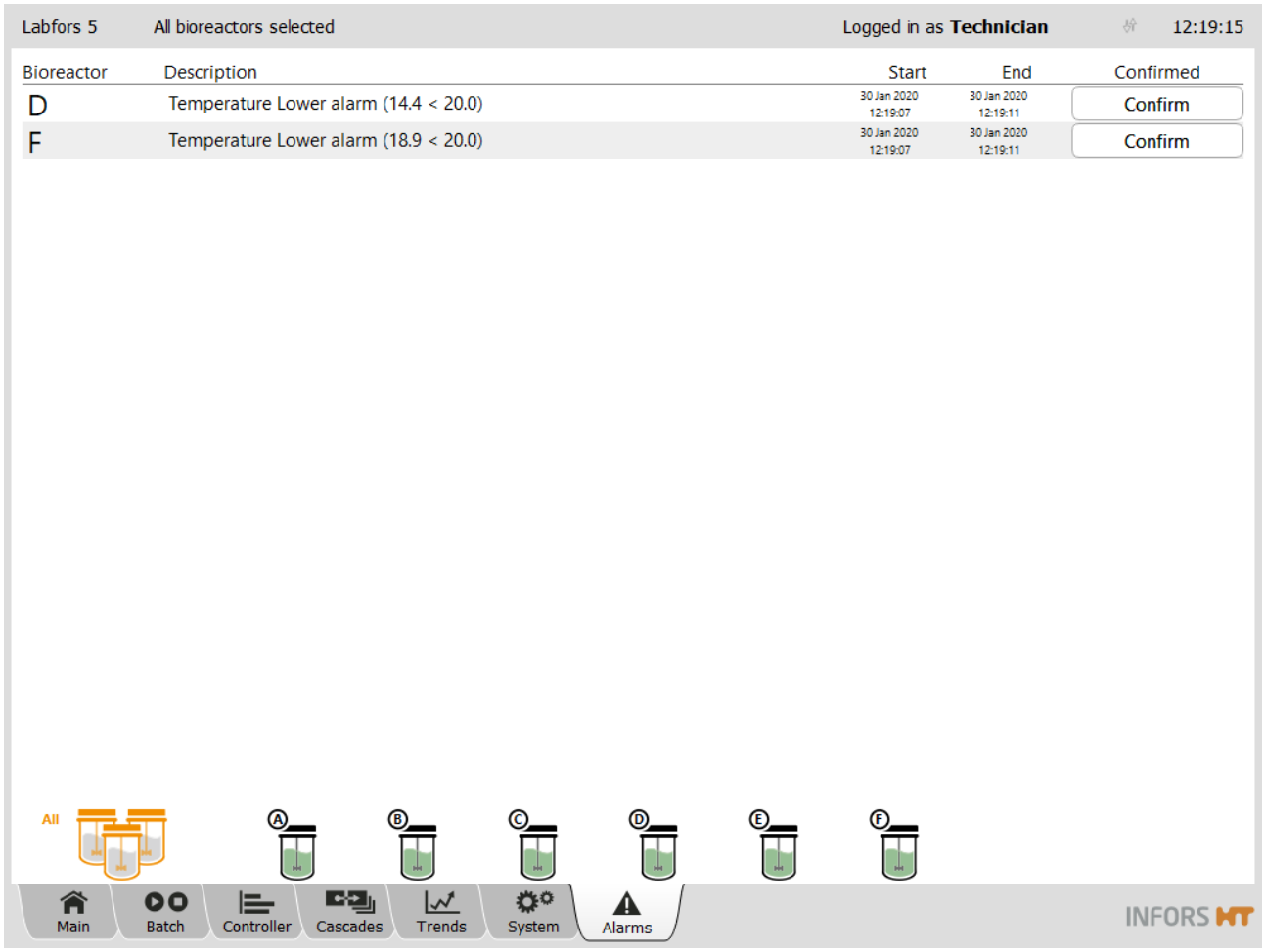
- **Licences**: Opens a menu with the licenses of all software libraries used.

The menu has 5 buttons which access the submenus with various functions:

- **Valves**: displays the status of the digital outputs.
- **Security**: for system log-in and log-off, passwords and user management.
- **Settings**: for the system and basic settings of the bioreactor(s)
- **Wipe Screen**: to lock the screen for 20 seconds, e.g. for screen cleaning
- **Shutdown**: to shut down the system.

A detailed description of the submenus can be found in the appropriately titled chapters.

2.7 Alarms – Parameter Alarms, User Alarms, System Alarms



The main menu *Alarms* lists the parameter alarms for all running bioreactors by time of occurrence. User and system alarms are shown here, too.

A parameter alarm is signalled by the *Alarm* tab flashing light red and dark alternately.

The screen contains the following columns:

- *Bioreactor*: displays the bioreactor (A to F) to which the parameter alarm refers.
- *Description*: describes the alarm
- *Start* and *End*: shows the date and time when the alarm started/ended.
- *Confirmed*: indicates via **Confirm** confirmed alarms with date, time and user.

The following user and system alarms are shown:

User alarm

- *Password Expiry:* the alarm for password expiry will be indicated during 10 days before expiry. Validity duration of the password is set when creating a new user login.

System alarms

- *Difference in board configuration*
- *Invalid modbus map for Parameter xy*

INFORMATION

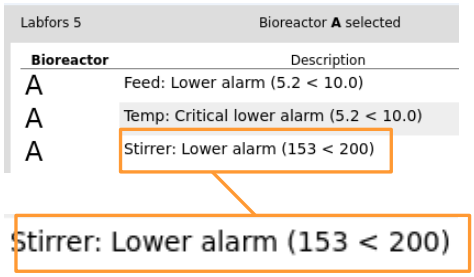
This alarm can only occur if modbus settings were modified. Modbus settings can only be modified on user level Service.

- *No communication*: no communication between control board and operating panel. For details refer to main chapter “Interferences”, chapter “Interferences Basic Operation and Operating Panel” in the separate operating manual of the device.
- *Requested specialized configuration not installed*: error occured while restoring saved data or during installation of a software update. For details refer to chapter “System Alarm – Difference in board configuration”.
- *System restarted after power failure*: for details refer to main chapter “Interferences”, chapter “Behaviour in Case of Power Interruption” in the separate operating manual of the device.

2.7.1 Parameter Alarms

A parameter alarm occurs as soon as the current value of a parameter is outside the set alarm tolerances.

A parameter alarm is triggered as soon as a value drops below the lower alarm value or exceeds the upper alarm value.

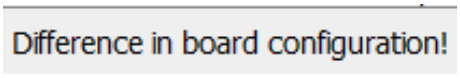


The example in the figure on the left shows: *Stirrer: Lower alarm (153 < 200)*. I.e. for biorecter A, the current value for parameter Stirrer (= 153 min^{-1}) is below the lower alarm value (= 200 min^{-1})

INFORMATION

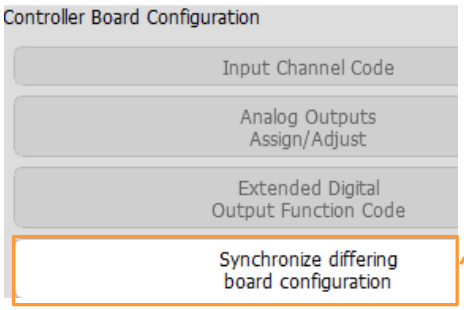
The values in brackets always refer to the current value compared with the setting of the alarm value or the critical value.

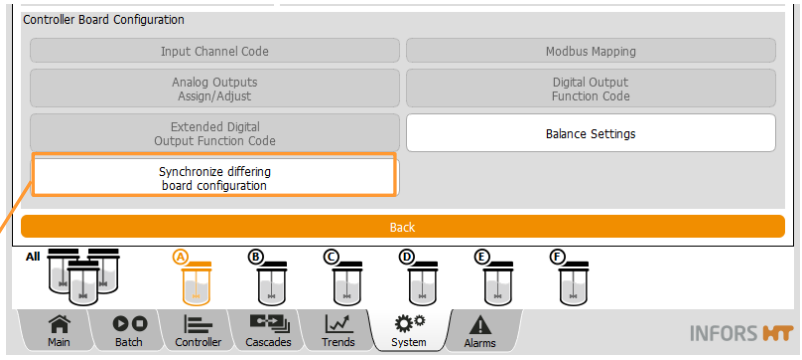
2.7.2 System-Alarm “Difference in board configuration”



A backup of each control board configuration of each satellite is stored in the touch screen. If there are differences between the backup and the current configuration after a firmware update / exchange of the control board respectively the touch screen, the alarm will *Difference in board configuration* occur. This signifies that the configurations do not correspond with each other.

To enable to select the appropriate configuration, the **Synchronize differing board configuration** appears and is enabled in the *Controller Board Configuration* section of the main menu Settings.





After selection of this function (pressing the button), the menu appears with the two following options:

- **Use current board configuration**: to replace the backup in the touch screen with the current configuration of the control board.

This is appropriate after exchange of a touch screen.

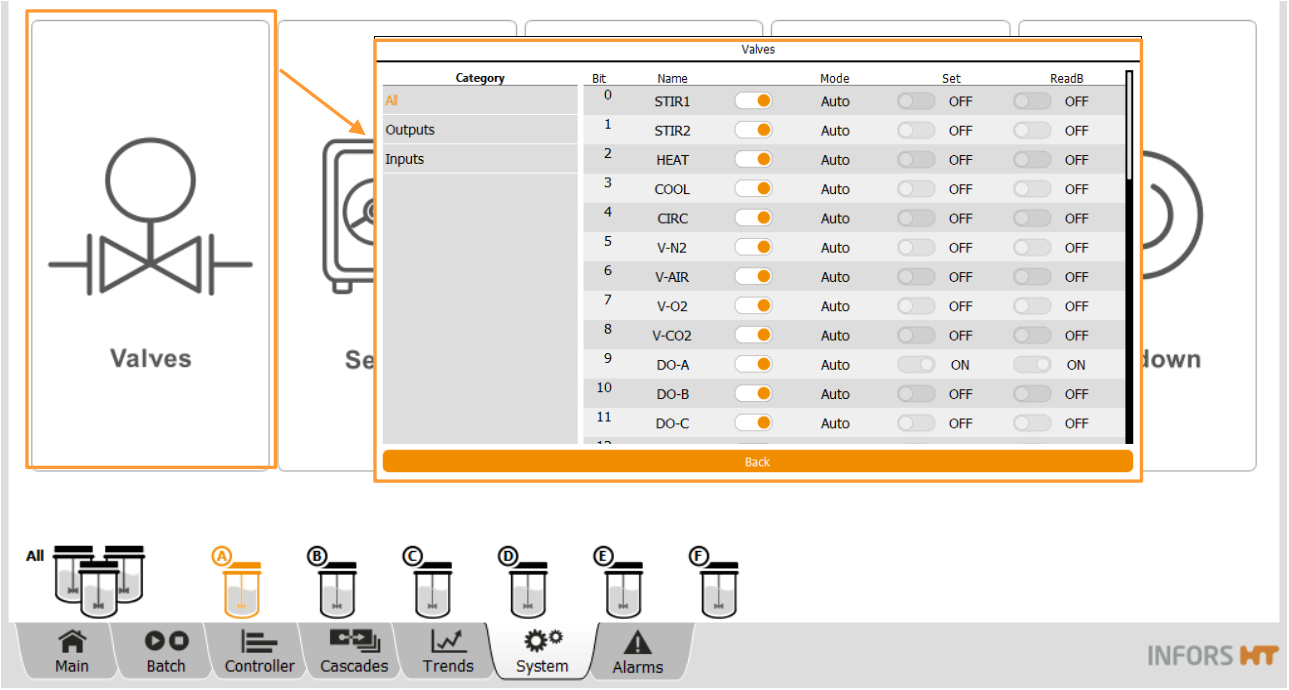
- **Use stored board configuration**: to overwrite the configuration of the control board with the configuration from the backup.

  This is appropriate after a firmware update, respectively replacement of a control board.

The alarm disappears as soon as the function is executed.

3 Submenus

3.1 Valves – Digital Outputs



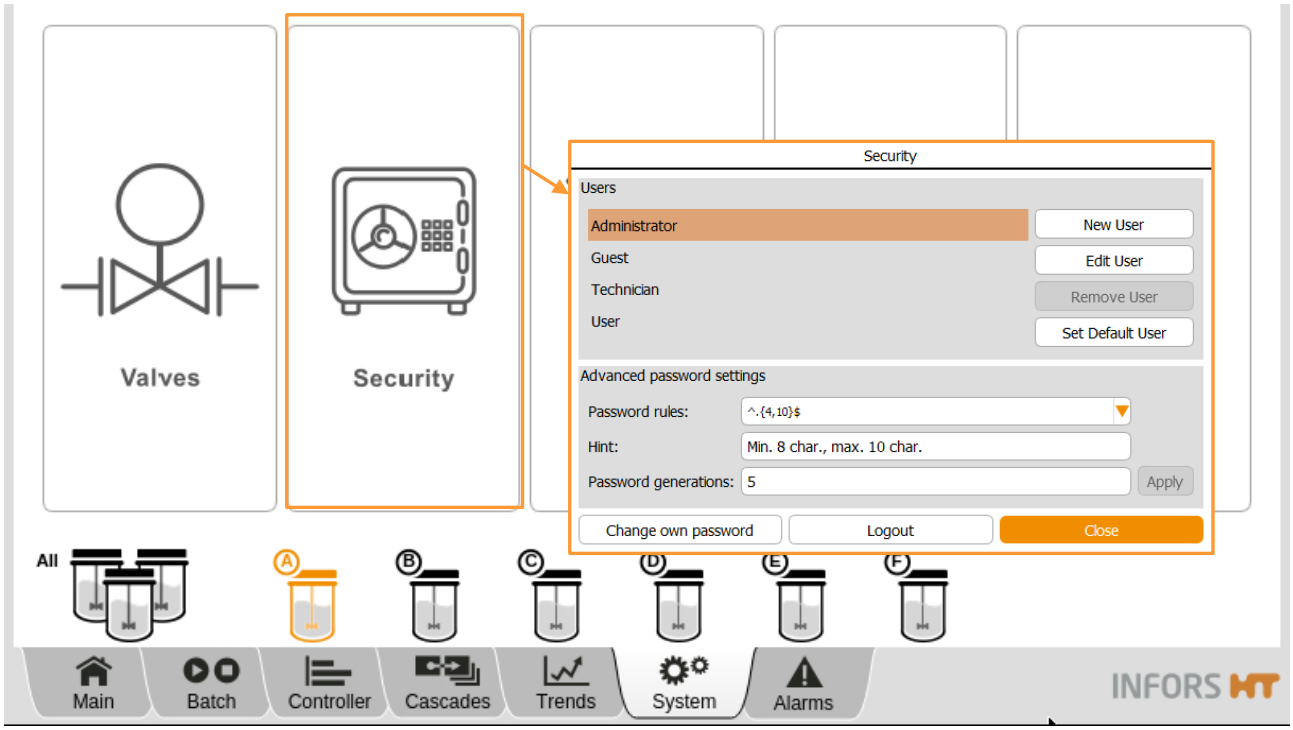
The submenu *VALVES* displays the digital outputs and inputs of the control board. The overview is predominantly used for fault diagnosis. All valves and digital outputs set to automatic mode (*Auto*) ex-factory. These settings must not be changed!

In column *Category* the view of all (*All*) digital inputs and outputs or only the display of the inputs or outputs can be selected.

The main column shows:

Hauptspalte		
Bit / Name		Channel number and designation
Mode	*Auto*	Automatic switching
	Manual	Manual switching, outputs are forced, i.e. the automatic switching is thus disabled.
Set (Switching status of the digital output)	*OFF / ON*	Output is switched off / on
ReadB (electronic feedback channel, which confirms the change in status.	*OFF / ON*	Readback is switched off / on
If the electrical connection is faulty, it is displayed as FALSE		

3.2 Security – User Management



The submenu *Security* is used for logging on and off the system. This is where users can also be added or deleted, passwords can be issued and access authorisations can be assigned.

More or less buttons may be enabled in this menu depending on the access authorisation of the registered user:

- **Login/Logout**: to log on/off to/from the system.
- **Change own password**: to change the own password.
- **New User**: to add a new user.
- **Edit User**: to edit user settings.
- **Remove User**: to delete a user.
- **Set Default User/Clear Default User**: to define/delete automatic user login.
- *Advanced password settings*: to define password rules for password security.

The different user levels, access authorisations and functions are described in the following chapters.

3.2.1 User Levels

The system has five user levels with different access authorisations. The user levels are designated and defined as *Groups*.

Service: This user group has access to all system and bioreactor settings. This user level is accessible for qualified INFORS HT service technicians only and access for all other users is blocked.

Administrators: This user group has access to basic system and bioreactor settings. New users can only be added, altered and deleted by users allocated to the user groups *Service* or *Administrators*. The default setting for the login to the system is predefined as *Administrator*.

Technicians: This user group has limited access to system and bioreactor settings. The default setting for the login to the system is predefined as *Technician*.

User: This user group only has restricted access to the system. The default setting for the login to the system is predefined as *User*.

Guests: This user group has viewing authorisations only and no access authorisations. Exception: users with this user level can select trend lines in the main *Trends* menu to display or hide them, change the background colour for the diagram display and select the time range for the diagram display. This user level serves as protection against unauthorised access to the system or unintentional changes to settings.

This user level is set automatically as long as no user is logged on to the system. This is indicated by the words *Guest mode* in the header on the screen.

The default password setting for the user groups *Administrators*, *Technicians* and *User* is the same: qwertyuiop.

INFORMATION

Passwords should be changed and managed by the authorised person (users with user level Administrators) after commissioning for the first time.

3.2.2 Access Authorisations of User Groups

The following tables group the various functions of the touch screen software with an indication of the access authorisations of the user groups.

Key:

- V (view) = visible, function cannot be executed
  Visible means that, depending on the function, the button or the menu/dialogue can only be viewed.
- E (execute) = Visible and function can be accessed for execution
  I.e. functions are executable
- Empty field = cannot be viewed and function cannot be executed

BIOREACTOR(S)	**User Groups**				
	Guests	User	Technician	Admin.	Service
Start / *Stop* Bioreactor(s)	V	E	E	E	E

RECIPES	**User Groups**				
	Guests	User	Technician	Admin.	Service
Load/Start	V	V	E	E	E
Save	V	V	E	E	E
Delete	V	V	E	E	E

PUMPS	**User Groups**				
	Guests	User	Technician	Admin.	Service
Calibrate (Pump calibration)	V	E	E	E	E
Reset (Resetting counter)	V	E	E	E	E
Pump factor (Setting pump factor manually)	V	E	E	E	E
Fill/Empty Pumps (Filling/emptying hoses manually and time-controlled)	V	E	E	E	E

PARAMETERS Standard	**User Groups**				
	Guests	User	Technician	Admin.	Service
Setpoint (changing setpoints)	V	E	E	E	E
Upper/Lower Alarm, Upper/Lower Critical (Setting alarm and critical values)	V	E	E	E	E

Submenus

Output active ON/OFF (Switching parameters on and off)	V	E	E	E	E
Calibrate pH / *Calibrate All pH* (Calibrating pH sensor(s), all variants, individually and all)	V	E	E	E	E
pH analogue: changing *Slope* and/or *Offset* (*Manual* calibration mode)		E	E	E	E
Calibrate pO2 / *Calibrate All pO2* (Calibrating pO_2 sensor(s), all variants, individually and all)	V	E	E	E	E
pO_2 analogue: Function *USE AS SETPOINT* in calibration menu		E	E	E	E
Function *USE AS SETPOINT* (if present) in calibration menus except for pO_2 analogue				E	E
Calibrate, all except for above mentioned			V	E	E
Calibrate, manually (*Manual* calibration mode), all except for above mentioned				E	E
PID			E	E	E
Options					E
PARAMETER Option	Guests	User	Technician	Admin.	Service
Turbidity, *Calibrate* (Calibrating the zero point of turbidity sensor Optek)	V	E	E	E	E

CASCADES	**User Groups**				
	Guests	User	Technician	Admin.	Service
Setting a cascade	V	E	E	E	E
Advanced option (Setting an advanced cascade)			E	E	E

TREND LINES (Trends)	**User Groups**				
	Guests	User	Technician	Admin.	Service
Change display settings	E	E	E	E	E

ALARMS (Alarms)	**User Groups**				
	Guests	User	Technician	Admin.	Service
Confirming alarms	V	E	E	E	E

DIGITAL INPUTS/OUTPUTS (System / Valves)	User Groups				
	Guests	User	Technician	Admin.	Service
Manually switching digital inputs and outputs	V	V	E	E	E

USER MANAGEMENT (System / Security)	User Groups				
	Guests	User	Technician	Admin.	Service
Login (Logging on to the system)	E	E	E	E	E
Logout (Logging out from the system)		E	E	E	E
Change Password (Changing password)		E	E	E	E
New User (Adding a new user)		V	V	E	E
Remove User (Deleting a user)		V	V	E	E
Edit User (Changing user settings)		V	V	E	E
Set Default User (Setting automatic user login)		V	V	E	E
List of all users				V	V

SYSTEM SETTINGS (System / Settings)	User Groups				
	Guests	User	Technician	Admin.	Service
Settings					
IP Settings (Network settings)	V	V	V	E	E
Change Time (Changing date and time)	V	V	V	E	E
Files					
Backup (Saving data)	V	V	V	E	E
Restore (Restoring data)	V	V	V	E	E
Service Menu (Settings in Service Menu)					E
Export Logs (Exporting log files)		V	E	E	E
Controller Board Configuration					
Input channel code (Setting codes for input channels)			V	V	E
Analog Outputs Assign/Adjust (Assigning/changing analogue outputs)			V	V	E
Extended Digital Output Function Code (Setting extended function codes for digital outputs)			V	V	E
Synchronize differing board configuration (Synchronising different configurations of the controller board)			E	E	E
Modbus mapping (Modbus settings)			V	V	E

Submenus

Digital Output Function Code (Setting function codes for digital outputs)			V	V	E
Balance Settings (Settings for balances)	V	V	V	E	E

TEMPORARY SCREEN LOCK (System / Wipe Screen)	**User Groups**				
	Guests	User	Technician	Admin.	Service
Activating the temporary screen lock	V	E	E	E	E

SYSTEM SHUTDOWN	**User Groups**				
	Guests	User	Technician	Admin.	Service
Shutting down the system	V	E	E	E	E

Labfors 5 Version for microorganisms / **Option LabCIP**	**User Groups**				
	Guests	User	Technician	Admin.	Service
LabCIP Settings	V	V	E	E	E
Starting the LabCIP (Perform CIP/SIP)	V	E	E	E	E

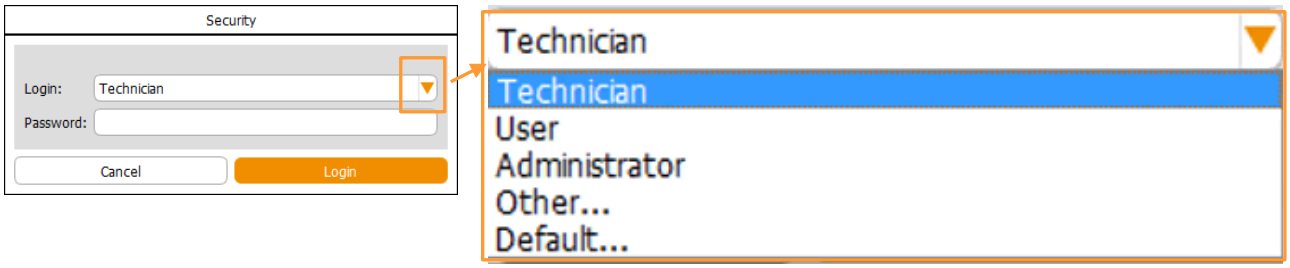
Labfors 5 Version for solid substrates and enzymatic bioprocesses / **Option Servo Motor**	**Benutzergruppen**				
	Guests	User	Technician	Admin.	Service
Activating/deactivating rotation speed limit (Set. Stirrer Max.)	V	E	E	E	E

3.2.3 Login / Logout – Logging on or off to/from the System

To log on to the system, proceed as follows:

Procedure

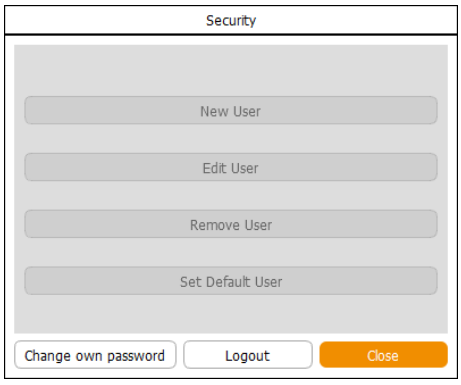
1. Call up the main menu *System* and press **Security**.
   Submenu *Security* appears.



The drop-down list (*Login*) lists all users available by default with factory settings.

- *User*
- *Technician*
- *Administrator*
- *Other*: for use by INFORS HT service employees only
- *Default*: automatic user login without entering a password if previously set using **Set Default User**.

2. Select the desired user, e.g. *Technician.*
3. Enter the password and press **Login**.
   The user is logged in.



The different functions are listed now as buttons in the *Security* menu.
The buttons **Change Password** for password changes**, Logout** for logging off from the system, and **Close** for leaving the menu are enabled on all user levels (except for *Guest*).

INFORMATION

On user level Administrator and above, the password rules can be configured here, too. For details refer to chapter “Password Security – Defining Password Rules”.

3.2.4 Change Password – Changing the Password

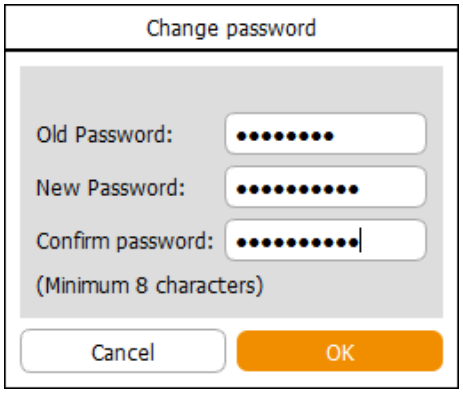
Users of all user groups can change their own password. In order to be able to change a password, the user must be logged on to the system.

Proceed as follows:

Procedure

1. Call up submenu Security and press **Change Password**.

   The *Change password* dialogue box appears.



2. Enter the old password.
3. Enter the new password and confirm it by entering it a second time.

   All inputs are displayed as dots.

INFORMATION

Depending on the password rule settings, the password must meet different conditions. Password rules are configured on user level Administrator and above. For details refer to chapter “Password Security – Defining Password Rules”.

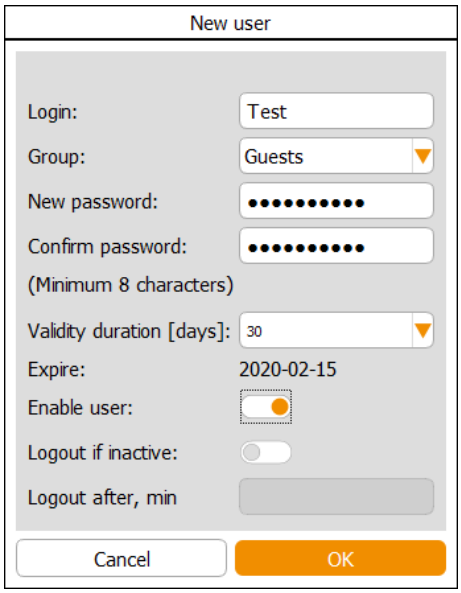
4. Press **OK**.

   The dialogue box disappears; the new password is saved.

3.2.5 New User – Adding a New User

To add a new user to the user list, proceed as follows:

Procedure



1. Log on to the system on user level Administrator.
2. Call up the submenu *Security* and press **New User**.

   The *New User* dialogue box appears.
3. Enter a new user in *Login*.
4. Select the desired user group in drop-down list *Group*.
5. Enter the password and confirm it by entering it again in

INFORMATION

Depending on the password rule settings, the password must meet different conditions. Password rules are configured on user level Administrator and above. For details refer to chapter “Password Security – Defining Password Rules”.

6. Select the validity duration of the password in drop-down list *Validity duration [days]*, choose “unlimited”, 30, 100 or 365 days.

   The corresponding expiry date is then displayed in *Expire.*
7. Activate/deactivate access authorisation of the new user in

   This function (enable user) is switched on by default.

INFORMATION

The user has no access rights and no password can be defined, if this function is deactivated.

8. Switch the automatic logout on/off when inactive after a predefined duration and set the expiration time in minutes, if given.
9. Press **OK**

   The dialogue box disappears, the new user is added and shown in the user selection list of submenu *Security*.

3.2.6 Edit User – Editing User Settings

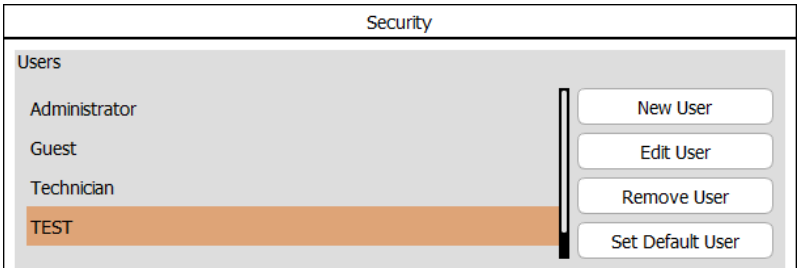
In **Edit User** the following settings can be changed for existing users:

- Assigning a new user group, see chapter “New User – Adding a New User”.
- Changing the password, cee chapter “Change Password”.
- Automatic user log-out when screen is inactive after a predefined time in minutes has elapsed. The first user level *Guests* is then set automatically.

To edit user settings, proceed as follows:

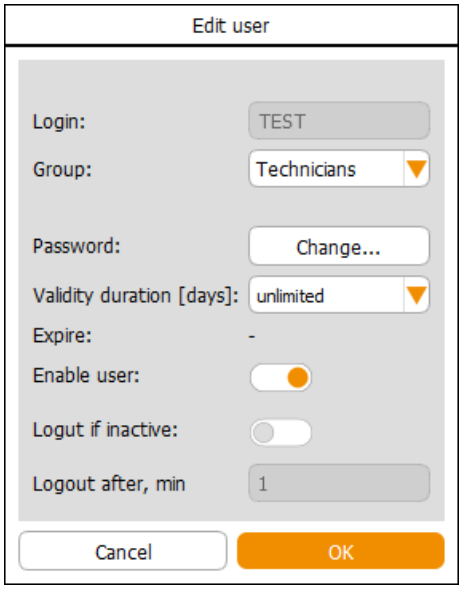
Procedure

1. Log on to the system on user level *Administrator* and call up submenu U *Security*.



2. Select the desired user (her: TEST) from the user selection list and press **Edit User**.

   The *Edit User* dialogue box appears with nearly identical options as for creating a new user in dialogue box *New User.*



3. Make required settings.
4. Press **OK**

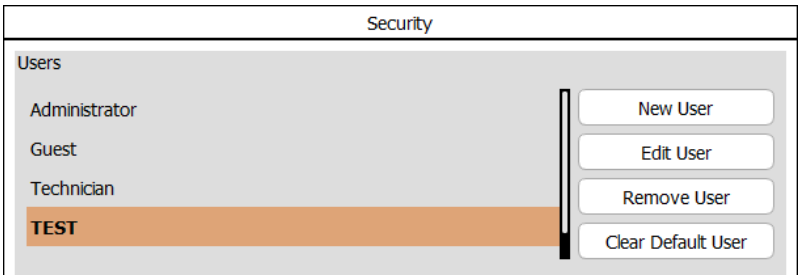
Settings are adopted; the dialogue box disappears.

3.2.7 Remove User – Deleting a User

To remove a user from the, proceed as follows:

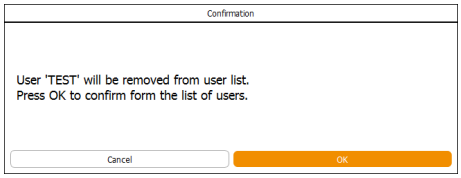
Procedure

1. Log on to the system on user level *Administrator* and call up submenu *Security*.



2. Select the user to be deleted (here: *TEST*) in the user selection list.
3. Press **Remove User**.

   The *Confirmation* dialogue box appears with information and prompt to confirm deletion of the user from the list.



4. Confirm deletion by pressing **OK.**

   The dialogue box disappears, the user *TEST* is deleted from the user selection list.

3.2.8 Set / Delete Default User – Setting or Deleting an Automatic User Login

Set Default User is used to set an automatic user login. I.e. a user can be defined who is then automatically logged on to the system the next time it is switched on.

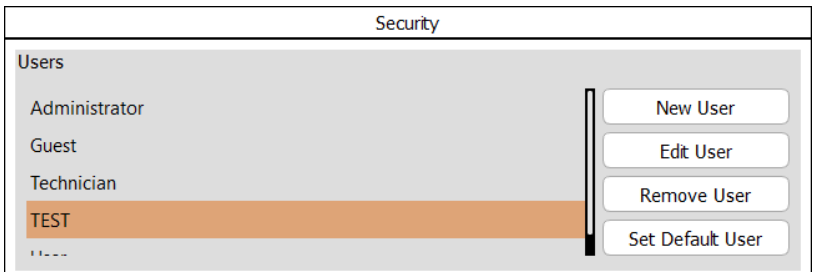
Clear Default User is used to delete the automatic login of a user.

Submenus

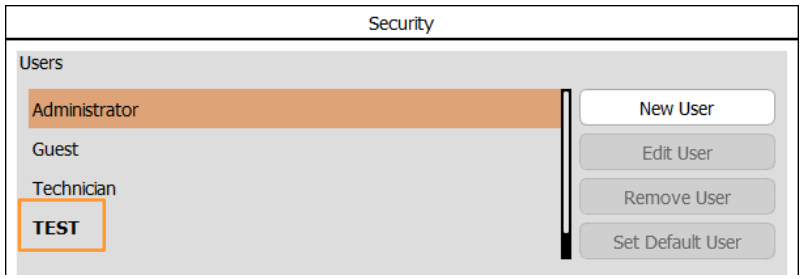
Proceed as follows:

Procedure

1. Log on to the system on user level *Administrator* and call up submenu *Security.*



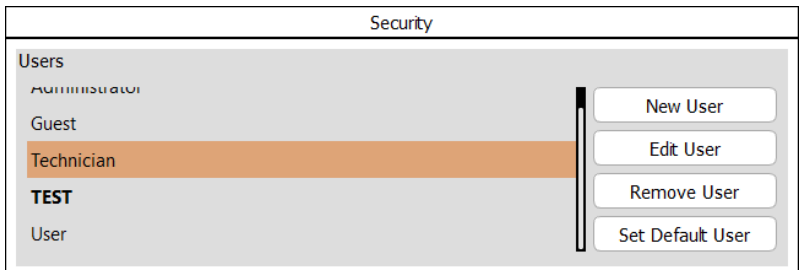
2. Select the desired user (here: *TEST*) in the user selection list.
3. Press **Set Default User**.



The defined user for automatic login is displayed in bold letters, the **Set Default User** button is only visible, but not enabled anymore.

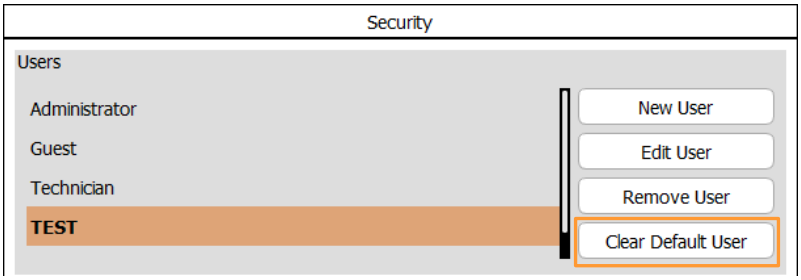
Changing the automatic user login

Another user can be defined here for automatic login, too (here: *Technician*). When selecting tis user, the **Set Default User** button is enabled again.



Deleting automatic user login

When selecting the defined user with the automatic user login setting in the list (here: *TEST*), the **Clear Default User** button is visible and enabled for deleting the automatic user login.



3.2.9 Password Security – Configuring Password Rules

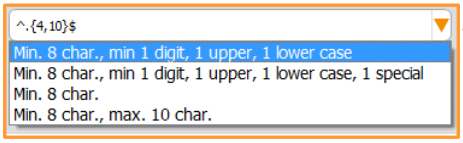
Conditions for creating new user passwords can be configured from user level Administrator on in submenu *Security*

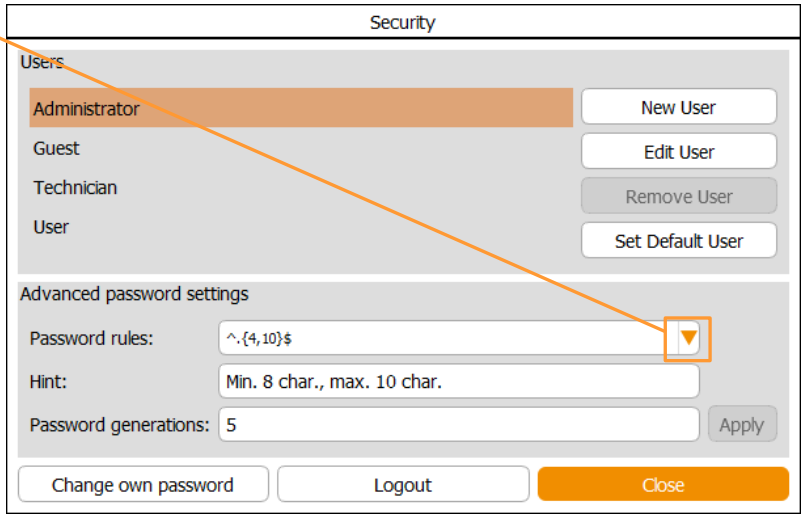
Proceed as follows:

Procedure

1. Login to the system on user level *Administrator* and call up submenu *Security*.

   The *Advanced password settings* area is visible and enabled now in the lower part of the menu:





   - *Password rules*: drop-down list with choice of four password rules (see figure to the top left). The password must have at least:

- 8 characters, containing at least 1 number, 1 capital letter and 1 lower case letter.
- 8 characters, containing at least 1 number, 1 capital letter and 1 lower case letter and 1 special character.
- 8 characters.
- 8 up to max. 10 characters.

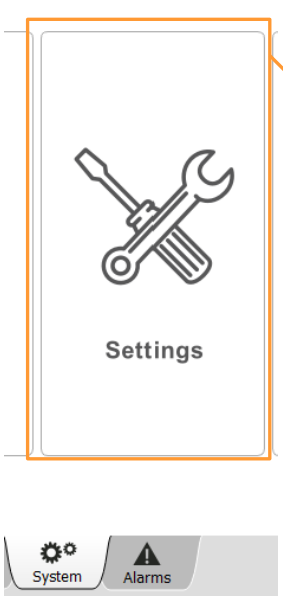
- *Hint*: shows which rules must be followed during creation of a new password.
- *Password generations*: defines the number of passwords that must be newly created, before a password may be reused.
- **Apply:** to instantly apply the rule when creating a new password. This button is enabled as soon as a rule is changed.

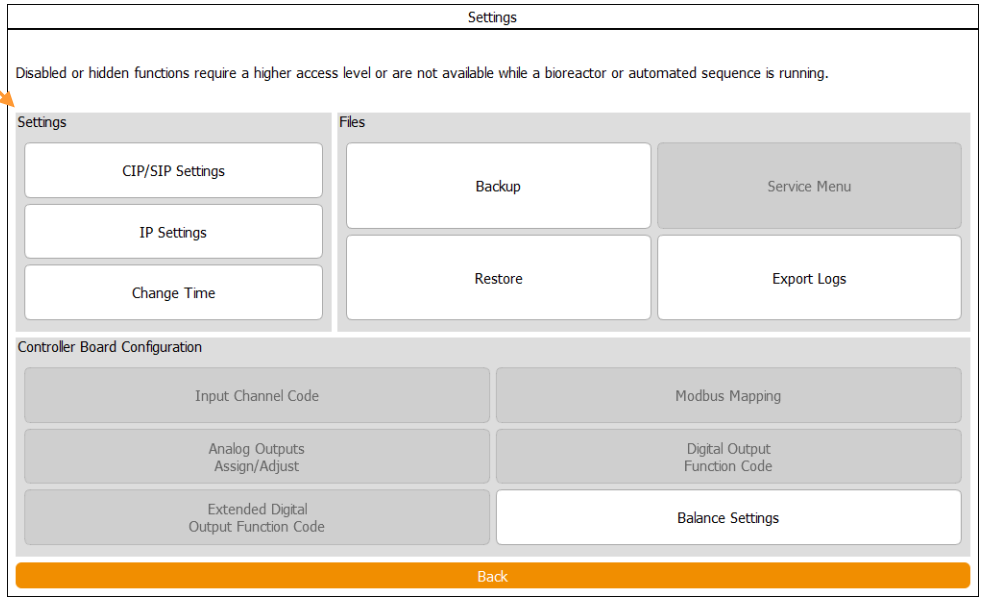
2. Select the desired rule to apply and the number of new passwords that must be created until reuse of an old password is allowed.
3. Press **Apply**.

   The rule is saved and will be shown when creating the next password.
4. Press **Close**.

   Submenu *Security* disappears.

3.3 Settings – Basic Unit Settings





In the submenu *Settings* basic settings for the device are made. Depending on the access authorisation, more or less buttons are visible and enabled (for details refer to the tables in chapter “Access Authorisations of User Groups”. The figure above shows the menu on user level *Administrator.*

The menu is divided into three areas with the following functions:

Settings

- **CIP/SIP Settings**: only visible and enabled for Labfors 5 with LabCIP. For details refer to the separate operating manual.
- **IP Settings**: for network settings.
- **Change Time**: to set the date and time.

Files

- **Backup**: to save data.
- **Restore**: to restore and upload saved data.
- **Service Menu**: access only for qualified Infors service or licensed dealer.
- **Export Logs**: to export log files.

Controller Board Configuration

- **Input Channel Code**: to set codes for input channels
- **Analog Outputs Assign/Adjust**: to assign/change analogue outputs.

- **Extended Digital Output Function Code**: to set function codes for extended digital outputs.
- **Synchronize differing board configuration**: to synchronize differing board configurations.

INFORMATION

This button is only visible, if the appropriate alarm (*Difference in board configuration!*) has been triggered and is displayed in main menu Alarms after an update of the firmware / change of a control board. For details refer to chapter “System Alarm Difference in oard configuration”.

- **Modbus mapping**: for Modbus settings.
- **Digital Output Function Code**: to set function codes for digital outputs.

INFORMATION

None of the functions concerning inputs and outputs, function codes and modbus mappings are described in this manual. These functions are only accessible for Infors service or Infors licensed dealers.

- **Balance Settings**: for balance settings.

Back directs back to the main menu *System*.

3.3.1 IP Settings – Network Settings

IP Settings is used to establish a network connection. This can be performed either automatically or manually.

INFORMATION

This is only possible, if a network cable is connected.

This manual does not describe how to setup a network connection.

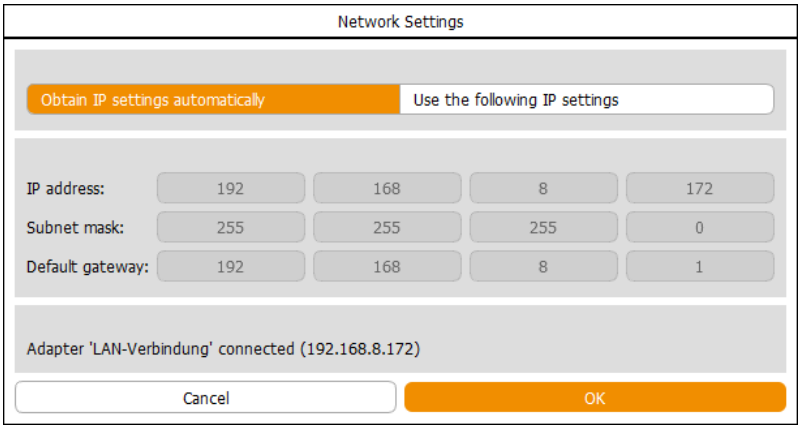
To call up the menu to make settings, proceed as follows:

Procedure

1. Log on to the system on user level Administrator and call up submenu *Settings*.

2. Press **IP-Settings**.

   The *Network Settings* menu appears with:



- **Obtain IP settings automatically**: to set IP settings automatically (default setting). Condition: a DHCP [1)] server is available in the network.
- **Use the following IP settings**: to use the following IP settings.

  Only after pressing this button, the following fields are enabled.
- *IP address*: shows current IP address or to enter IP address manually.
- *Subnet mask*: displays default gateway or allows manual input.
- *Default gateway*: shows default gateway or allows manual input.

INFORMATION

The status message …*connected* indicates that correct network connection is established. If this is not the case (no signal), the message "*No active LAN connection"* appears.

1) *Dynamic Host Configuration Protocol*

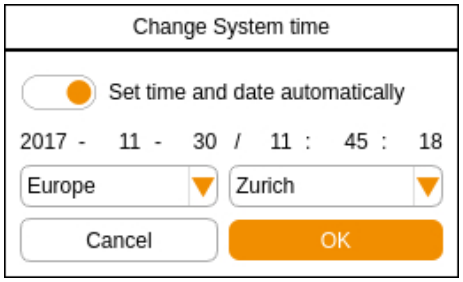
3.3.2 Change Time – Changing Date and Time

Change Time enables adjusting the system date and time to the local conditions. The system is set for automatic synchronisation with the time server ex-factory. I.e. the display is corresponding with the selected time zone. Alternatively, these settings can be manually adjusted.

To make settings, proceed as follows:

Procedure

1. Log on to the system on user level *Administrator* and call up submenu *Settings*.
2. Press **Change Time**.



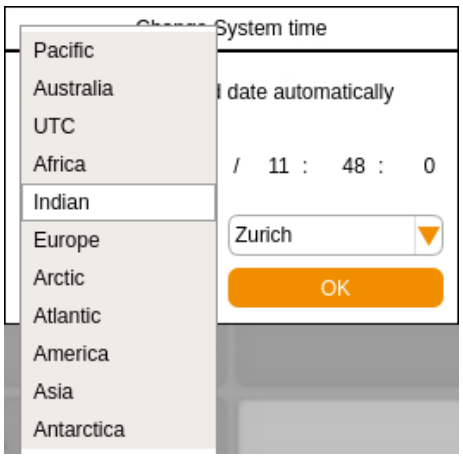
The *Change System time* dialogue box appears with the default configuration ex-factory:

- **ON/OFF** switch *Set time and date automatically* is in position **ON.**
- Display (from left to right) for year, month, day, hours, minutes and seconds.
- Drop-down lists for time zone and city: default = Europe / Zurich

Changes with automatic adjustment

Proceed as follows:

Procedure



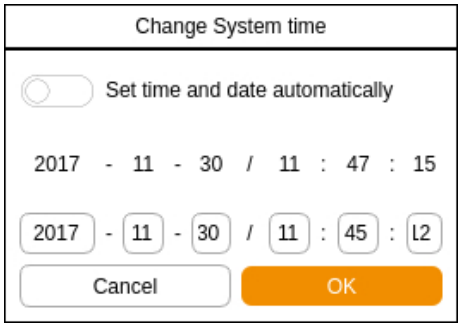
1. Select the time zone and city in the drop-down lists.
2. Press **OK.**

Settings are saved, dialogue box disappears.

Manual changes

Proceed as follows:

Procedure



1. Switch automatic time and date setting **off.**

   Input fields (from left to right) for year, month, day, hours, minutes and seconds appear.
2. Enter desired values.
3. Press **OK.**

   Inputs are saved, dialogue box disappears.

3.3.3 Backup – Saving Data

The Backup function is used to save the entire settings of the touch screen software and the control board of all connected bioreactors. These data can be restored using the Restore function.

Note the following:

- Data can be saved on the internal memory or on a USB stick.
- A data backup is only executable when all bioreactors are stopped, i.e. no fermentation/cultivation is running.

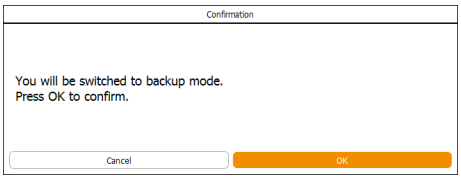
To execute a backup, proceed as follows.

Procedure

Only when using a USB stick, otherwise go to step 2:

1. Use the special cable provided with the device and connect it to the appropriate connector (see figure on the left) on the rear side of the operating panel and connect the USB stick.
2. Log on to the system on user level *Administrator*, call up main menu *System* and select submenu *Settings*.
3. Press **Backup** in the *Files* area.

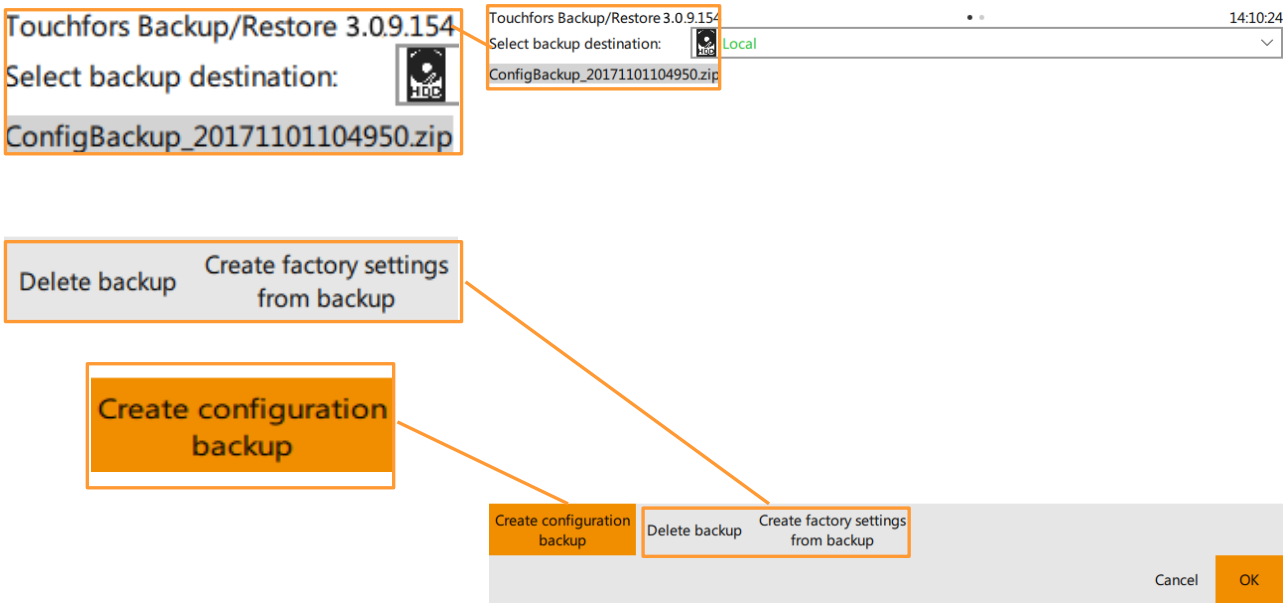
Submenus



The *Confirmation* dialogue box appears with information and prompt to confirm switching to backup mode.

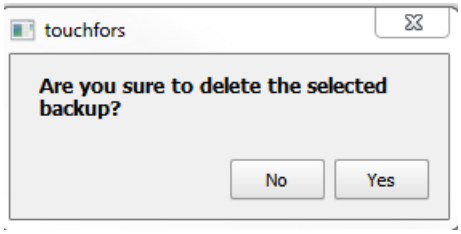
4. Press **OK**.

The menu for data backup opens with:



- *Select backup destination*:
  - *local*: to locally save the backup.
  - *external*: to save the backup externally on a detected and connected USB stick.
- **Create configuration backup**: to create the backup.
- **Delete backup**: to delete the backup.
- **Create factory settings from backup**: to create factory settings from the backup.

5. Select the backup destination and press **Create configuration backup** to create the backup.
6. Press **OK** to save the backup and leave the menu.



Deleting a backup

Pressing **Delete backup** opens a dialogue box with inquiry and prompt to confirm deletion.

If backup on USB stick:

7. Remove the USB stick and the cable.

3.3.4 Restore – Restoring Saved Data or Restoring Factory Settings

The Restore function enables to restore data, which have previously been saved using the Backup function. Data will be uploaded to the system again. It is also possible to restore factory settings using this function.

INFORMATION

Factory settings usually represent the settings of the bioreactor/bioreactors in as-delivered condition. In case of retrofitting of one or several bioreactors, these settings can be updated, too. Both is exclusively carried out by an Infors service technician or a licensed dealer.

Note the following:

- Data are either restored from the internal memory or from a USB stick, see chapter “Backup – Saving Data”.
- The Restore function is only executable when all bioreactors are stopped.

Submenus

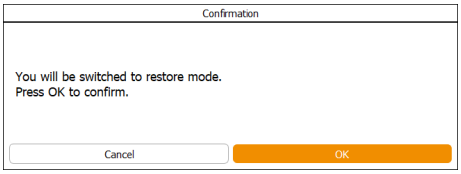
To execute the Restore function, proceed as follows:

Procedure

Only when using a USB stick, otherwise go to step 2:

1. Use the special cable provided with the device and connect it to the appropriate connector on the rear side of the operating panel and connect the USB stick with the saved date (Backup data).

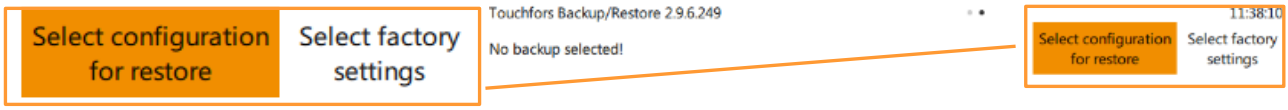
2. Log on to the system on user level *Administrator*, call up main menu *System* and select submenu *Settings*.
3. Press **Restore**.



The *Confirmation* dialogue box appears with notice and prompt to confirm switching to restore mode.

4. Press **OK**.

The menu for data restoring appears with:

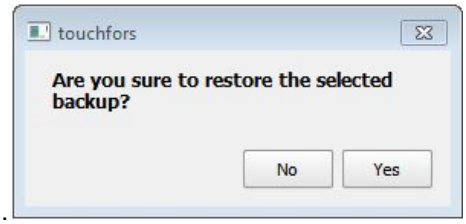


- **Select Configuration for restore**: to select the backup data for restoring.
- **Select factory settings:** to select factory settings.

Executing the backup for data restoring

Pressing **Select configuration for restore** changes the menu display and shows with *Select backup source* the choice of the possible data sources:

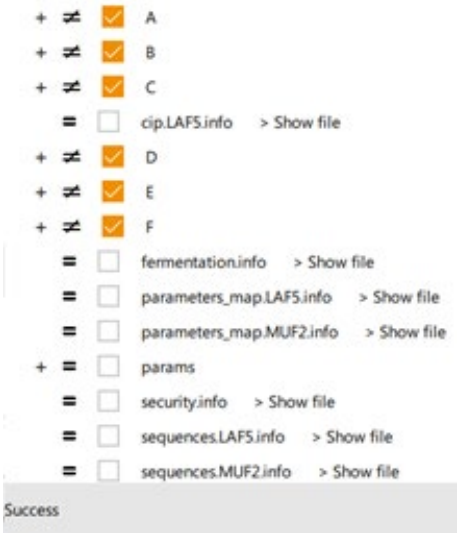
- local: internal memory
- xy (drive) / external: detected and recognised USB stick
- **OK**: To confirm selection.



After selection of the data source, a dialogue box appears with inquiry and prompt to confirm restoring.

5. Press **Yes**.

The screen changes and lists data for configuration comparison.



- **≠** signifies a difference between Backup and current configuration.
- **=** No difference between Backup and current configuration.
- **+/-** To open/close tree
- Show file / Show difference: To display file / difference

INFORMATION

This view for showing the difference within a file is for information purposes and mainly foreseen for Infors service or licensed Infors dealers. It shows the differences between the settings of the file to restore and the currently used version in unified format (also *unidiff*).

- **Cancel**: to cancel the backup process and leave the menu.
- **OK**: to execute the backup for restoring data.

3.3.5 Export Logs – Exporting Log Files

The Export Log functions enables to save all log files (protocol files) as well as alarms and error messages on a USB stick.

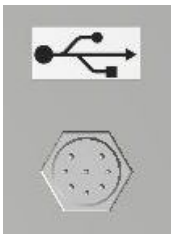
Note the following:

- A USB stick is needed for the export.
- Export is only executable when all running processes are stopped.

Submenus

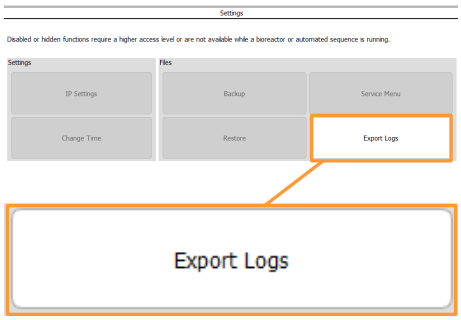
Proceed as follows:

Procedure



1. Use the special cable provided with the device and connect it to the appropriate connector (see figure on the left) on the rear side of the operating panel.

2. Connect the USB stick.
3. Log on to the system on user level *Technician* or *Administrator*.
4. In main menu *System*, call up submenu *Settings*.



5. Press **Export Logs**.

   Data export is started.

   Once the export is finished, the *Information* dialogue box appears with message *Log files successfully exported to: xxxxx*

6. Press **OK**.

   The dialogue box disappears. The Zip file is stored on the USB stick now.

3.3.6 Balance Settings

This function is used to set up to a maximum of 7 connectable balances (via the switchbox of the device manufacturer).

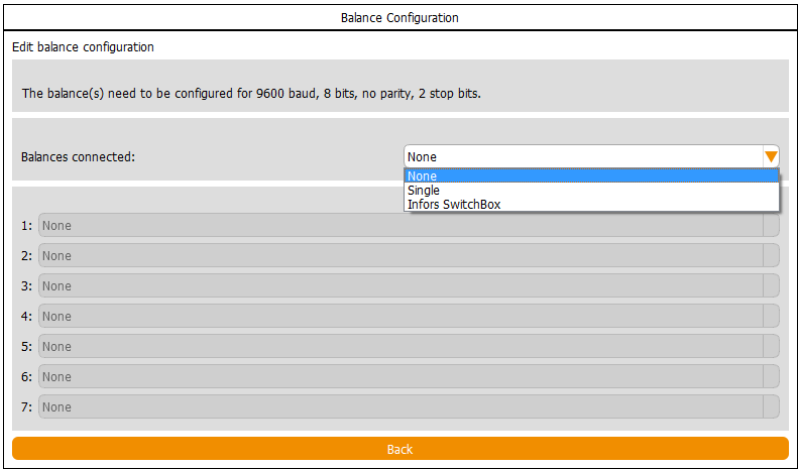
Balances must be configured with the following values: Baud rate 9600, 8 bits, no parity, 2 stop bits.

Proceed as follows:

Procedure

1. Connect the balance(s) or switchbox
2. Log on to the system on user level *Administrator*.
3. In main menu *System*, call up submenu *Setting*s.
4. Press **Balance Settings.**

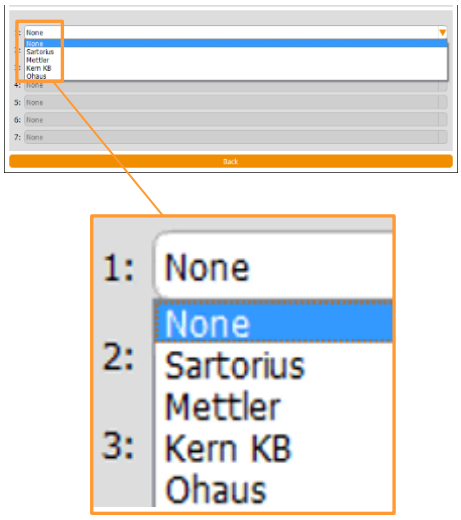
   The menu *Balance Configuration* appears with:



- Information with the above-mentioned configuration values for balances.
- Drop-down list *balances connected*: to select number of connected balance(s).
  - *None*: no balance
  - *Single*: one balance (without Switchbox)
  - *Infors SwitchBox*
- 7 drop-down lists, of which one or all are enabled, once one option has been selected.

5. Select the number of balance(s).

Submenus



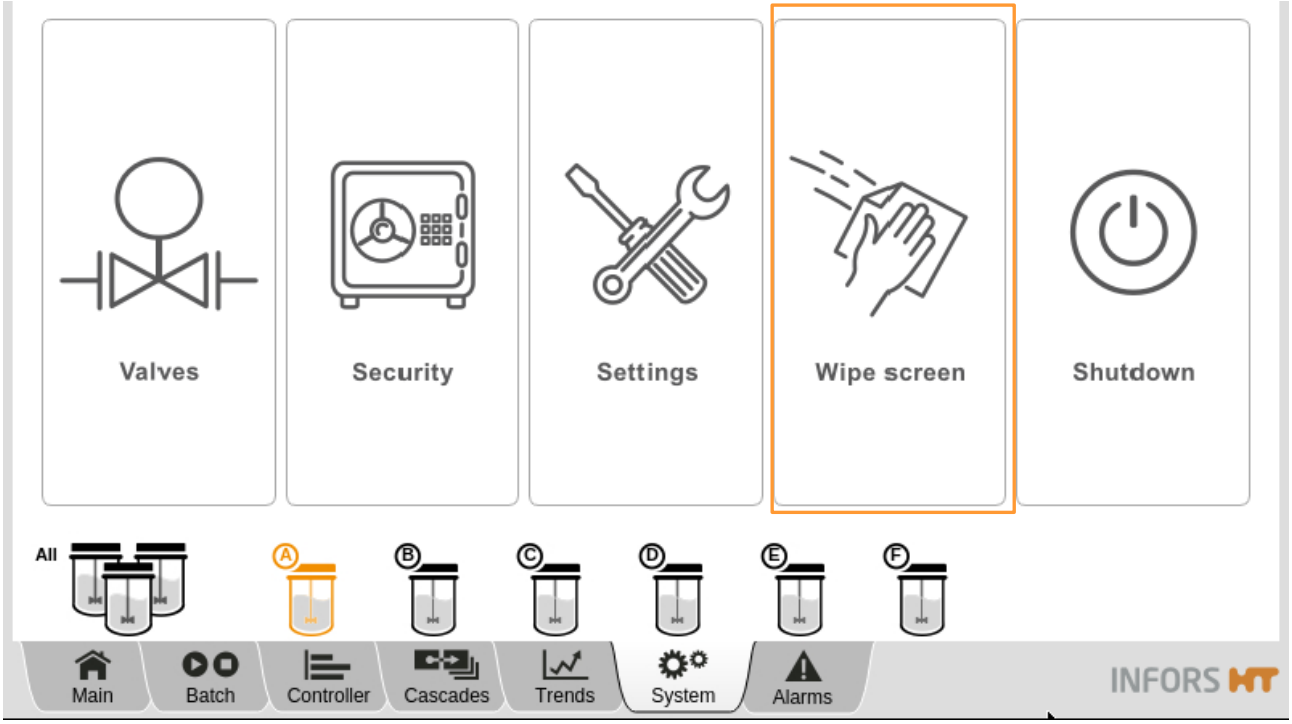
Drop-down list(s) for selection of the balance type(s) connected appear(s). The choice contains the following types: none (no balance), Sartorius, Mettler, Kern KB und Ohaus.

6. Select the balance type(s).

7. Press **Back**.

Settings are adopted, submenu Settings reappears.

3.4 Wipe Screen – (Temporarily) Locking the Screen



The submenu Wipe Screen has one function only: It locks the screen to prevent any inputs on the screen for 20 seconds. This allows e.g. cleaning the screen for 20 seconds if required.

To activate the temporary screen lock, proceed as follows:

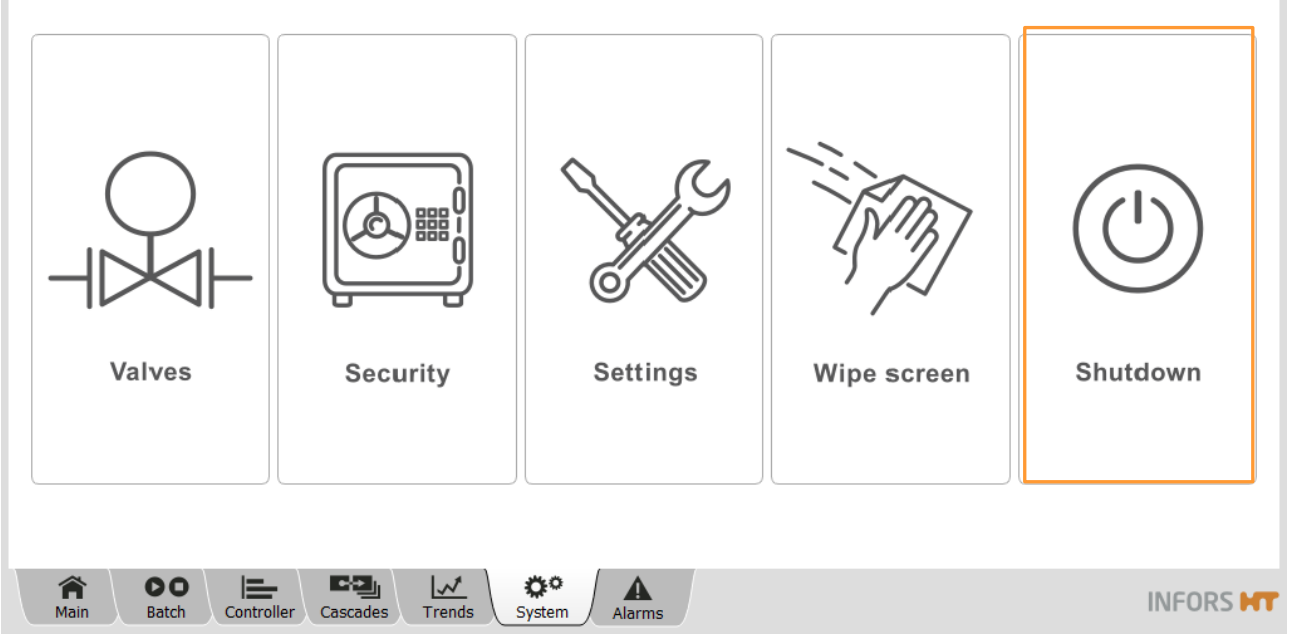
Procedure

1. In main menu *System*, press **Wipe Screen**.

   The screen turns white, the remaining time is displayed in seconds.

   Once the time has elapsed, the last screen reappears automatically.

3.5 Shutdown – Shutting Down the System



The submenu *Shutdown* has one function only: it shuts down the system. The system can only shut down, if all bioreactors are in idle (stopped) state.

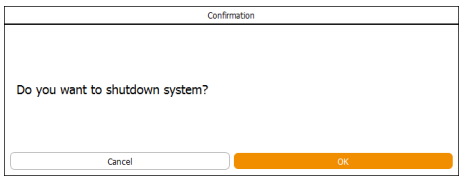
INFORMATION

ALWAYS shut down the system first, only then switch off the device at the power switch.

Proceed as follows:

Procedure

1. Stop any running bioreactors by pressing **Stop** in the main menu *Batch*, if necessary.
2. Call up the main menu *System* and press **Shutdown.**



The *Confirmation* dialogue box appears to confirm the shutdown.

3. Press **OK**.

The system shuts down.

4 Recipes

The various buttons for the Recipes function in main menu *Batch* can be used to load and start, save or delete what are referred to as recipes. This means all parameter settings (including cascade settings) for a cultivation process can be saved and re-used for re-curring operating processes later.

INFORMATION

All parameter settings, cascade settings and calibration data of sensors are saved. Pump calibration data are not saved. Calibration data of sensors are not uploaded.

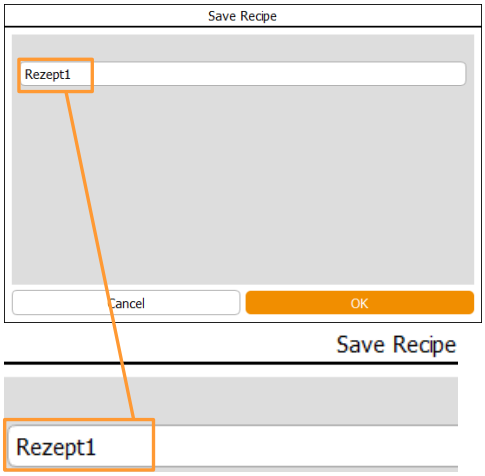
4.1 Save Recipe – Saving a Recipe

Recipes can be saved when the bioreactor is running or stopped. Recipes can only be saved individually for each bioreactor.

To save a recipe, proceed as follows:

Procedure

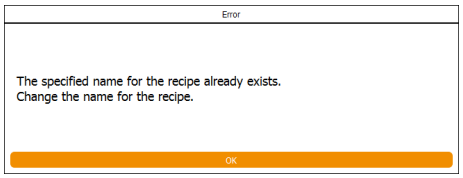
1. Log on to the system on user level *Technician* or above.
2. Select the desired bioreactor.
3. Call up main menu *Batch* and press **Save Recipe**.



The *Save Recipe* dialogue box appears.

4. Enter the desired file name.
5. Press **OK**.

The dialogue box disappears, the recipe is saved.



Recipe file name used twice

If the file name for a recipe has been used twice, an *Error* dialogue box appears with the appropriate information and instruction.

4.2 Load/Start Recipe – Loading and Starting a Recipe

A recipe has to be loaded for each individual bioreactor. One bioreactor recipe can also be used for all other bioreactors.

All preparations for a cultivation process should be made before loading and starting a recipe.

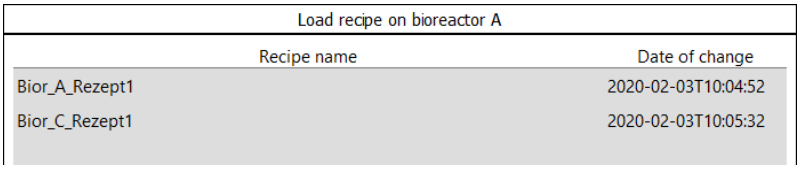
Loading recipe from bioreactor for same bioreactor

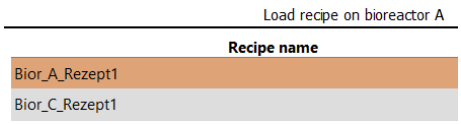
The following example shows how to load a saved recipe of bioreactor A to the same bioreactor. Proceed as follows:

Procedure

1. Log on to the system on user level *Technician* or above.
2. Select bioreactor A.
3. Call up main menu *Batch* and press **Load/Start Recipe**.

   The *Load recipe on bioreactor A* dialogue box appears with a list of all saved recipes of all bioreactors with date and time.



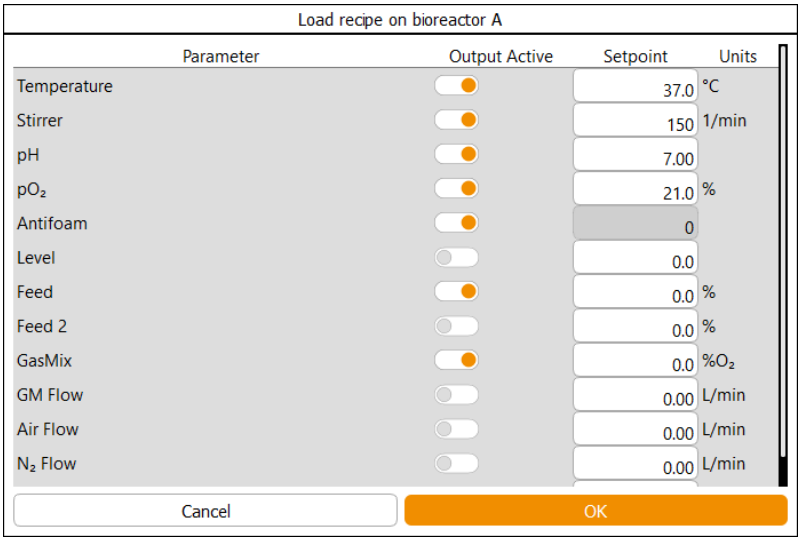


4. Select the recipe.

   The selected recipe is displayed with an orange background.

5. Press **Next**.

The dialogue box changes views.

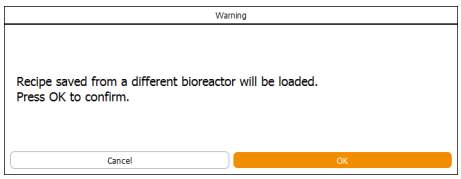


All parameters used in the recipe are listed here. Setpoints can be subsequently changed and parameters can be switched on or off. The bioreactor is started with **OK**.

6. If applicable, change setpoints and/or switch parameters on/off.
7. Press **OK**.

   The dialogue box disappears, bioreactor is A started.

Loading recipe from a bioreactor to another bioreactor



The recipe of one bioreactor can also be used for other bioreactors. To do this, proceed in the same way as for loading for the same bioreactor. Before saving after pressing **Next**, a corresponding notice appears.

4.3 Delete Recipe – Deleting a Recipe

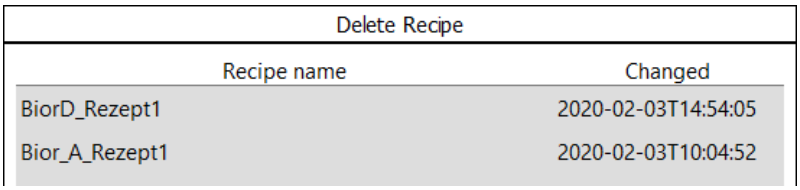
Recipes can only be deleted one by one. Recipes can also be deleted during a running cultivation process.

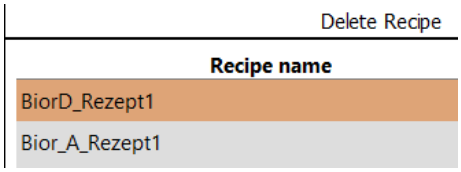
To delete a recipe, proceed as follows:

Procedure

1. Log on to the system on user level *Technician* or above.
2. Select any bioreactor or all bioreactors.
3. Call up main menu *Batch* and press **Delete Recipe**.

   The *Delete Recipe* dialogue box appears and lists all saved recipes.

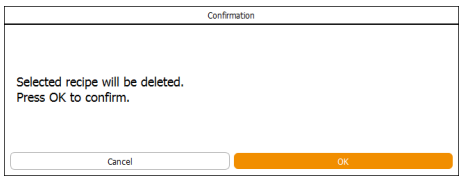




4. Select the recipe.

   The recipe is displayed with an orange background.

5. Press **OK**.



   The *Confirmation* dialogue box appears with notice and prompt to confirm the deletion of the recipe.

6. Press **OK.**

   The dialogue box disappears; the recipe is deleted.

5 Parameters

The touch screen operating panel can display and control a maximum of 24 parameters. Depending on the equipment and its configuration, more or fewer parameters are visible and available in the system.

The following describes first the default integrated parameters and their function. It then describes the frequently used optional parameters and their intended function.

Further application-specific parameters, whose configuration and function differ from those described here, are available on request. As a result of the various combination options, not all possible configurations are described.

5.1 Temperature

Measures and controls the temperature in the culture vessel. The measured values are recorded by a platinum resistance thermometer (Pt100 sensor).

The control range varies depending on the temperature control system and can be found in the technical specifications in the operating manual of the equipment.

5.2 Stirrer

Measures and controls the rotation speed of the stirrer shaft. This depends on factors such as the type of vessel volume, drive system, culture viscosity and number and kind of impellers and can be found in the technical specifications of the equipment's operating manual.

Set Stirrer Max. – rotation speed limit

This function is only present and relevant for the benchtop bioreactor Labfors 5, version for solid substrates and enzymatic bioprocesses with the servomotor (high torque) option.

The maximum rotation speed for this equipment version and specific configuration is limited to 300 min^{-1} by default. This limit may be removed under certain circumstances so that that the max. rotation speed is up to 1000 min^{-1}.

Parameters

It is compulsory, that the following conditions are fulfilled before removing the rotation speed limit:

- The stirrer is **NOT** operated with helix impellers of any type.
- Viscosity of the medium in the culture vessel corresponds to that of water.

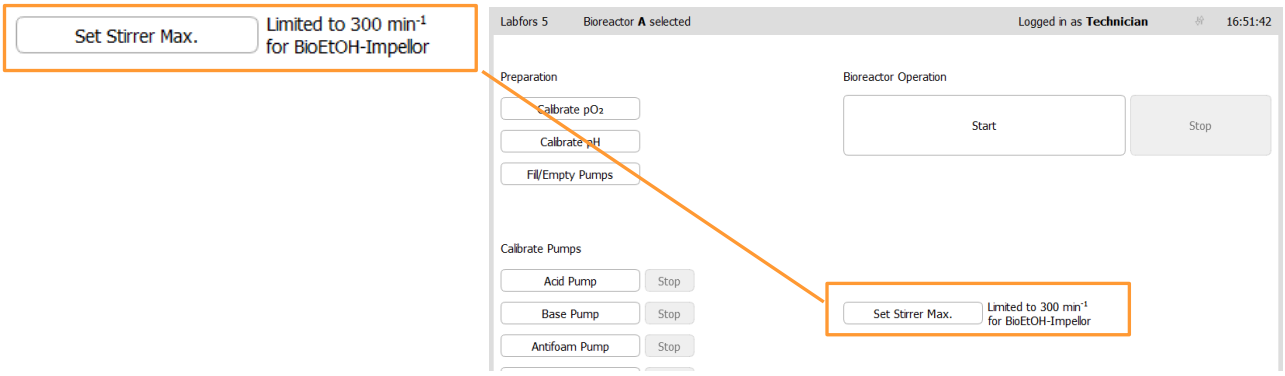
ATTENTION

The glass vessel, the impeller or the motor may be damaged when operating the stirrer at unauthorised excessive rotation speed or when using the wrong impellers.

– Never use helix impellers when operating the stirrer with rotation speed higher than 300 min^{-1}!

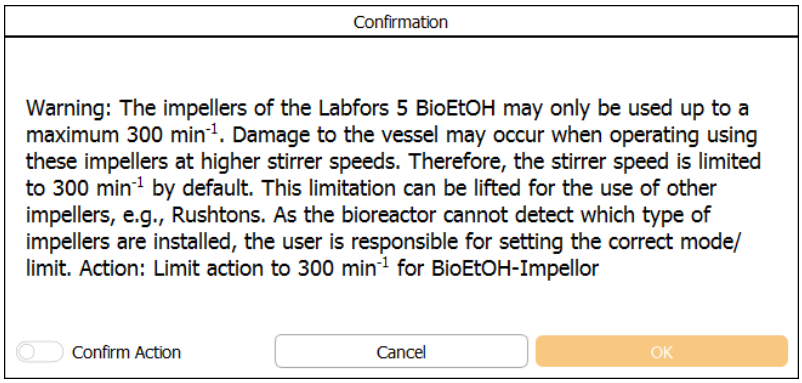
– Only when the medium is completely liquefied, rotation speed may be set higher than 300 min^{-1}!

The limitation is activated or deactivated via the **Set Stirrer Max**. button in main menu *Batch*. Which setting is active is displayed next to **Set Stirrer Max**.

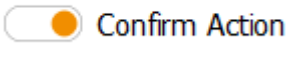


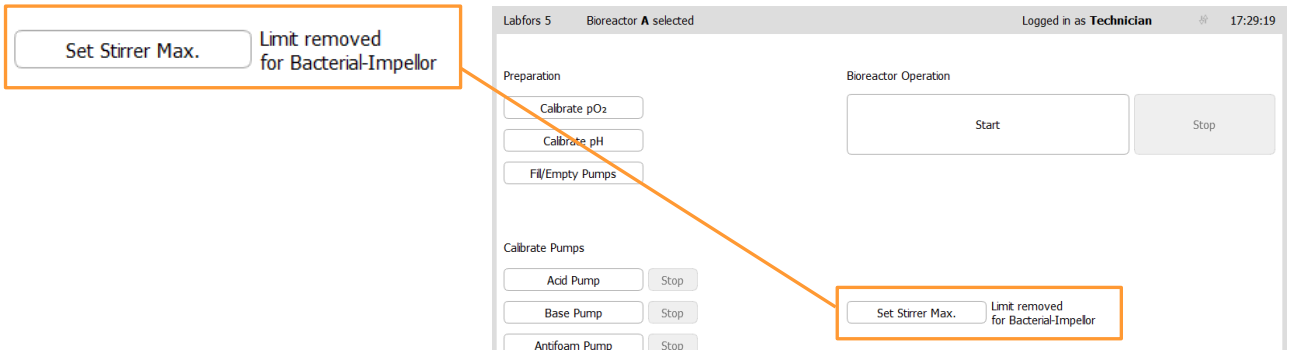
The display *Limited to 300 min^{-1} for BioEtoH Impellor* indicates an activated speed limitation.

After pressing **Set Stirrer Max**. a dialogue box appears with the corresponding warning and the mentioned instructions for the possible removal of the rotation speed limit:



The **Confirm Action** switch allows switching between the modes.





The display *Limit removed for Bacterial-Impellor* indicates a deactivated speed limitation.

5.3 pH

res and controls the pH. The range of control is from pH 2 to 12. Depending on the selected variant, the measuring system is analogue or digital.

The pH is controlled by adding acid and base via the two peristaltic pumps *Acid* and *Base*. CO_2 can also be used instead of acid. In this case it is added via a magnetic valve or a mass flow controller in the gas line. This configuration requires a corresponding cascade control with a factory preset. The activity of the pumps is time dependent. This means that they always operate in start/stop

mode at the same speed. Control is made by a PID loop. A dead band can be used to prevent unwanted rapid dosing.

Temperature compensation is a special function of the pH parameter when using the analogue pH sensor from the manufacturer METTLER. This function must be switched on during cultivation so that the temperature dependency of the measurement principle is corrected.

INFORMATION

pH of liquids is also temperature dependent which is why the pH also reacts on temperature changes when temperature compensation is switched on.

5.4 pO_2

Measures and controls the saturation of dissolved oxygen. Depending on the selected variant, the measurement system is analogue or digital.

In comparison, for example, with pH measurement, which is calibrated to absolute measurements, calibrating the oxygen measurement is always performed to a relative reference point. To do this the calibration is to 100 % relative oxygen saturation, generally determined with air to a max. stirrer speed and maximum gassing rate. The absolute concentration of dissolved oxygen in mmol/l can therefore differ for 100 % saturation depending on the process.

The PID controller output from pO_2 is generally cascaded to other parameters such as *Stirrer*, *Flow*, *Feed* or *GasMix*.

5.5 Antifoam

Measures the foam formation and regulates the addition of antifoam agent. The antifoam pump is activated as soon as the antifoam sensor comes into contact with foam.

The activity of the pump is time dependent. This means that it always operates in start/stop mode at the same speed.

- The *Dose time* must be set in seconds instead of the setpoint.
- The *Wait time* must be set in seconds instead of setting an alarm limit.

5.6 Level

Measures the level in the culture vessel by means of the level sensor. A signal is generated (*Output* of parameter *Level* = 100 %), as soon as the level sensor detects liquid. To regulate the level in the vessel, a pump can be assigned to parameter *Level* using a simple cascade.

5.7 Feed

Regulates the analogue peristaltic pump *Feed* for addition of the nutrient solution. The pump speed is adjustable and can be set in steps of 0.1 % within a range of 0 % to 100 %.

5.8 Feed 2 and Feed 3

Regulate the optional analogue peristaltic pumps *Feed 2* and *Feed 3*. The pump speed is adjustable and can be set in steps of 0.1 % within a range of 0 % to 100 %.

5.9 Flow

Measures and regulates the volume flow of two or more process gases in the culture vessel via a single mass flow controller (thermal mass meter with integrated control valve). The measurement system is entirely electronic, and the measurement is displayed according to the present configuration in L min^{-1} respectively in mL min^{-1}.

If the parameter *Flow* is available this means that the individual process gas lines are equipped with magnetic valves, which are switched using the *Gasmix* parameter.

5.10 Air Flow, O_2 Flow, N_2 Flow

All these flow parameters measure and regulate the volume flow of the appropriate process gas in the vessel via an individual mass flow controller (thermal mass meter with integrated control valve) per gas. The measurement system is entirely electronic, and the measurement is displayed is displayed according to the present configuration in L min^{-1} or mL min^{-1}.

5.11 GasMix

Controls the oxygen concentration in the inlet air. This is achieved by switching between air and oxygen or air and nitrogen for a 2-gas-mix system or air, oxygen and nitrogen for a 3-gas-mix system.

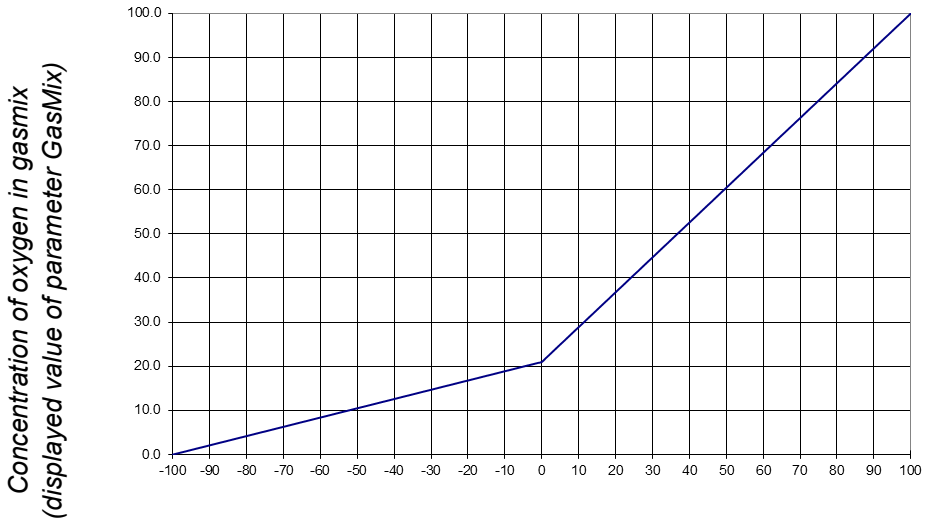
Depending on the existing configuration this means that the relevant solenoid valve is switched on or the individual gas flow parameters are controlled.

INFORMATION

If the parameter *GasMix* combined with the parameter *GM Flow* and the parameters *Air Flow*, *O_2 Flow* and/or *N_2 Flow* is installed and configured, the specified parameters are preconfigured by the device manufacturer in an advanced cascade for pO_2 control.

The following applies to the setpoint input and value display in the touch screen software:

Setpoint GasMix	Meaning	Value display
-100 %	Nitrogen only	0 % O_2
0 %	Air only	21 % O_2
100 %	Oxygen only	100 % O_2



Example

2-gas-mix system with air and oxygen, supplied via a magnetic valve.

The solenoid valves are switched according to the pre-set cycle duration in parameter option *PID* of the *GasMix* parameter.

Settings

- cycle duration: 10 seconds (*Eval. Time (s)* in option *PID*)
- setpoint *GasMix*: 20

This means that:

- the solenoid valve for oxygen opens for 2 seconds
- the solenoid valve for process air opens for 8 seconds

Setpoint 100 ≙ 10 seconds

Setpoint 20 ≙ 2 seconds

INFORMATION

For this described configuration of the 2-gas-mix system with air + oxygen with two solenoid valves, the oxygen portion of the gas mixture cannot fall below 20.95 %.

5.12 GM Flow

Sets the gassing rate of the gas mixture (GasMix parameter). This parameter can only be used and set in conjunction with the parameters *GasMix*, *Air Flow* and O_2 *Flow* and/or N_2 *Flow*.

From the gassing rate of the gas mixture (*GM Flow*) and the setpoints of the GasMix parameters the device calculates the volume flow rates of the individual gases (e.g. *Air Flow*, O_2 *Flow* etc.)

Only a setpoint input for the *GM Flow* parameter is required, the values of the parameters specified above are automatically determined and controlled.

ATTENTION

Addition input of setpoints for individual flow parameters when using the GM Flow parameter causes controller errors!

Should the flow parameters be individually controlled, the parameters *GM Flow* **and** *GasMix* **need to be switched off**.

5.13 CO_2 Flow

Measures and regulates the volume flow of carbon dioxide in the culture vessel via a mass flow controller (thermal mass meter with integrated control valve). The measurement system is entirely electronic and the measurement is displayed according to the present configuration L min^{-1} or mL min^{-1}.

Labfors 5 version for phototrophic organisms

If the parameter *pCO_2* is available, parameter *CO_2 Flow* is pre-configured for control of the *pCO_2* parameter ex-factory.

5.14 Weight

Displays the measurement of a connected external scale.

5.15 Turbidity

Is used to determine the turbidity of the culture. Turbidity can be used to draw conclusions regarding the biomass concentration in the culture. The measuring system comprises a sensor with integrated transmitter. Measuring range of absorption: 0 to 4 CU. The parameter *Turbidity* is set to this measuring range, too.

Labfors 5 / Multifors 2 – version for microorganisms

Two measuring systems are available here. In addition to the above-mentioned variant, a sensor with transmitter is available for non-invasive measurement of scattered light in culture. Measurements are performed in a range from 0 to 1000.

5.16 Exit CO_2 and Exit O_2

Measure the gas concentration of carbon dioxide (CO_2) and oxygen (O_2) in the exit gas of the bioreactor via a combined gas sensor and are used for exit gas analysis. Depending on the selected variant of the measurement system, the measurement ranges and application areas of the gas sensors are different.

5.17 Capacitance

Measures the capacity that correlates to the live biomass. This is measured using an ABER FUTURA biomass sensor. The measurement range is 0 pF cm^{-1} to 400 pF cm^{-1}.

Sensors of the ABER Futura systems measure the permittivity (also: *capacitance*) and conductivity of the culture. This measured data can be used to determine a correlation with the live biomass concentration, for example, using the soft sensor in eve® or data evaluation.

INFORMATION

The sensor with the corresponding transmitters must be purchased directly from the manufacturer ABER. INFORS HT offers a connection to the transmitter on the basic unit.

5.18 Conductivity

If the bioreactor is equipped with an ABER FUTURA biomass sensor, this can also be used to measure conductivity. In this case the measurement range is: 0 to 40 mS cm^{-1}.

Sensors of the ABER Futura systems measure the permittivity (also: *capacitance*) and conductivity of the culture. This measured data can be used to determine a correlation with the live biomass concentration, for example, using the soft sensor in eve® or data evaluation.

INFORMATION

The sensor with the corresponding transmitters must be purchased directly from the manufacturer ABER. INFORS HT offers a connection to the transmitter on the basic unit.

5.19 Redox

Measures the reduction/oxidation potential (redox) in the medium in mV. Depending on the selected variant, the measurement system is analogue or digital. The measurement range is -2000 mV to +2000 mV (analogue system) or -1500 mV to +1500 mV (digital system).

5.20 Ext. Pump

Regulates the external peristaltic pump of the type 120U/DV from the manufacturer Watson Marlow. The pump speed is adjustable and can be set in steps of 0.1 % within a range of 0 % to 100 %.

5.21 pCO_2

Measures the saturation of dissolved carbon dioxide (CO_2) in the culture by means of a digital CO_2 sensor with integrated temperature sensor. Measured values are displayed on the associated transmitter and in the touchscreen software. The measurement display of parameter *pCO_2* is set to a range from 0 to 1000 hPa, analogous to the measurement display of the transmitter.

If a CO_2 gas line is available with a mass flow controller (*CO_2 Flow* parameter), this can be used to control the pCO_2, e.g. by cascades.

5.22 Pressure

Labfors 5

Measures and controls the pressure in the culture vessel, if the option is present [1)]. The measurement is performed by a piezoresistive pressure sensor and control takes place by a solenoid valve. Control range: 0 to 400 mbar.

[1)] *does not apply to version for phototrophic organisms*

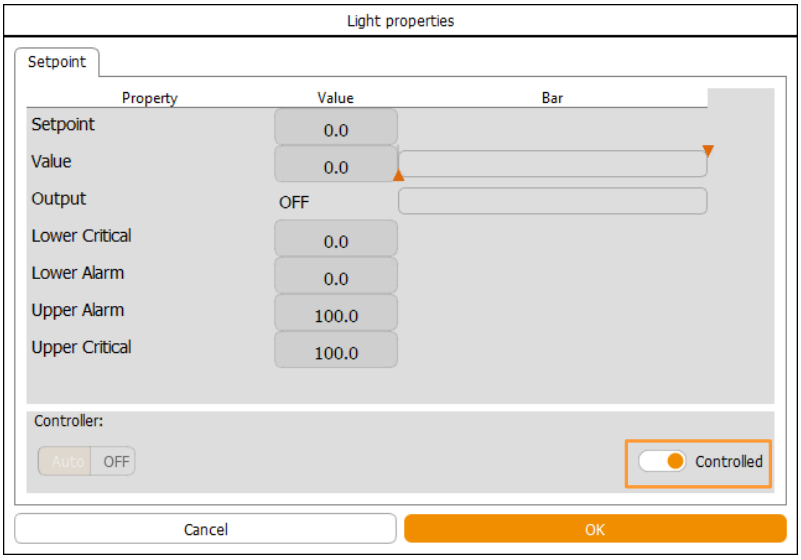
5.23 Light

Labfors 5 – version for phototrophic organisms

Controls the light intensity of the LEDs on the irradiation unit. Setting range: 0 % – 100 %, settings can then be made in increments of 0.1 %.

When using the optional light sensor, the Light parameter is calibrated based on the absolute light intensity range of the built-in irradiation unit. The value is indicated in µmol m^{-2} s^{-1}.

Also luminostat operation is possible, if the light sensor is used.



In this case, the *Controlled* function (check box) in parameter option *Setpoint* must be activated to enable control. The light intensity reaching the light sensor, is then used to define a setpoint.

The controller modifies the light intensity of the irradiation unit so that the same light intensity reaches the sensor allowing for varying culture density conditions. In other words: the biomass always “receives” the same quantity of light.

The bioreactor can also be converted for turbidostat operation on request (Infors service technician). Here, the light intensity is recorded by the separate parameter *Light Sensor.* A pump can also be cascaded to this parameter in order to dilute the culture, if the measured light intensity decreases. Over time, the biomass is adjusted so that the average light intensity per biomass is kept constant.

5.24 JTemperature

Labfors 5 – version for solid substrates and enzymatic bioprocesses

As a result of the high solid content inside the vessel, the heat transfer from the vessel jacket to the culture vessel is not ideal, which means that there can be a high temperature drop from the jacket to the vessel content. In some circumstances this may lead to inactivating enzymes/bacteria close to the vessel jacket. It can therefore be useful to limit the maximum temperature of the vessel jacket.

To do this you need to create a cascade for the parameter *Temperature* (temperature), whereby the *JTemperature* is specified as a control parameter. Within the limits of the minimum and maximum setpoint, the vessel jacket temperature of the system varies to reach the required setpoint for the parameter *Temperature*.

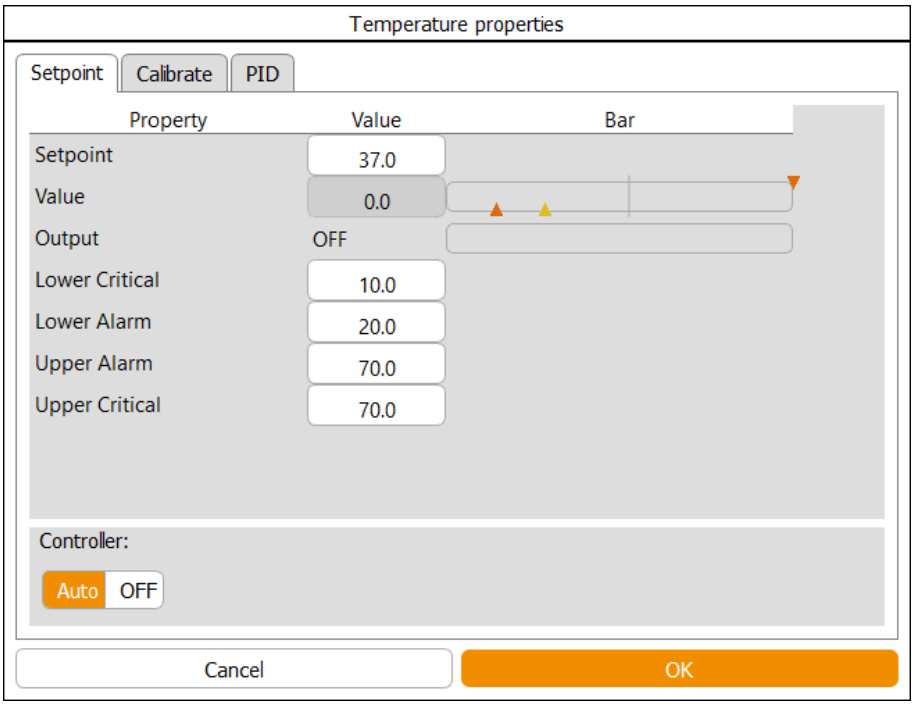
5.25 Torque

Labfors 5 – version for solid substrates and enzymatic bioprocesses

When using the optional servomotor (High Torque), it is possible to measure the power, which allows conclusions to be drawn about the actual torque. The measured torque is displayed in parameter *Torque*. This value can in turn be used to control the motor.

The current torque can serve as an indicator of the progress of the hydrolysis process. By cascading with the Stirrer parameter, it is also possible, for example, to automatically adjust the stirrer speed for operation at constant torque. In this way, an overload of the motor at the start of the process can be avoided and the mixing during the hydrolysis can be increased.

6 Parameter Options



Parameter options are setting menus for the parameters. They are shown as tab pages in the *Properties* dialogue box for the selected parameter. The figure above shows the example of the *Temperature properties* dialogue box (temperature parameter).

The parameters and their options (setting menus) for each individual bioreactor are called up in main menu *Controller*.

Depending on the access authorisation and the type of the parameter, more or less options may be available. For details on user levels and their access authorisations see the chapter “Access Authorisation of User Groups”.

- **OK**: to save inputs and close the dialogue box
- **Cancel**: to close the dialogue box without changes

Most parameters have the following options:

- *Setpoint*: this is where setpoint values, alarm values and critical values can be set and where parameters can be switched on and off.
- *Calibrate*: this is where the sensors’ measured values are calibrated.

Parameter Options

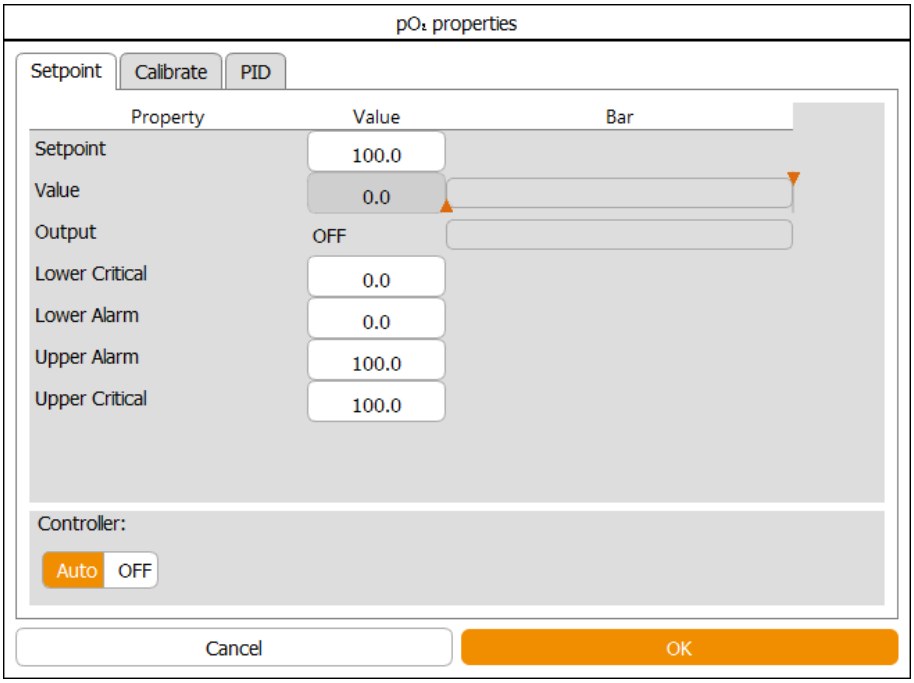
This option is only available for calibration of the measured values of the pH, pO_2 and turbidity sensors (OPTEK system) on user levels *User* and *Technician*. All other calibration menus are only accessible on user level Administrator and above.

- *PID*: This is where controller settings are made.
- *Options*: This is where the basic parameter settings are made.

  This option is only accessible to the manufacturer's qualified personnel. This option is not visible or enabled at any other user level.

The following chapters describe the content and function of the individual tab pages, i.e. parameter menus. Each menu description is followed by either detailed setting instructions or a cross reference to the respective corresponding in these operating instructions.

6.1 Setpoint



The tab page for the *Setpoint* option is divided up into a three-column main area with input fields and view boxes and a *Controller* area.

Columns

- *Property*: designation of the input fields and view boxes
- *Value*: values of the input fields and view boxes
- *Bar*: graphic display of the values as in main menu Controller. For details refer to chapter “Main Menus”, “Controller – Value Display”.

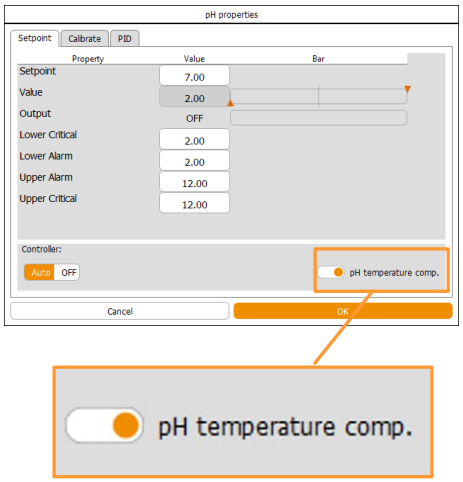
Input fields and view boxes

- *Setpoint*: to enter the setpoint
- *Value*: displays the current value
- *Output*: shows the controller output as a percentage.
- *Lower Critical* and *Upper Critical*: to enter the lower critical and upper critical value
- *Lower Alarm*: to enter the lower alarm value
- *Upper Alarm* and *Lower Alarm*: to enter the upper alarm and lower alarm value

Controller

- **Auto**: to switch on the parameter into automatic mode. In this mode, it is possible to switch the parameter on or off by touching the controller output (displayed value *OFF* or %) in main menu *Controller* during a running cultivation.
- **OFF**: to switch off the parameter. This mode deactivates the controller output in main menu *Controller*, too.

pH temperature compensation



If the pH measurement system with analogue pH sensors from the manufacturer METTLER is present, parameter pH has the additional function *pH temperature comp*. (pH temperature compensation). With digital pH measurement systems, this function is integrated into the pH sensor.

pH temperature compensation must be switched on during cultivation so that temperature-compensated values can be generated. That means, the temperature dependency of the measuring principle will be corrected.

INFORMATION

pH of liquids is temperature-dependent, too. Therefore, pH will still be responsive to temperature variation, although temperature compensation is switched on.

This function must also be switched on to calibrate the pH sensor whilst simultaneously measuring the temperature of the pH buffer solution or manually entering the temperature of the buffer solution.

6.1.1 Setting Setpoint Values, Switching Parameters ON / OFF

Parameter setpoint values are basically set in the configuration dialogue for one bioreactor or all bioreactors. Once the bioreactor(s) is/are running, setpoint values can be changed then via main menu *Controller* for each bioreactor individually.

Parameters can be switched on or off in the configuration dialogue or via main menu *Controller* once the bioreactor(s) is/are running, if their controller output is set to automatic mode in the *Setpoint* option of the parameter.

In stopped state of a bioreactor, all its parameters are automatically switched off and cannot be switched on.

INFORMATION

Bioreactor(s) is/are always started with the settings in the configuration dialogue. Changes to these settings are saved and transferred to the next configuration dialogue. If setpoint values are changed or parameters are switched on/off whilst a bioreactor is running, these settings are only adopted for the current cultivation process.

Note the following for setting setpoints:

When using a lightly foaming medium, set the setpoints in parameters *Stirrer* (stirrer speed) and the different *Flow* parameter(s) as low as possible if this does not have a negative effect on the oxygen supply to the culture.

If there is still heavy foaming, a chemical antifoaming agent will need to be used. In this case the *Dose time* and *Wait time* in the parameter *Antifoam* must be set accordingly.

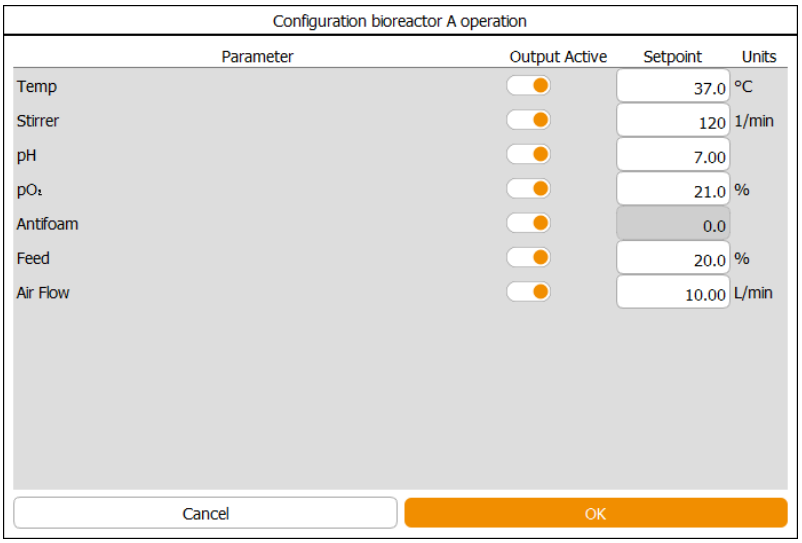
Settings in the configuration dialogue

To make the settings in the configuration dialogue, proceed as follows:

Procedure

1. Select the desired bioreactor.
2. Call up main menu *Batch* and press **Start**.

   The *Configuration bioreactor operation* dialogue box (configuration dialogue) of the selected bioreactor appears.



- The left side lists all available parameters (depending on the equipment configuration).
- On the right side are the switches for switching the parameters on or off and the starting setpoints. The setpoints can be changed here.

INFORMATION

The on/off switches are present if the *Controller* is in automatic (*Auto*) mode in the *Setpoint* option of the parameter.

3. If necessary, change the setpoints of the parameters individually via ***Setpoint***.
4. Switch on/off parameters as required.
5. Press **OK**.

   The dialogue box disappears, the settings are saved, and the bioreactor is started.

   When all bioreactors are selected (*ALL*), they are all started with the same settings.

   Changed settings are transferred to the next configuration dialogue.

Settings on the running bioreactor

To make the settings on the running bioreactor, the following two options are available:

a) Directly via the *Setpoint* input field/view boxes and the controller output buttons in the *Output* column of the main menu *Controller*.

b) In the *Setpoint* menu of the selected parameter in the *Parameter* column of the main menu *Controller*.

INFORMATION

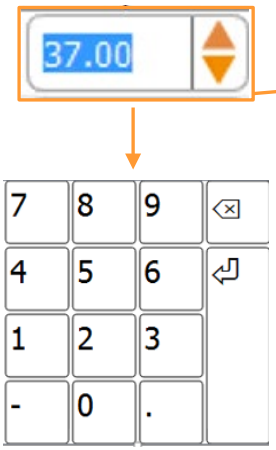
Changed settings are adopted for the cultivation process in progress only.

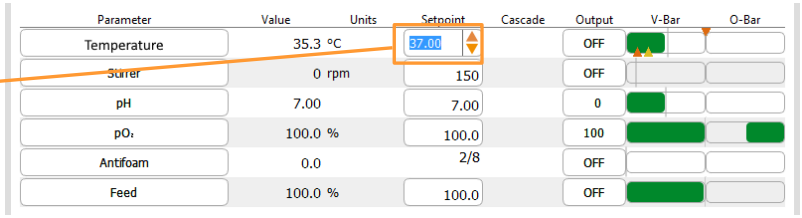
Proceed as follows:

Variant a)

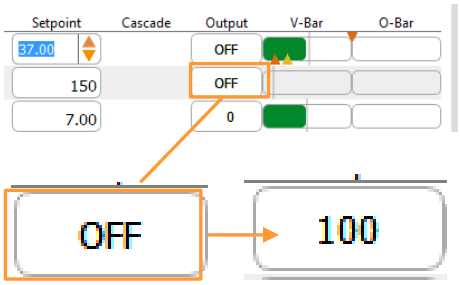
Procedure

1. Call up main menu *Controller*.





2. Press the *Setpoint* input field/view box of the desired parameter and enter the desired setpoint via numeric keypad



3. Switch the parameter on via controller output button **OFF**.

The parameter is switched on, the controller output changes from *OFF* to the display of the corresponding numeric value in %.

INFORMATION

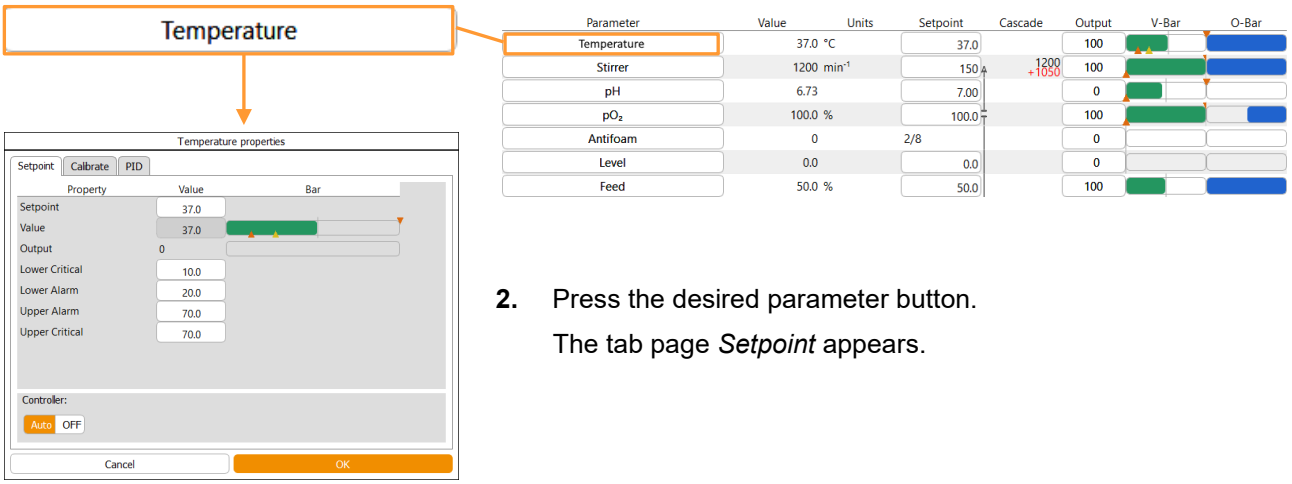
To switch the parameter i.e. controller output on or off here, is only possible, if the controller of the parameter is set to automatic (Auto) mode in its *Setpoint* option. See also next procedure in variant b).

Parameter Options

Variant b)

Procedure

1. Call up main menu *Controller*.



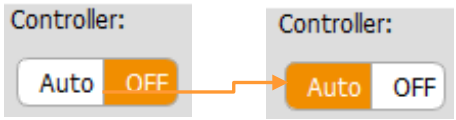
2. Press the desired parameter button.

The tab page *Setpoint* appears.

3. Enter the desired setpoint via ***Setpoint***.

4. Change alarm values and critical values as required.

For details about alarm value and critical value settings refer to chapter „Setting Alarm Values and Critical Values”.



5. Ensure the controller output is switched to automatic mode (**Auto)**, change setting as necessary.

The parameter is set switched on now.

6. Press **OK**.

The dialogue box disappears, the settings are saved.

6.1.2 Setting Alarm Values and Critical Values

Alarm values and critical values can be set symmetrically or asymmetrically.

- Symmetrically: The difference between the setpoint value and the upper alarm value or the upper critical value = the difference between the setpoint value and the lower alarm value or the lower critical value.
- Asymmetrically: The difference between the setpoint value and the upper alarm value or the upper critical value ≠ the difference between the setpoint value and the lower alarm value or the lower critical value.

Upper alarm values can be set ≤ upper critical values. Lower alarm values can be set ≥ lower critical values.

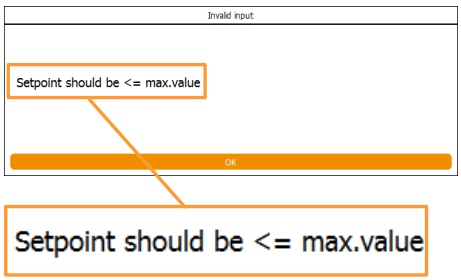
A parameter alarm is triggered as soon as a value drops below the lower alarm value or exceeds the upper alarm value. For details see the chapter “Alarms – Parameter Alarms, User Alarms, System Alarms”, “Parameter Alarms”.

INFORMATION

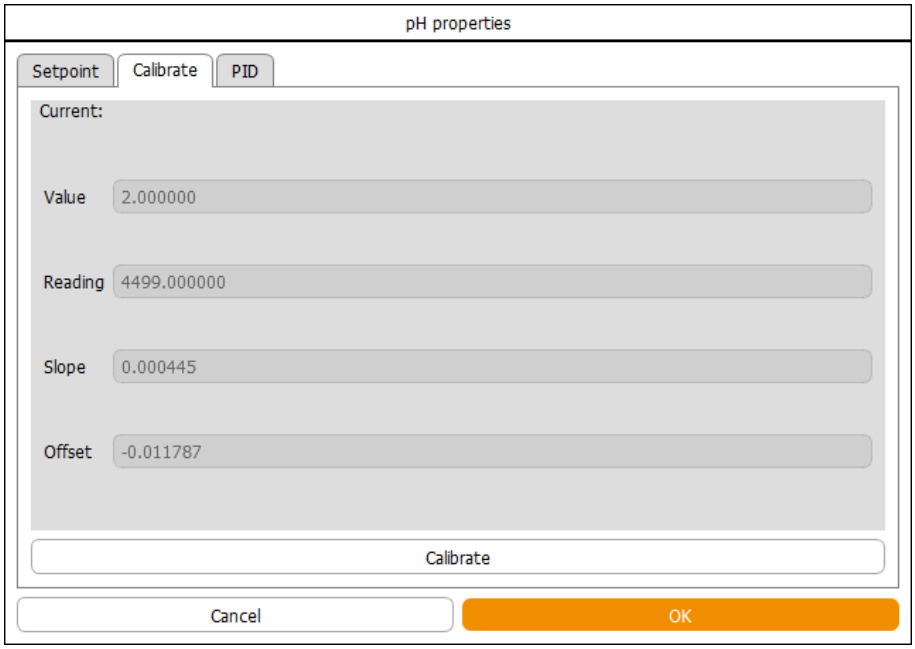
Alarm values and critical values have to be set individually for each bioreactor by selecting the desired parameter in the main menu Controller and calling up its *Setpoint* option menu. The setting procedure remains the same as for setpoint values. The bioreactor can be in stopped or running state while entering these values.

Invalid setpoint value or alarm limit input

When an invalid setpoint, alarm or critical alarm value is entered, a corresponding *Invalid input* dialogue box appears with the appropriate notice.



6.2 Calibrate - Calibration



The tab page for the *Calibrate* option contains four view boxes and a button:

- *Value*: shows the current measured value depending on the last calibration
- *Reading*: shows the current measured value in digital units
- *Slope*: shows the digital value of the calculated slope of the calibration line
- *Offset*: describes the intersection point of the calibration line with the X axis
- **Calibrate**: to open the calibration menu

Reading, *Slope* and *Offset* are not relevant for measurement systems of the digital pH and pO_2 sensors. These values are stored directly in the integrated electronics of the respective sensor.

INFORMATION

The calibration menus for pH and pO_2 can also be called up directly via **Calibrate pH** and **Calibrate pO_2** in the main menu *Batch*.

General Information on calibration

Sensors for measurement of pH, pO_2 and turbidity (variant OPTEK only) are usually recalibrated before each cultivation. Depending on the sensor and measurement system, either a 2-point calibration or a 1-point calibration or a zero adjustment is sufficient. Detailed information on calibration can be found in the separate documentation provided by the sensor manufacturers.

The various calibrations are described in the following chapters.

Calibrate All pH/pO2 – Calibration of all pH-/pO_2 sensors

The **Calibrate ALL pH** and **Calibrate ALL pO_2** buttons in main menu *Batch* are available, as soon as more than one bioreactor (= culture vessel) is controlled using the touch screen software. These functions enable a simultaneous calibration of several or all connected pH sensors or pO_2 sensors.

A maximum of 6 bioreactors can be controlled using an operating panel with the touch screen software. For the bench-top bioreactors Labfors 5 and Multifors 2 this means:

- Labfors 5: 1 device = 1 bioreactor (= 1 culture vessel)
  max. 1 master device with 5 satellite devices is possible
- Multifors 2: 1 device = 2 bioreactors (= 2 culture vessels)
  max. 1 master device with 2 satellite devices is possible.

6.2.1 pH Sensor Calibration

The calibration must be carried out before sterilisation, i.e. before mounting the pH sensor in the culture vessel.

Depending on the version selected, the device is equipped and configured with a digital or analogue pH measurement system.

Digital sensors

The pH buffers and their temperature dependencies are stored in these pH sensors and are automatically detected during calibration. It is therefore not necessary to carry out a separate temperature measurement of the buffer solution.

INFORMATION

If a digital pH sensor has already been calibrated externally, the bioreactor will use this data and the calibration procedure in the touch screen software is not necessary.

Analogue sensors

If very exact calibration values are required, the exact temperature of the buffer solutions should be determined. The measurement can be made directly with the temperature sensor of the device during calibration. Another possibility is to measure the temperature exactly and enter the value manually in the touch screen software. In both cases, temperature compensation must be switched on in the SETPOINT option of the pH parameter. This corrects the temperature dependence of the measurement principle. Without temperature measurement or input, a puffer temperature of 20 C is assumed.

Detailed information on calibration, general use, service and maintenance can be found in the separate documentation provided by the sensor manufacturers.

6.2.1.1 pH Sensor (Digital) Calibration

To calibrate a digital pH sensor in the touch screen software, proceed as follows:

Procedure

1. Connect the sensor cable.
2. Carefully remove the watering cap from the pH sensor and rinse the pH sensor with distilled water, do not rub!

ATTENTION

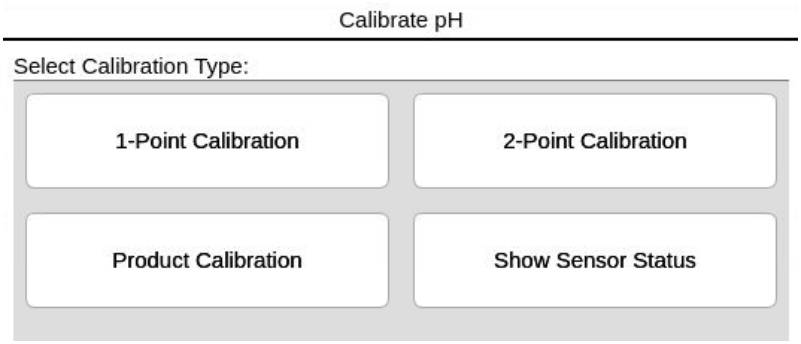
Dry wiping or rubbing a pH sensor after rinsing can cause electrostatic charge. This can greatly increase the response time and generate incorrect measurements. At most, gently dab a pH sensor after rinsing, **NEVER** rub or wipe it!

INFORMATION

Only sensor type Easyferm Plus ARC: the ERROR Glass resistance too high which may appear after initialization can be ignored. It may occur if the sensor is in contact with air or nonconductive liquid such as distilled water.

3. Call up main menu *Batch* and press **Calibrate pH**.

The calibration menu opens with four options:

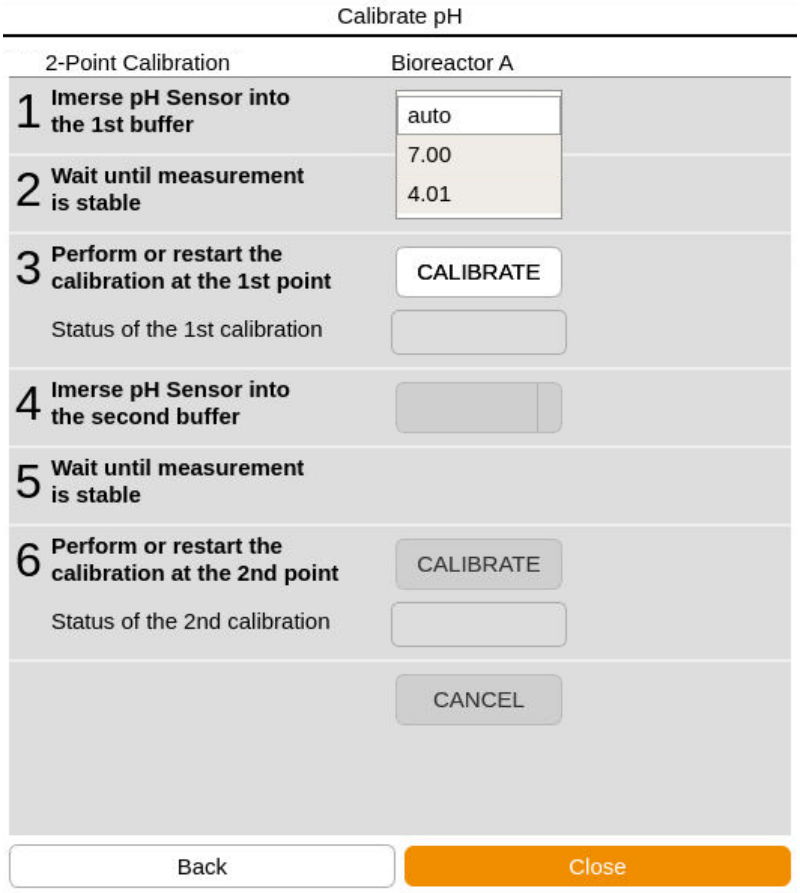


- **1-Point Calibration** and **2-Point Calibration**: to select 1-point or 2-point calibration.
- **Product Calibration**: to select product calibration. For details see chapter “pH Sensor (Digital) Product Calibration”.
- **Show Sensor Status**: shows data and values produced by the firmware of the sensor manufacturer that is integrated in the sensor. For more details see section “Sensor Status”.

4. Select 2-point calibration.

Parameter Options

The menu opens and leads step by step (1 to 6) through the calibration:



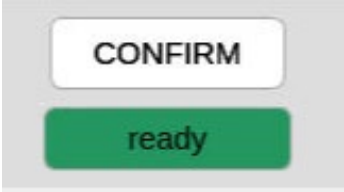
- **Drop-down list**s (step 1 and 4) for selection of the 1st, respectively the 2nd reference value. If the connected sensor allows the use of different calibration buffers or an automatic recognition of the calibration buffer (“auto”), it can be selected. Otherwise, the calibration buffer to be used is displayed.
- Measured value display (step 2 and 5)
- **CALIBRATE** and status display (step 3 and 6): to start the calibration procedure.

  As soon as the bar of the status display is filled up and shows *Ready*, the button changes to **CONFIRM** to save the calibration point. **CANCE**L for possible abortion of the calibration process becomes available.

INFORMATION

The calibration process can be continued at any time from the last stored point if the menu has been left via **Close**. This does not apply, however, if another calibration process is started

5. Hold the pH sensor into the appropriate buffer solution of the first calibration point and if possible, select reference value or automatic buffer recognition in the drop-down list (step 1).
6. Wait until the measurement is stable (step 2).
7. Press **CALIBRATE** (step 3a).



The calibration process begins. The **CALIBRATE** button changes to **CONFIRM**.
The status display slowly turns green, indicating the ideal waiting time until a stable measured value is reached.

INFORMATION

If the measured value is assumed to be already stable, the waiting time can be skipped by pressing **CONFIRM** to continue with the second calibration point.

8. Press **CONFIRM** (step 3b).

   The calibration point is stored.

INFORMATION

If the calibration process fails, an error message is displayed with a corresponding note. Restart calibration in this case.

If the calibration is successful, the drop-down list for selection of the second reference value and the **CALIBRATE** button become available to calibrate the second point.

The calibration procedure for the second point remains the same as for the first point. After rinsing the pH sensor with distilled water, the same *ERROR* may occur. This can also be ignored here.

After successfully storing the 2nd calibration point via **CONFIRM** the calibration is finished and the menu can be left via **Close**.

Sensor Status

Show Sensor Status is used to call up data and values that are output by the firmware of the sensor manufacturer integrated in the sensor. In addition to sensor type and calibration information, the following two values are displayed for METTLER ISM sensors:

- **ACT** (Adaptive Calibration Timer in days): determines the time of the next calibration to ensure optimum measurement performance. It is reset to its initial value after successful calibration.
- **DLI** (Dynamic Lifetime Indicator in days): displays the number of days remaining and is preset by the sensor manufacturer.

6.2.1.2 Calibration of All (Digital) pH Sensors

The procedure for calibrating all digital pH sensors simultaneously remains the same as the calibration procedure for a single digital pH sensor. Therefore, the individual steps are not described in detail in this chapter.

It is possible to handle the pH sensors and buffer solutions in various ways.

For example:

a) Place all pH sensors in a container with the buffer solution at the same time and calibrate the first and the second point one after the other.

b) Place each pH sensor in the buffer solution individually (or in pairs for Multifors 2) and calibrate the first point of each pH sensor one after the other. Repeat the same process for the second point.

c) Place all pH sensors in a container with the buffer solution individually and calibrate the first and the second point one after the other.

Proceed as follows for calibration:

Procedure

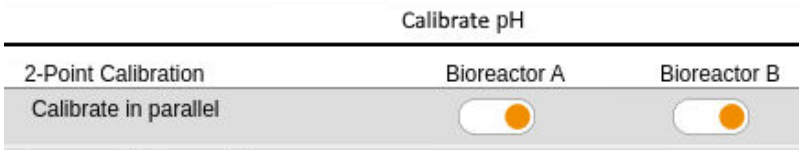
1. Depending on the desired method, prepare a container, e.g. measuring beaker, with both buffer solutions at a known temperature for each pH sensor individually or for all pH sensors.
2. Connect all sensor cables.
3. Select all (*All*) bioreactors via selection bar.
4. Call up main menu *Batch* and press **Calibrate All pH**.

   The calibration menu opens with the different calibration options as for the single calibration.

5. Select 2-point calibration.

   The menu opens with up to 6 (bioreactor A to F) bioreactors. The example below shows the 2-point calibration menu for bioreactor A and B.

   The calibration menu leads through the calibration step by step (1 to 6) in the same way as for a single pH sensor.



   Calibrate in parallel: only this function is additionally available here. This defines whether the calibration steps of one, several or all pH sensors should be carried out simultaneously (function ON) or individually (function OFF) one after the other

6. Switch the function on/off as required.

7. Rinse the pH sensors with distilled water, (do not rub!) and hold them into the appropriate buffer solution of the first reference point.

INFORMATION

Observe the notes on electrostatic charging and possible error message *ERROR Glass resistance too high in chapter* “pH Sensor (Digital) Calibration”.

8. Proceed with calibration as described from step 6 in the chapter “pH Sensor (Digital) Calibration”.

6.2.1.3 pH Sensor (Digital) Product Calibration

Adapting the calibration curve to the current process conditions is possible by performing a product calibration. This could be necessary if there is a possibility of drift of the displayed pH during a long-term cultivation, for example.

INFORMATION

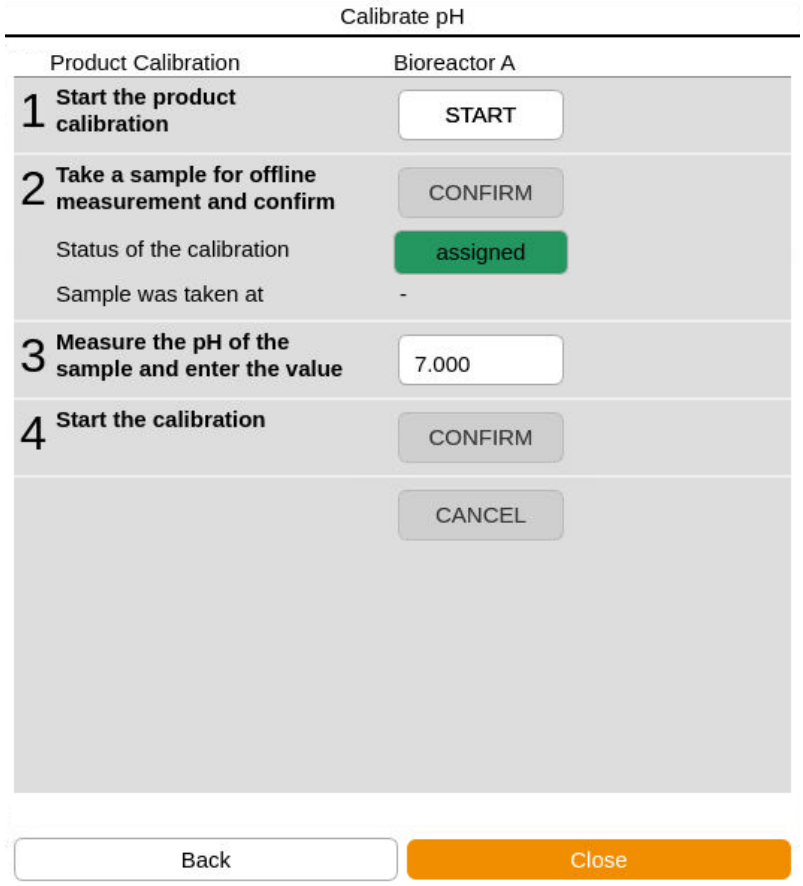
Product calibration can only be carried out and is only effective if the externally measured and entered pH value does not deviate from the original pH value by more than 2 pH units.

Proceed as follows for product calibration:

Procedure

1. Call up the calibration menu of the pH sensor and press **Product Calibration**.

The product calibration menu opens and guides step by step (1 to 4) through the product calibration:



- Step 1 +2: start product calibration via **START** and confirm sampling via **CONFIRM** to generate a time stamp (*Sample was taken at*).

  Status display of the calibration with the following possible displays:
  - *ready*: time stamp for sampling can be generated via **CONFIRM**.
  - *measured*: time stamp was generated.
  - *assigned*: last product calibration was successful and is active. Performing a new product calibration is possible.
  - *aborted:* last product calibration was aborted via **CANCEL** or was not successful, restart product calibration.
- Step 3 + 4: enter external measured value and confirm entry via **CONFIRM** to start calibration.

Parameter Options

INFORMATION

The calibration process can be continued at any time from the last stored point if the menu has been exited via **Close**. This does not apply, however, if another calibration process is started.

2. Press **START**.
3. Take a sample from the process (culture in the vessel).

   There are two possible approaches:

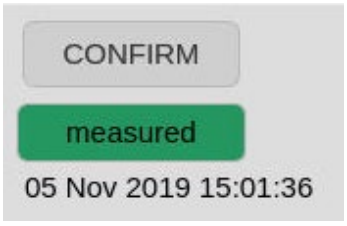
   a) Confirm the sampling (generate a time stamp), carry out a laboratory measurement of the pH value for the sample, enter the measured value and carry out product calibration.

   OR:

   b) Confirm the sampling (generate a time stamp), leave the calibration menu via **Close** and carry out the product calibration with an external measured value at a later time.

Variant a)

Procedure



1. Press **CONFIRM**.

   Status display changes to *measured.*
   Date and time of sampling are now displayed below.

2. Carry out a laboratory measurement of the pH value for the sample.

3. Enter the measured pH value of the sample, in the example to the left, pH 7.0.
4. Press **CONFIRM** to start calibration.

5. Wait until the calibration is complete.

This means that the status display changes to *assigned*. This status allows to perform a new product calibration or to exit the menu.

6. Leave the menu via **Close**.

INFORMATION

A new product calibration or a 1-point or 2-point calibration cancels the active product calibration.

Variant b)

Procedure

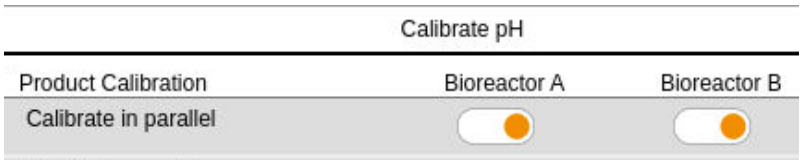
1. Press **CONFIRM**.

   As in variant a), the status display changes to *measured* and the date and time of sampling are displayed below.

   This indicates that sampling is successful, but product calibration is not yet active. If a sample is lost, step 1 can be performed again.
2. Exit calibration menu via **Close** and perform laboratory measurement of the pH value for the sample at a later time.
3. To perform the product calibration, proceed as described in variant a) from step 2.

Product calibration of all (digital) pH sensors

The procedure for simultaneous product calibration of all digital pH sensors remains the same as for a single pH sensor.



Calibrate in parallel: only this function is additionally available in the calibration menu. This defines whether the calibration steps of one, several or all pH sensors should be carried out simultaneously (function ON) or individually (function OFF) one after the other.

6.2.1.4 pH Sensor (Analogue) Calibration

To calibrate an analogue pH sensor in the touch screen software, proceed as follows:

Procedure

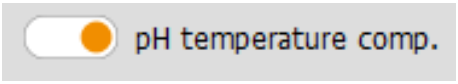
1. Connect the sensor cable.

   Ensure the cable is not buckled or twisted.

ATTENTION

The integrity of the sensor cable can be damaged by buckling or twisting. This may lead to faulty measurements.

If the externally measured temperature of the pH buffer solutions is to be entered or if their temperature is to be measured with the temperature sensor:



2. Switch pH temperature compensation on in *Setpoint* option of parameter *pH*.

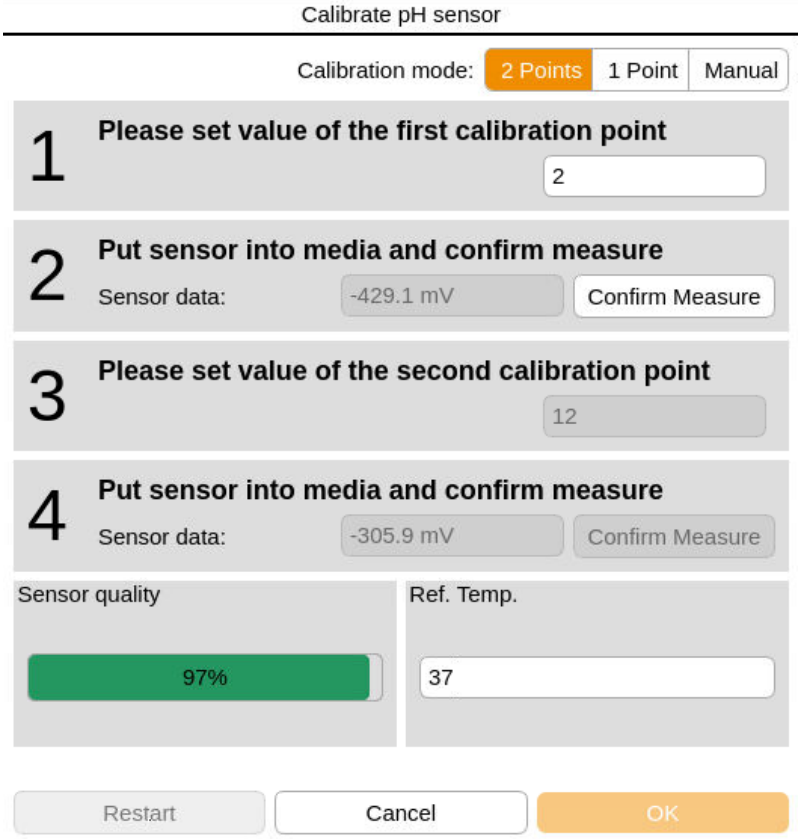
3. Carefully remove the watering cap from the pH sensor and rinse the pH sensor with distilled water, do not rub!

ATTENTION

Dry wiping or rubbing a pH sensor after rinsing can cause electrostatic charge. This can greatly increase the response time and generate incorrect measurements. At most, gently dab a pH sensor after rinsing, **NEVER** rub or wipe it!

4. Call up main menu *Batch* and press **Calibrate pH**.

The calibration menu *Calibrate pH sensor* appears and leads step by step (1 to 4) through the calibration.



The 2-point calibration mode is automatically selected. The *Ref. Temp* input field/view box is displayed.

INFORMATION

Without switching pH temperature compensation on before, this field is not visible.

The *Sensor quality* display bar charts the quality of the sensor in a scale from 0 to 100 %.

5. Enter the value of the low (or high) reference buffer in the input field on line 1.

INFORMATION

The order in which the reference points are calibrated is irrelevant.

With activated temperature compensation:

6. Enter the temperature of the buffer solution in the *Ref. Temp*. view box/input field or hold the temperature sensor together with the pH sensor into the relevant buffer solution at step 7.
7. Hold the pH sensor into the relevant buffer solution.

   The measurement (in mV) is displayed in line 2 in *Sensor data*.

   As soon as the measurement is stable:
8. Press **Confirm Measure** in line 2.

   The calibration value is accepted. The input fields and buttons in line 3 and 4 are available now.

INFORMATION

The signal characteristics are asymmetric. In other words, the closer the signal comes to the real value, the slower the change. The calibration is inaccurate, if the measurement is confirmed with **OK** before the sensor signal has completely stabilised. Wait a few minutes before confirming with **OK** and check the reading again, if in doubt.

9. Rinse the pH sensor with distilled water, do not rub!
10. Repeat the same steps for the second point like for the first point.

    Once the second calibration value is accepted:
11. Press **OK**.

    The dialogue box disappears, the calibration values are stored.
12. Rinse the pH sensor with distilled water, do not rub!

6.2.1.5 Calibration of All (Analogue) pH Sensors

If the exact temperature of the buffer solution is to be determined for the calibration of all pH sensors, this must be done externally; it cannot be measured here with the temperature sensor. If the temperature of the buffer solution is not entered, a buffer temperature of 20 °C is assumed.

Proceed as follows for calibration:

Procedure

1. Depending on the desired method, prepare a container, e.g. measuring beaker, with both buffer solutions at a known temperature for each pH sensor individually or for all pH sensors.
2. Connect all sensor cables and ensure they are not buckled or twisted.

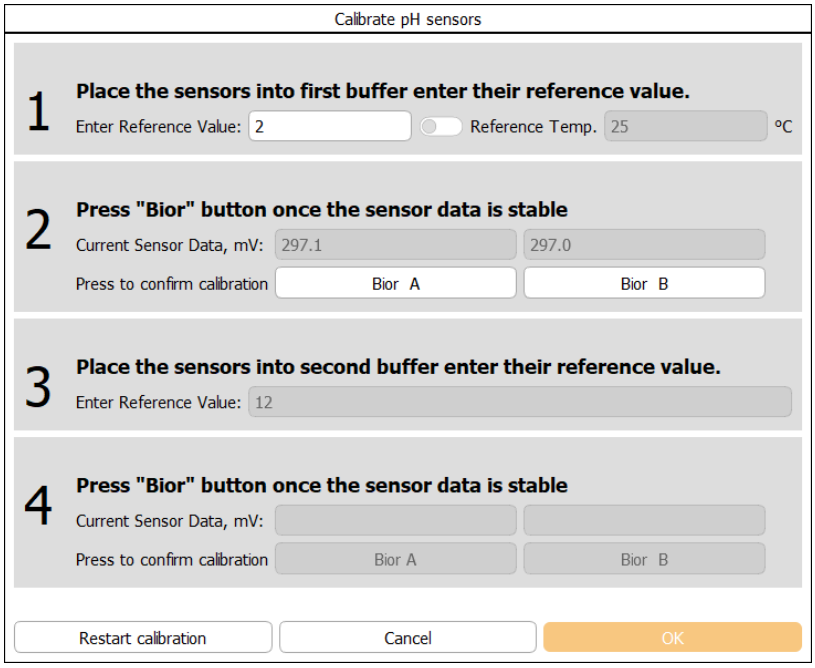
ATTENTION

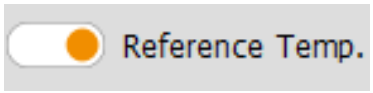
The integrity of the sensor cable can be damaged by buckling or twisting. This may lead to faulty measurements.

3. Select all (*All*) bioreactors via selection bar.
4. Call up main menu *Batch* and press **Calibrate All pH**.

Parameter Options

The menu opens with up to 6 (bioreactor A to F) bioreactors. The example below shows the 2-point calibration menu for bioreactor A and B. The menu leads through the calibration step by step (1 to 4).





5. Switch on the *Rerence Temp*. function for manual input of the buffer solution temperature as required

INFORMATION

When using this function, it must be ensured that temperature compensation (*pH temp compens*) is switched on for the individual bioreactors in the pH parameter option *Setpoint.*

6. If necessary, enter the measured temperature value of the buffer solution in the *Reference Temp*. input field
7. Rinse all pH sensors with distilled water, do not rub!

ATTENTION

Dry wiping or rubbing a pH sensor after rinsing can cause electrostatic charge. This can greatly increase the response time and generate incorrect measurements. At most, gently dab a pH sensor after rinsing, **NEVER** rub or wipe it!

8. Enter value of lower (or upper) reference buffer in input field on line 1

   The order in which the reference points are calibrated is irrelevant.

9. Hold the pH sensors into the relevant buffer solution.

   Measured values (in mV) of the pH sensores are displayed in *Current Sensor Data* in line 2 above the **Bior** buttons.

   As soon as all measured values are stable:

10. Press the **Bior** buttons one after the other.

    The calibration values are accepted. The input fields and buttons in line 3 and 4 are now available.

INFORMATION

The signal characteristics are asymmetric. In other words, the closer the signal comes to the real value, the slower the change. The calibration is not accurate, if the measurement is confirmed with **OK** before the sensor signal is completely steady. Wait a few minutes before confirming with **OK** and check the reading again, if in doubt.

11. Rinse all pH sensors with distilled water, do not rub!
12. Repeat the same steps for the second calibration point as for the first.

    As soon as the second calibration value of all pH sensors has been accepted:

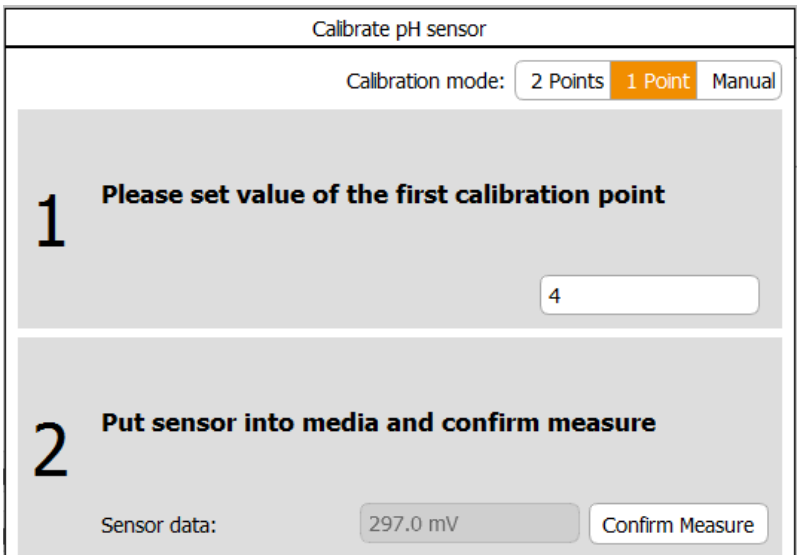
13. Press **OK**.

    The menu disappears, the calibration values are stored.

14. Rinse all pH sensors with distilled water, do not rub!

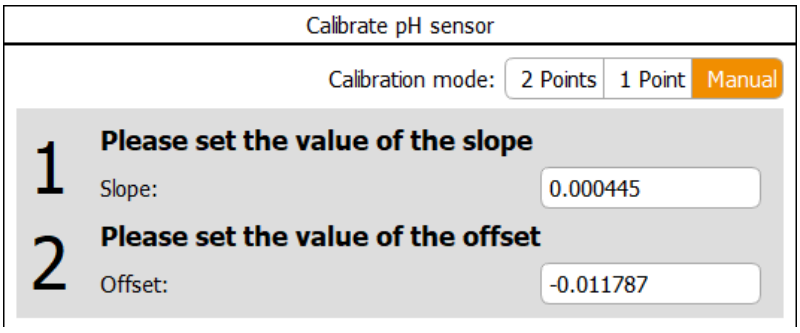
6.2.1.6 pH Sensor (Analogue) Recalibration

To compensate for a deviation (drift) in the measurement of an analogue pH sensor over a long-term cultivation, it is possible and sufficient to recalibrate with a 1-point calibration.



This means that the pH of a sample measured using an external measurement device is accepted as the new reference value in 1-point calibration mode.

The same effect is achieved by manually correcting the offset (deviation). In other words, the difference between the externally determined measurement and the displayed measurement in the culture needs to be added to or subtracted from the last calculated offset value depending on the result.



The correction is made in manual calibration mode.

6.2.2 pO_2 Sensor Calibration

A 1-point calibration to 100 % is usually sufficient for exact measurement and should be carried out before each cultivation. If requirede, a 2-point calibration to 100 % and 0 % is also possible.

INFORMATION

The prerequisites for exact calibration results can be found in the separate documentation of the sensor manufacturer. The calibration conditions and how they are achieved are defined by the operator and are not the subject of this operating manual.

Depending on the version selected, the device is equipped and configured with a digital or analogue pO_2 measurement system.

Digital sensors

The 2-point calibration can only be carried out in the correct sequence: 1st calibration point = 100 %, 2nd calibration point = 0 %.

INFORMATION

Digital pO_2 sensors are preconfigured by the device manufacturer to the measurement value %-sat.

Analogue sensors

A 2-point calibration of the analogue pO_2 sensors can be performed in the 2-point calibration mode or successively in the 1-point calibration mode.

The 2-point calibration **must** be carried out in the correct sequence: 1st calibration point = 0 %, 2nd calibration point = 100.

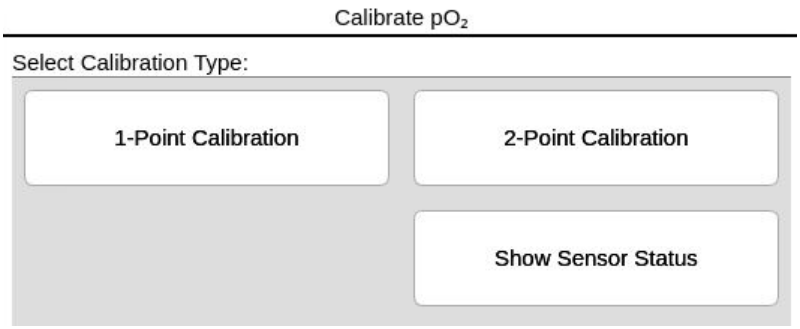
6.2.2.1 pO_2 Sensor (Digital) Calibration

The following example describes a 2-point calibration of a digital pO_2 sensor. Here the first calibration point is 100 %, the second calibration point is 0 %.

Proceed as follows, once desired calibration conditions for 100 % calibration are achieved:

Procedure

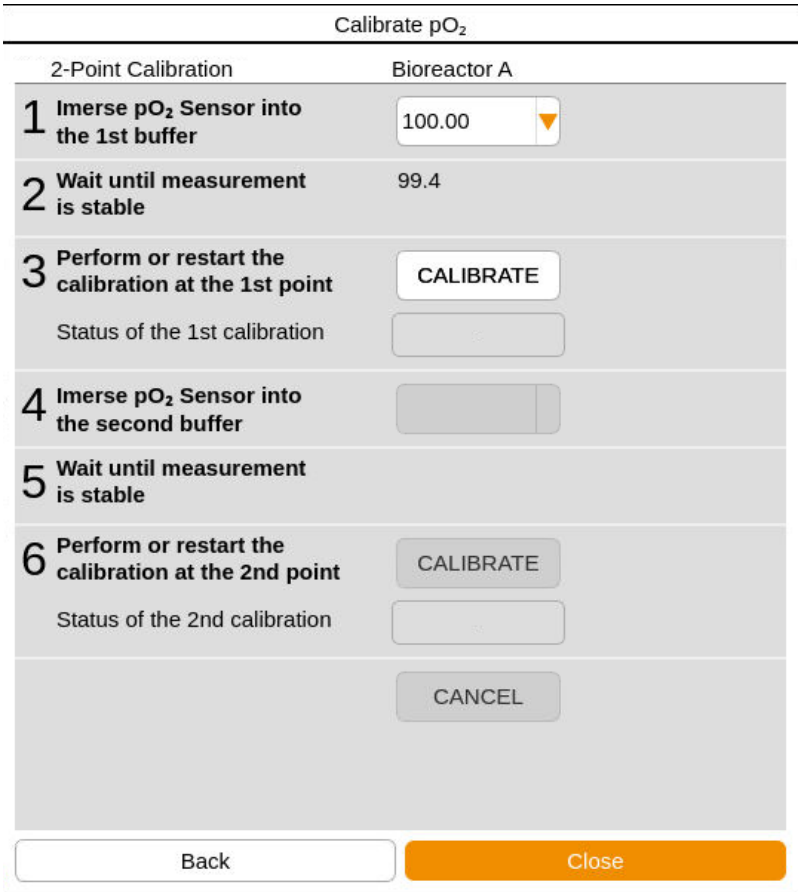
1. Call up main menu *Batch* and press **Calibrate pO_2**.
   The calibration menu appears with three options:



   - **1-Point Calibration** and **2-Point Calibration**: to select 1-point or 2-point calibration.
   - **Show Sensor Status**: shows data and values produced by the firmware of the sensor manufacturer that is integrated in the sensor. For more details see chapter “pH Sensor (Digital) Calibration”, section “Sensor Status”.

2. Select 2-point calibration.

The menu opens and leads step by step through the 2-point calibration.



- **Drop-down lists** (step 1 and 4) for selection of the 1st, respectively the 2nd reference value. If the connected sensor allows the use of different reference values or an automatic recognition of the reference value (“auto”), it can be selected. Otherwise, the reference value to be used is displayed.
- Measured value display (step 2 and 5)
- **CALIBRATE** and status display (step 3 and 6): to start the calibration procedure.

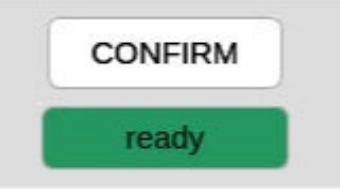
  As soon as the bar of the status display is filled up and shows *Ready*, the button changes to **CONFIRM** to save the calibration point. **CANCEL** for possible abortion of the calibration process becomes available.

Parameter Options

INFORMATION

The calibration process can be continued at any time from the last stored point if the menu has been left via **Close**. This does not apply, however, if another calibration process is started.

3. If possible, select reference value **100** (= 100 %) in drop-down list (step 1)
4. Wait until the measurement is stable (step 2).
5. Press **CALIBRATE** (step 3a).



The calibration process begins. The **CALIBRATE** button changes to **CONFIRM**.
The status display slowly turns green, indicating the ideal waiting time until a stable measured value is reached.

INFORMATION

If the measured value is assumed to be already stable, the waiting time can be skipped by pressing **CONFIRM** to continue with the second calibration point.

6. Press **CONFIRM** (step 3b).

   The calibration point is stored.

INFORMATION

If the calibration process fails, an error message is displayed with a corresponding note. Restart calibration in this case.

If the calibration is successful, the drop-down list for selection of the second reference value and the **CALIBRATE** button become available to calibrate the second point.

7. Create correct calibration conditions for 0 % calibration.

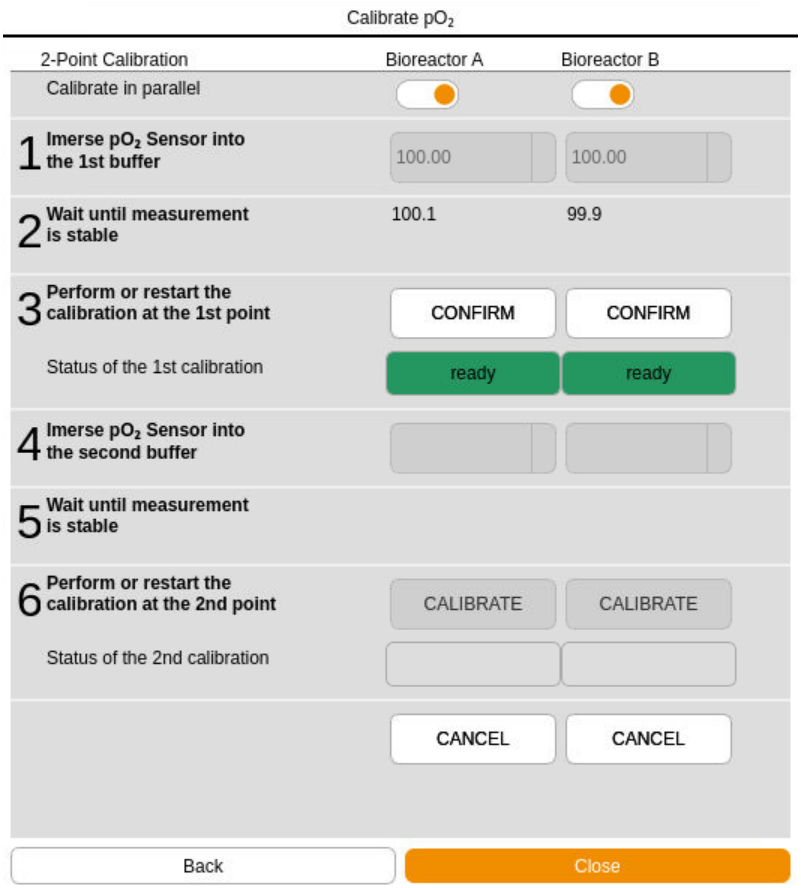
   Once achieved:
8. Proceed the same way as described from step 4 on for the second calibration point with 0 %.

   After successfully storing the 2nd calibration point via **CONFIRM** the calibration is finished and the menu can be left via **Close**.

6.2.2.2 Calibration of All (Digital) pO_2 Sensors

The procedure for calibrating all digital pO_2 sensors simultaneously remains the same as the calibration procedure for a single pO_2 sensor. The individual steps are therefore not repeated in this chapter.

The figure shows the 2-point calibration menu for bioreactor A and B. In the example shown here, both measured values of the first calibration point are stable and ready for storage via **CONFIRM**.



Calibrate in parallel: only this function is additionally available here. This defines whether the calibration steps of one, several or all pO_2 sensors should be carried out simultaneously (function ON) or individually (function OFF) one after the other

6.2.2.3 pO_2 Sensor (Analogue, Polarographic) Polarisation

Polarographic pO_2 sensors must be polarised at initial operation or after disconnection from the voltage source. Correct calibration is not possible otherwise.

For polarisation, the sensor cable must simply be connected to the pO_2 sensor and the device must be switched on at the main switch.

Duration of polarisation (= polarisation time) depends on how long the pO_2 sensor has been disconnected from the voltage source (= depolarisation time)

As a general rule: if depolarisation time > 30 minutes, the minimum polarisation time is 360 minutes.

More details about polarisation can be found in the separate documentation from the sensor manufacturer.

6.2.2.4 pO_2 Sensor (Analogue) Calibration

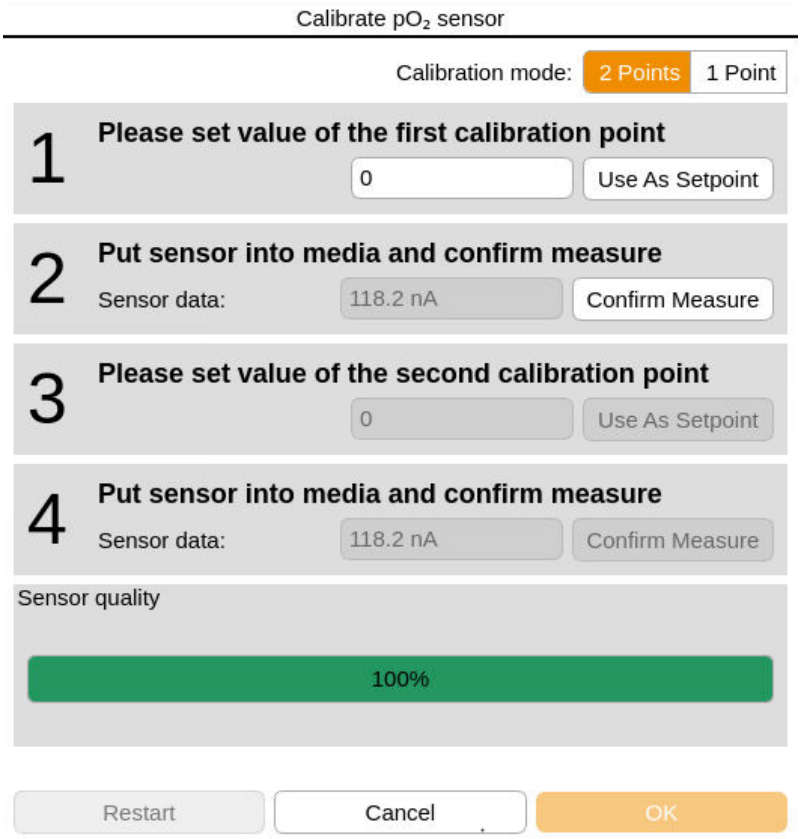
The following example describes a 2-point calibration of an analogue (amperometric/polarographic) pO_2 sensor. This must be done in the correct order. This means that the first calibration point is 0 % (zero point), the second calibration point is 100 %.

Proceed as follows, once desired calibration conditions for 0 % calibration are achieved:

Procedure

1. Call up main menu *Batch* and press **Calibrate pO_2**.

The calibration menu appears.



The 2-point calibration mode is automatically selected. The menu leads step by step (1 to 4) through the calibration.

INFORMATION

The **Use As Setpoint** button is only usable and relevant under certain circumstances, see next section “Function Use As Set-point analogue pO_2 sensors”.

2. If not preset: enter value **0** (zero = 0 %) for the first calibration point in line 1
3. Wait until the measured value (*Sensor data*, line 2) is stable.
4. Press **Confirm Measure** in line 2.

   Value is accepted as 0 % oxygen.
5. Create correct calibration conditions for 100 % calibration.

   Once achieved:
6. Enter value **100** (= 100 %) for the second calibration point in line 3.

7. Wait until the measured value (*Sensor data,* line 4) is stable.
8. Press **Confirm Measure**.

   The value is accepted as 100 % oxygen saturation.
9. Press **OK**.

   The dialogue box disappears, the calibration values are stored.

Use As Setpoint function analogue pO_2 sensors

The **Use As Setpoint** buttons in the calibration menu of the analogue pO_2 sensors can only be used by the operator under the following circumstances:

- Gasmix configuration with air/O_2/N_2 is present
- Parameter *Gasmix* is configured in a cascade for the pO_2 control.

INFORMATION

For all other parameters the Use As Setpoint button is only relevant to INFORS HT service technicians.

How it works

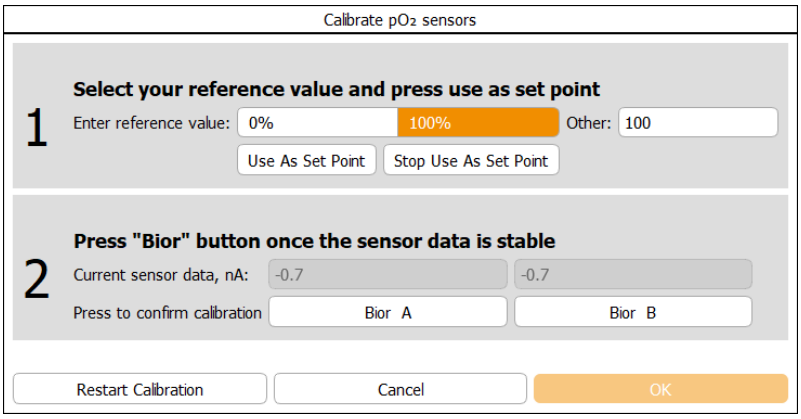
In the calibration menu of the *pO_2* parameter (METTLER sensors):

- 0 % calibration: The input ***0*** (%) in the input field of the first calibration point and pressing the **Use As Setpoint** button causes the *Gasmix* parameter to switch to nitrogen for this value.
- 100 % calibration: (2nd point), before entering the ***100*** value: The input ***21*** (%) in the input field of the second calibration point and touching the **Use As Setpoint** button causes the *Gasmix* parameter to switch to air for this value. The value can then be changed to ***100*** (%) in the input field and the calibration completed.

6.2.2.5 Calibration of All (Analogue) pO_2 Sensors

The procedure for calibrating all analogue pO_2 sensors simultaneously remains the same as the calibration procedure for a single pO_2 sensor. The individual steps are therefore not repeated in this chapter.

The calibration menu (shown below) for all analogue pO_2 sensors is slightly different from the calibration menu for a single pO_2 sensor



- There is no 2-point calibration mode available. A 2-point calibration is performed one after the other in the correct sequence (zero point before 100 %).
- The **Bior** buttons are available for confirming the measured values.

For details on the special function “Use As Setpoint”, see the section “Use As Setpoint Function Analogue pO_2 Sensors” in chapter “pO_2 Sensor (Analogue) Calibration”.

6.2.3 Turbidity Sensor Calibration

Optek turbidity sensors are pre-calibrated in the factory. Inserts are available for reference measurement.

Due to the different light absorption of different media, zero point calibration of the turbidity sensor should be performed before each cultivation process. This can be done either **before or after** sterilising, depending on the application in question.

Conditions for zero point calibration of the sensor

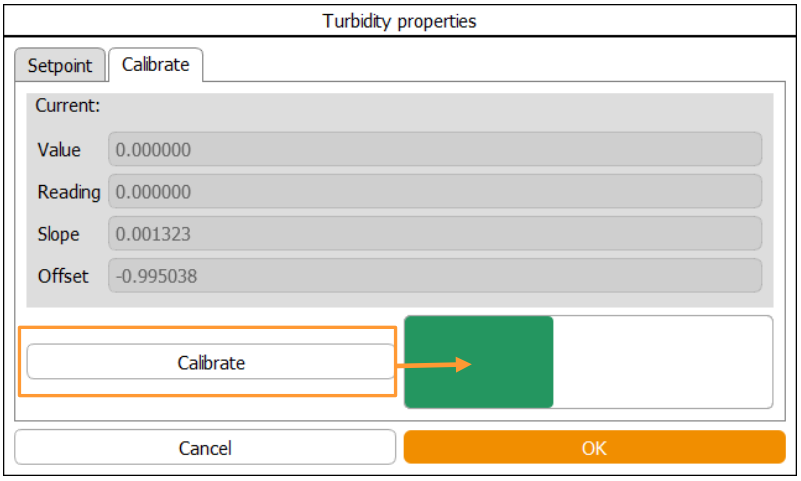
The sapphire windows of the optical density sensor must be clean and free of air or gas bubbles.

The light absorption of the medium before activation of the gassing and before inoculation can be used as a reference value for the zero point.

To calibrate the zero point of the turbidity sensor, proceed as follows:

Procedure

1. Call up the main menu *Controller* and wait until the measured value (parameter *Turbidity*) is stable
2. Call up the *Calibration* menu of the parameter and press **Calibrate.**

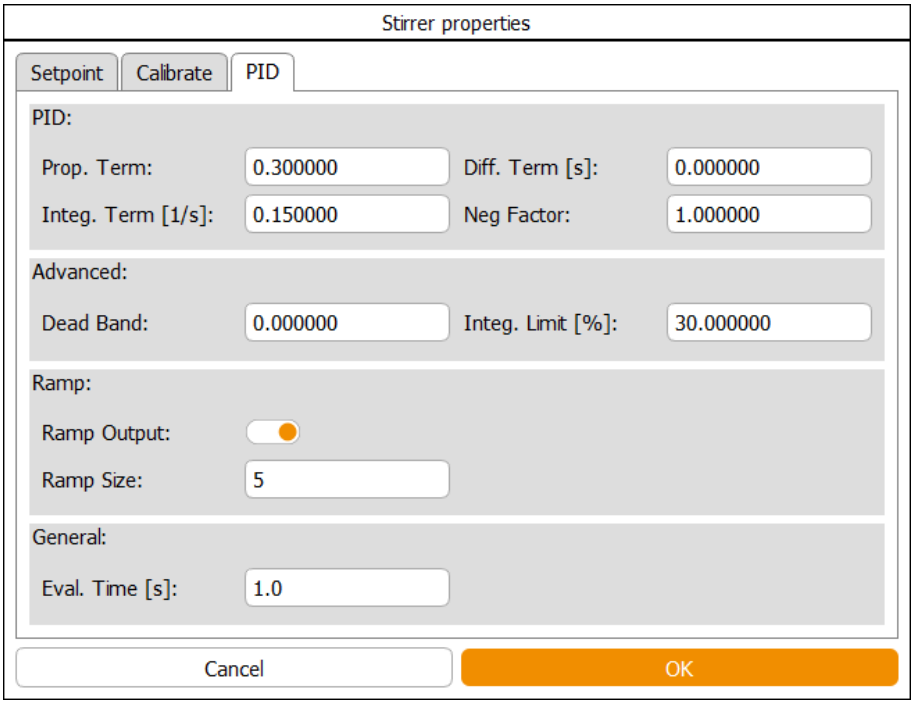


Calibration is started and a view bar appears to the right side of the **Calibrate** button which charts the course of the calibration. The progress is shown by a green colour. If the view bar disappears after a few seconds, the calibration is completed.

3. Press **OK.**

   Calibration is saved, menu disappears.

6.3 PID (Control)



The *PID* tab page is split into four horizontal areas and contains input fields for PID (Proportional Integral Derivative) control settings. The table in the following chapter explains the function of the individual setting values in more detail.

Note the following:

- If the ramp output is switched off, the value in the Ramp Size-input field is not relevant.
- In the case of parameters which are not controlled but only measured, only the value in the Eval Time (s) input field is relevant. This value is always > 0.

6.3.1 Table with Setting Values for PID Control

Setting value	Description
Prop. Term	Proportional factor: The greater the discrepancy between the set-point value and the actual value the greater the controller output.
Integ. Term [1/s]	The integral factor aggregates all errors over the time. If the setpoint is not achieved using the proportional factor, the integral factor adjusts the output successively until the setpoint value is achieved. An integral factor set too high will lead to oscillation of the control loop.
Diff Term [s]	The differential quotient calculates the change in the actual value over the time and counteracts this change to limit any overshoot.
Neg. Factor	The negative factor can be used to add weighting to two-sided control (+100 to -100 %) (e.g. heavy acid, light alkali). In the process 1 is the balance and 0.5 or 2 equate to the half or double the controller output accordingly. Example: Nitrogen influences the pO_2 value less than oxygen, thus a negative factor of 2 can compensate for the reaction of the controller.
Dead Band	If a dead band is entered, no control is implemented within this value at either side of the setpoint value (symmetrically, + / -). I.e. the controller output is = 0. The dead band is used for pH control.
Integ. Limit [%]	The integral influence is used to ensure that the integral factor cannot increase over an indefinite period. This limits erroneous accumulation. The integral influence is set between 0 and 100 % of the controller output.
Ramp output	In order to perform changes slowly or step-by-step, a ramp can be introduced. This is useful above all for the stirrer speed or a mass flow valve.
Ramp Size	Period of time during which the controller set point is gradually brought up to the newly entered set point.
Eval Time [s]	The evaluation time determines the intervals in seconds at which the PID value is recalculated. The controller speed is defined this way. A scanning time of 10 seconds is a good average value.

6.3.2 Explanations of PID Control

The PID function is based on a generic formula provided as example:

$$Error_n = \frac{Set - Act}{Max.Value - Min.Value}$$

$$Output_n = P.Term * \left\{ Error_n + I.Term \cdot \int_{i=0}^{n} Error_i + D.Term \cdot (Error_n - Error_{n-1}) \right\}$$

Explanation of the formula

- Error = deviation between setpoint value and actual value.
- P = proportional factor, proportional response to an error, used to reach a setpoint.
  The bigger the value, the sharper the control.
- I = integral factor, integration of the error in 1/second.
  A typical integral factor is < 0.05.
- D = differential quotient, derivative of the error, set in seconds (mostly to 0).

Be aware of the following relating to the individual factors:

Proportional factor

The change of the proportional factor has a considerable effect on a running process.

If the proportional factor is increased excessively, this causes oscillations in the control loop around the setpoint value.

<u>Example, the pH parameter</u>

To achieve the setpoint value, a little acid, then a little base, acid again, then base etc. is added.

If the proportional factor is reduced excessively, the controller hardly reacts to the deviations and never achieves the setpoint value.

Integral factor

The integral factor should have a low value and only be changed a little in small steps with long pauses.

The ideal approach is to switch off the device briefly after changing the integral factor in order to delete the pending error calculation.

Parameter Options

A typical integral factor is < 0.05. It should equate to the reciprocal value of double to quadruple the system's cycle duration. The higher the entered value, the less the time (in seconds) remains for control.

A higher value than 0.05 is generally of no use as it exceeds the time minimum for which the control is required. This causes fluctuations in the control circuit.

Example of calculation of the integral factor

The cycle duration of system oscillations is measured at 50 seconds from amplitude to amplitude. The integral factor is thus calculated as follows:

$1 / (50 \text{ s} \times 2) = 0.01 \text{ s}^{-1}$

$1 / (50 \text{ s} \times 4) = 0.005 \text{ s}^{-1}$

Integral factor	Seconds
0.1	10
0.05	20
0.001	100
0.005	200

Differential quotient

The differential quotient is rarely required. It is set to 0 (zero) at the beginning.

A high value is only necessary if major changes are made in quick succession. In all circumstances it causes the controller output to react stronger.

6.3.3 Changing the PID Controller Settings

When making changes to the PID controller settings proceed as follows:

Procedure

1. Make a note of the factory settings, i.e. make sure they can be restored, if necessary.
2. For readjustment of a PID controller, start with the setting for the proportional factor. Select a proportional band width as large as possible.
3. Reset the integral factor and the differential quotient to zero.
4. Increase the proportional factor until the controller causes the actual value to oscillate.
5. Measure the oscillation duration, e.g. with eve®, the bioprocess platform software from the device manufacturer.
6. Halve the proportional factor and vary the integral factor between the reciprocal value of the doubled and quadrupled oscillation duration.

7 Cascade Control

The main menu *Cascade* provides the option of setting up a cascade control of a process parameter – mostly pO_2. This means that the controller output parameter (=Output) of the master controller (e.g. pO_2) is used as a master parameter for the slave controller(s).

INFORMATION

The master controller and slave controllers are also called master and slave.

Serial cascade

A deviation of the setpoint of the parameter to be controlled (master controller) influences the setpoint of the first parameter (slave controller) in the cascade.

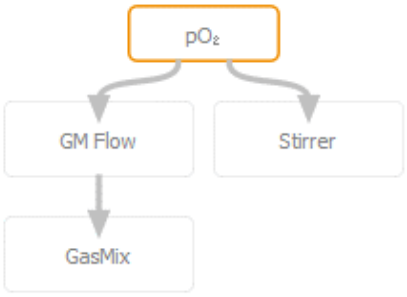
If the first parameter in the cascade reaches its maximum or minimum setpoint and the setpoint of the parameter being controlled is not yet achieved, the next parameter in the serial cascade is activated and so it continues.

In the example of the left-hand figure:
The parameter *Stirrer,* the 1st slave controller, is activated first in the cascade, to control the *pO_2* parameter, the master controller.
The parameter *AirFlow,* the 2nd slave controller, is only activated when the setpoint of parameter *pO_2* has not been achieved by the *Stirrer* parameter.

Parallel cascade

A deviation of the setpoint of the parameter to be controlled (master controller) influences the setpoint of all parameters (slave controllers) that are in the cascade.

In the example of the left-hand figure:
The parameters *Stirrer* and *Air Flow*, both slave controllers, are activated at the same time to control the *pO_2* parameter, the master controller.



Parallel serial cascade

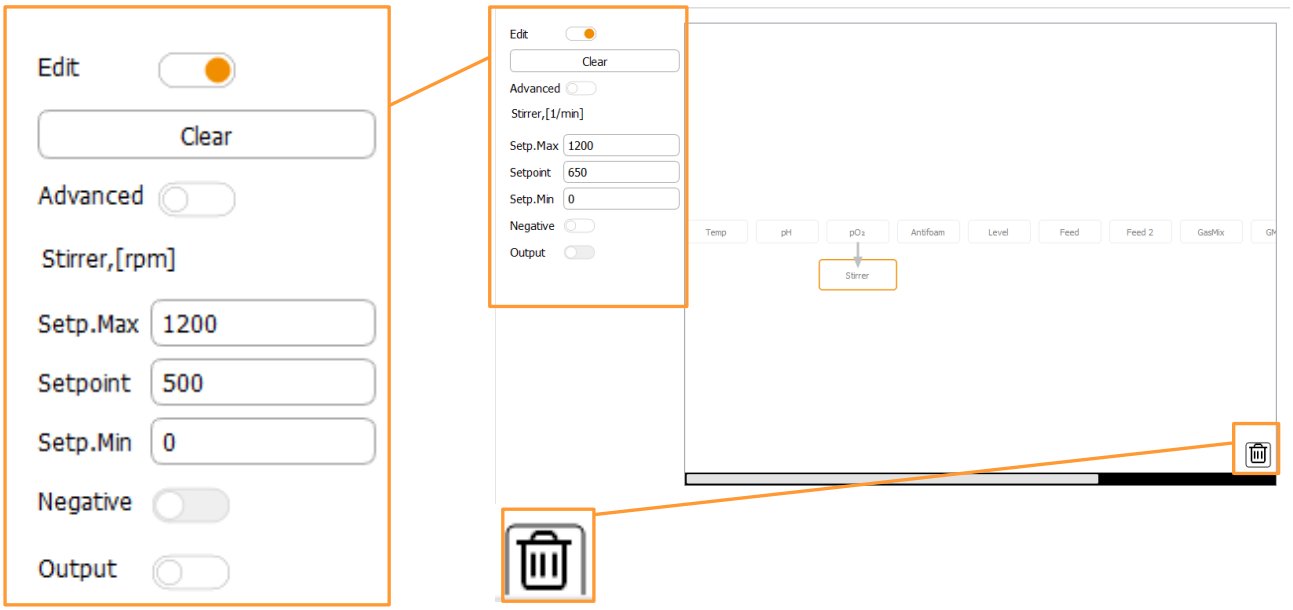
A deviation of the setpoint of the parameter to be controlled (master controller) influences the setpoint of all parameters (slave controllers) that are parallel and the first element in the cascade.

If the parameters that are connected in parallel reach their maximum or minimum setpoint and the setpoint of the parameter being controlled is not yet achieved, the next parameter(s) in the cascade is/are activated.

In the example of the left-hand figure:
The parameters *Stirrer* and *Air Flow* (master controller) are activated at the same time to control the pO_2 parameter.
The parameter *GasMix* (slave controller) is only activated when the setpoint of parameter pO_2 has not been achieved by the *Stirrer* and *AirFlow* parameters.

7.1 Setting a Cascade

The different cascade settings are made in the left-hand side of the main menu *Cascade*. The process parameters can be merged to a cascade in the main area of the menu using drag & drop.



Cascade elements (parameters) can be removed and dropped off in the recycle bin using drag&drop.

- *Edit*: to switch on/off the edit function of the cascade.

  Switching off this function will also deactivate the display of the present process parameters in the main area of the menu.

  Once the edit function is switched on, all parameters can be merged to one or even several cascades using drag&drop.

  Each parameter can only be used once and in one cascade only.
- **Clear**: to call up warning dialogue and delete cascade after confirmation.
- *Advanced*: to switch on/off the setting mode for advanced cascade.

INFORMATION

Advanced cascades are used for customised device configurations. They are only set from the device manufacturer at the factory. Their settings and possible adjustments are device-specific saved at the factory. If required, they may be obtained upon request from the manufacturer.

- Parameter name, (e.g. *Stirrer*): selected parameter with unit.

  The selected parameter visually stands out from the other parameters in the main screen area. The input fields for min./ max. and setpoint values are visible and enabled at the same time to the left-hand side.
- *Setp. Max*. und *Setp. Min*.: factory settings for min. and max. setpoint values which define the adjustable value range of the selected parameter in which the cascade can change the setpoint of the cascaded parameter to control the setpoint of the master controller. These values are adjustable within this predefined value range.
- *Setpoint*: setpoint of the parameter.
  - Master controller: the setpoint to be controlled.
  - Slave controller: the starting setpoint of the parameter from which the setpoint of the parameter of the cascade can be varied within the value range of *Setp. Min. up to Setp. Max.*

INFORMATION

In most cases, it is recommended to set the setpoint for the slave controller to the lower end of the value range (Setp. Min.)

- *Negative*: to switch on/off the negative function of a cascade. Can be used for slave controller, if an increase of the setpoint

of the slave controller leads to a decrease of the current value of the slave controller.

- *Output*: to switch on/off the cascade and all used parameters in the cascade hereby.

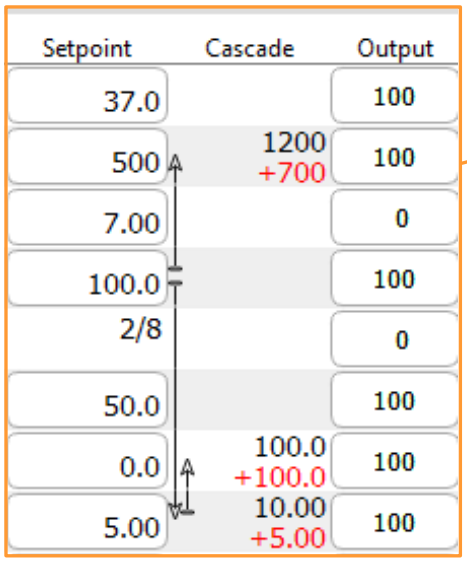
  Each parameter in the cascade must be switched on (*Output ON*) for the cascade to function.

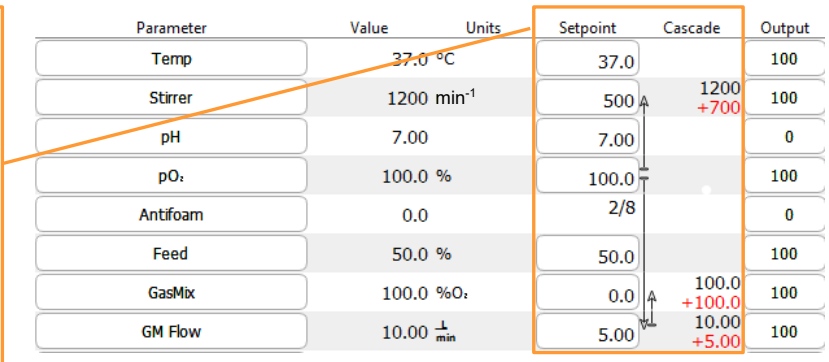
  The parameters can also be switched on and off in the *Controller* main menu.

  If a parameter is switched off (*Output OFF*), all of the following parameters are uncoupled from the cascade.

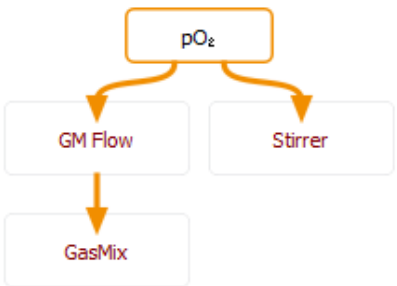
Cascade progress display

A cascade and its progress can be seen in the *Controller* main menu.





In addition to arrows showing the direction of the cascade control, the setpoint and the control output of the cascade that is added to or subtracted from the setpoint is displayed in the *Cascade* column. These values are given in the relevant parameter unit.



The colour of the added/subtracted setpoint in the *Controller* menu and the name of the parameter in the *Cascade* menu indicates the progress of the cascade and the remaining scope of the cascade within the value range of a slave controller to control the master controller according to the following scheme:

Colour	Utilisation of value range
Grey	Inactive
Green	0 – 90 %
Yellow	90 – 99 %
Red	100 %
Blue	0 %

Example of calculation

Stirrer, e.g. for slave controller from setpoint to max. setpoint.

- Setpoint: 500
- Setpoint max. 1200
- Value range: 1200 – 500 = 700

700 = 100 % / 630 = 90 %

500 + 630 = 1130 = setpoint, from which 90 % of the value range are reached.

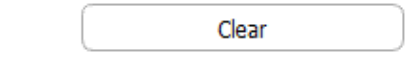
This means for the display according the colour scheme mentioned:

- Green: up to 1130
- Yellow: up to 1193
- Red: at 1200

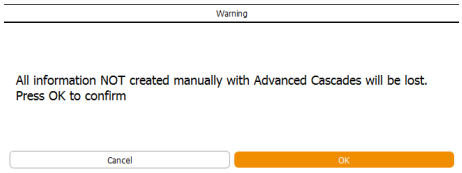
7.2 Deleting a Cascade

To delete all settings of a cascade (does not apply to advanced cascade), proceed as follows:

Procedure



1. In main menu *Cascade*, press **Clear**.



A dialogue box appears with the warning that all entries that have NOT been made in advanced cascade mode will be deleted.

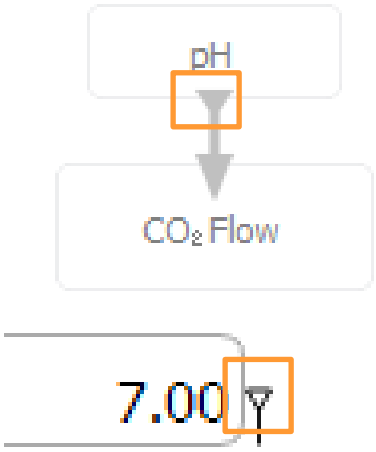
2. Press **OK**.

Cascade is deleted.

7.3 Negative Function of a Cascade

The *Negative* function causes a change in sign of the controller output. This means, a negative controller output causes the addition of a positive value for the set point of the cascaded parameter and vice versa.

The pH control with base and CO_2 instead of acid is a classic example of this: to reduce the pH, the CO_2 flow rate (*CO_2 Flow* parameter) needs to increase.



The fact that the *Negative* function has been switched on is illustrated by the triangle symbol on the arrow that indicates the direction of the cascade control.

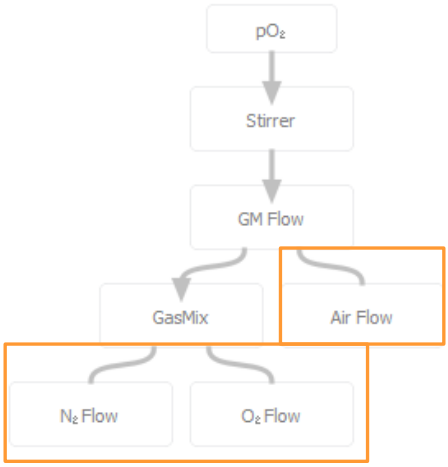
This arrow shape can be seen both in the *Cascade* menu as well as in the *Controller* menu.

7.4 Special Configurations

For bioreactors with gassing strategy “High End” (configuration with several mass flow controllers for flow control and gas mix) the gases to be used e.g. *Air Flow*, *N_2 Flow* and *O_2 Flow*, must be assigned to both parameters that control the gas mixture, i.e. parameters *GasMix* and *GM Flow*, in the cascade configuration.

For this purpose, setup the following cascades additionally to the desired cascade configuration, if the appropriate parameters are present:

- Parameter *Air Flow* as slave controller to parameter *GM Flow*
- Parameter *O_2 Flow* as slave controller to parameter *GasMix*
- Parameter *N_2 Flow* as slave controller parameter *GasMix*



If parameters *O_2 Flow* and *N_2 Flow* are present, then they are setup as a parallel cascade below parameter *GasMix*.

To make a distinction between the allocation of these parameters and regular cascade elements, the connections are shown without arrow.

8 Pumps and Settings

The pumps are controlled in accordance with the corresponding parameters:

Standard

- *Acid* pump (digital): in accordance with the *pH* parameter
- *Base* pump (digital): in accordance with the *pH* parameter
- *Antifoam* pump (digital): in accordance with the *Antifoam* parameter
- *Feed* pump (analogue): in accordance with the *Feed* parameter

Optional

- *Feed 2* and *Feed 3* pumps (analogue): in accordance with the *Feed 2* and *Feed 3* parameters.

Digital pumps have a set speed and are time controlled. I.e., they always run at the same speed in start/stop mode. The pump speed of analogue pumps is adjustable and can be set in steps of 0.1 % within a range of 0 % to 100 %. Both digital and analogue pumps are controlled within a range of 0 % to 100 %.

Example

- Analogue: 50 % of the maximum feed rate = pump runs at half speed.
- Digital: 50 % of the maximum feed rate = pump runs during half the time

The following pump settings are possible:

- Setting the pump speed for feed pump(s) and dosing/waiting time for the antifoam pump
- Calibrating the pumps
- Resetting the delivery rate manually to zero
- Filling or emptying the pump hoses manually or time controlled.

INFORMATION

This function is only present for the four integrated standard pumps.

For details on how to change the settings for the feed pump(s) and the antifoam pump refer to the appropriate chapters in chapter “Parameters”. Calibration, pump counter and filling/emptying of the pump hoses is described in detail in the following chapters.

8.1 Calibrating a Pump

Calibrating a pump makes it possible to display and record the actual delivered volume. The delivery rate is indicated in millilitres.

Note the following points:

- Always use hoses of the same kind with the same dimensions for calibration and pumping media.
- Pump calibration must be executed before sterilisation in the autoclave.

Aid

- Graduated measuring cylinder/jug or scale/balance and an empty vessel
- Reagent bottle equipped with silicone hose, filled with the reagent to be delivered, the nutrient solution or a liquid which has the same viscosity

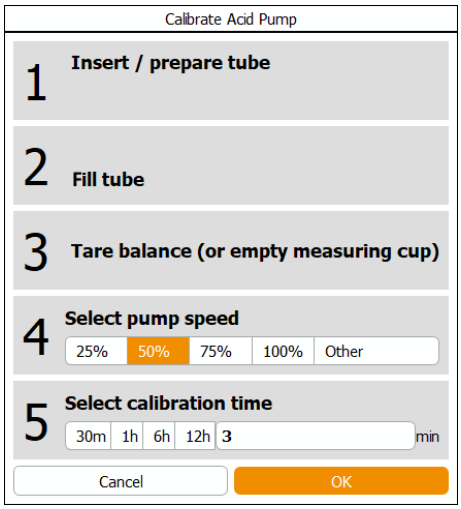
INFORMATION

To obtain precise results, the reagent bottle should be put on a scale which is linked to the bioreactor or to the bioprocess platform software eve® installed on a PC or laptop.

In order to calibrate a pump, e.g. the acid pump of bioreactor A, proceed as follows:

Procedure

1. Connect the reagent bottle to the pump.
2. Place the output end of the hose in a measuring cylinder/jug. Or: Place the reagent bottle on a scale and tare to zero, place the output end of the hose in an empty vessel
3. Completely fill the hose.
4. Select bioreactor A from the selection bar.
5. Call up the main menu *Batch* and press **Calibrate Acid**.



The *Calibrate Acid Pump* dialogue box appears and leads step by step through the calibration.

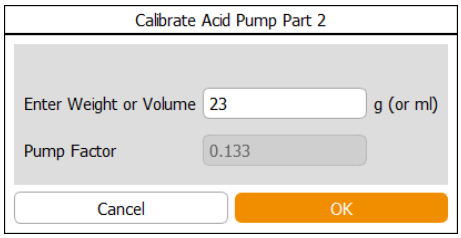
6. At step 4, select the pump speed in percent or enter another value in % after pressing **Other**.

> **INFORMATION**
>
> To obtain most accurate results, the pump should be calibrated at the same speed as it is to be expected to run during cultivation.

7. At step 5, select calibration duration or enter it manually.
8. Press **OK**.

Calibration is started.

The remaining time in h/min/s is shown next to the **Stop**-button.



Once the time has elapsed, the dialogue box with part 2 appears.

9. Enter the delivered liquid in mL or g.

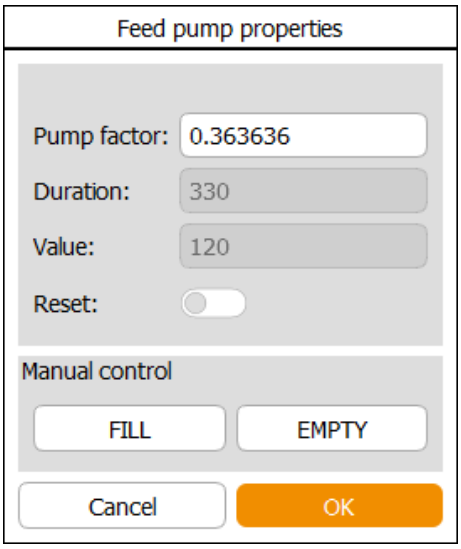
   After entering the pumped quantity, the automatically calculated pump factor is displayed.
   The pump factor is always ≠ 1 with a calibrated pump.
10. Press **OK**.

The dialogue box disappears; the calibration value is saved.

Completed at with date and time next to the **Stop** button indicates that and when the pump was calibrated.

8.2 Resetting the Pump Counter to Zero

The number of pump revolutions and the delivered quantity (in mL) of calibrated pumps are displayed constantly during a running cultivation process. The display remains in place after completion of the process (when the bioreactor is stopped) until a new cultivation process is started again (when the bioreactor is started). The counter can also be reset to zero manually, proceed as follows:



Pressing one of the pump buttons in the main menu *Main* of the selected bioreactor opens the pump properties dialogue box, e.g. of the Feed pump, as shown to the left.
The displayed number of pump revolutions (*Duration*) and the delivered quantity in mL (*Value*) can be reset using the Reset-switch.

INFORMATION

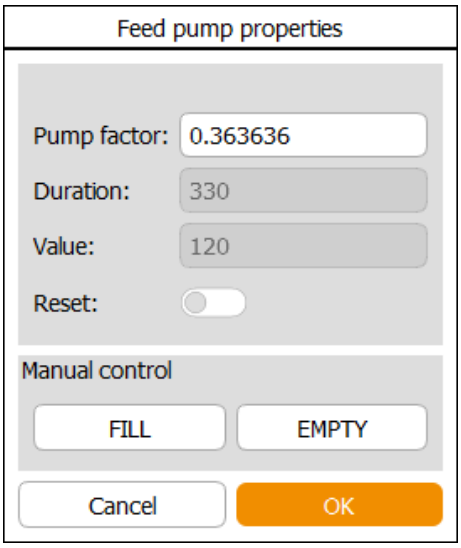
Manual change of the pump factor leads to rejection of the previous calibration value. The pump factor is always ≠ 1 with a calibrated pump.

For details about FILL and EMPTY see chapter “Filling and Emptying the Pump Hoses”

8.3 Filling and Emptying Pump Hoses

The pump hoses of the standard pumps can be filled and emptied manually individually or all at the same time, time controlled. Both functions are only available when all bioreactors are stopped.

Manual filling and emptying



Pressing one of the pump buttons in the main menu *Main* of the selected bioreactor opens the pump dialogue box with the **FILL** and **EMPTY** buttons for filling and emptying. The pump runs as long as the corresponding button is pressed.
The picture on the left shows the pump dialogue box of the feed pump

Time controlled filling and emptying

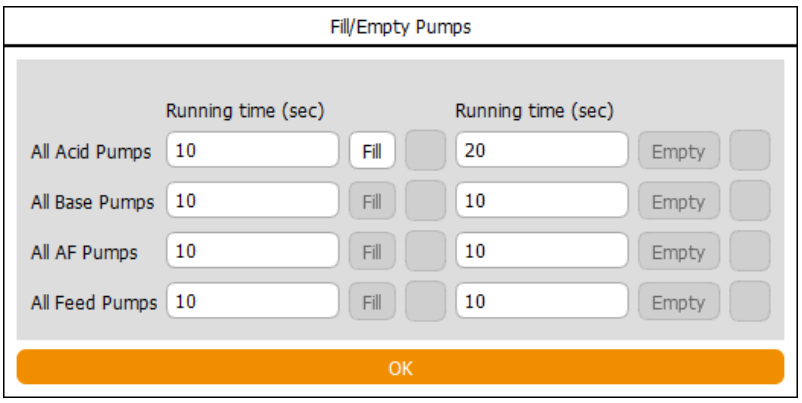
If all (*All*) bioreactors are selected, **Fill/Empty Pumps** in main menu *Batch* allows automatic, time-controlled filling or emptying of the pump hoses of all standard pumps.

INFORMATION

If only one bioreactor is available, the function is also possible by selecting the bioreactor in the selection bar.

Fill/Empty Pumps in main menu *Batch* allows the automatic filling or emptying of the pump hoses of the standard pumps when the bioreactor is in idle state.

The figure below shows the *Fill/Empty Pumps* dialogue box.



The pumps are grouped by function, thus, for example, all acid pump hoses are filled or emptied simultaneously without affecting the base pumps etc. For each pump group, an individual filling/emptying duration in seconds can be defined. The filling or emptying procedure is started via **Fill** and **Empty**. Stop buttons are provided next to each of these buttons for immediately stopping the filling or emptying process.

INFORMATION

If a filling or emptying procedure is active, the remaining filling or emptying duration is displayed. The menu cannot be closed while at least one filling or emptying procedure is active.

Note the following:

- The pump duration of a pump should preferably be tested with the liquid which has the same or similar viscosity as the liquid to be pumped.
- Observe hose lengths and hose sizes of the pumps/pump groups and, if necessary, test the pump duration of each pump/pump group considering the same conditions mentioned above.

9 Starting and Stopping the Bioreactor(s)

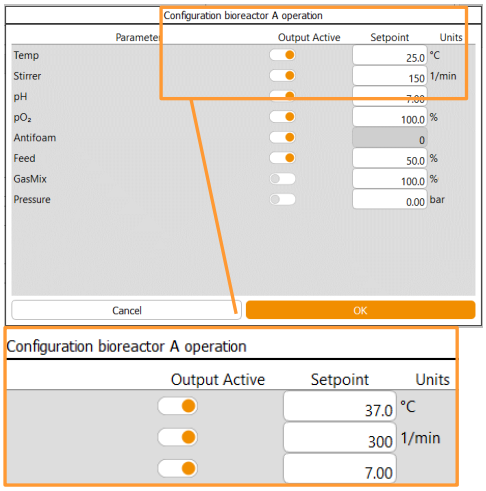
9.1 Starting the Bioreactor(s)

To start one bioreactor (= 1 culture vessel) or all available bioreactors, proceed as follows:

Procedure

1. Select the desired bioreactor, e.g. bioreactor *A* (icon to the left) left) or *All* bioreactors (icon to the right) from the selection bar.

2. In main menu *Batch*, press **Start** or **Start All**.



The configuration dialogue box of the selected bioreactor (picture to the left) or of all bioreactors appears containing more or less controlled parameters, depending on the device configuration.
Setpoint settings of the previous cultivation are visible here.

INFORMATION

The bioreactor(s) is/are started witht the settings in the configuration dialogue box. Changes to these settings are saved and transferred to the next configuration dialogue box. If setpoint values are changed or parameters are switched on/off whilst the bioreactor(s) is/are running, these settings are only adopted for the current cultivation process.

3. Make settings as necessary and press **OK**.

   The bioreactor(s) (cultivations) is/are started. That and how long the process is running is indicated by *in progress since* with running time in h/min/s in main menu *Batch* of each running bioreactor.

- Current values and controller outputs for the parameters are visible in the main menu *Controller*.
- A recording of the current values and a diagram are visible in the main menu *Trends*.

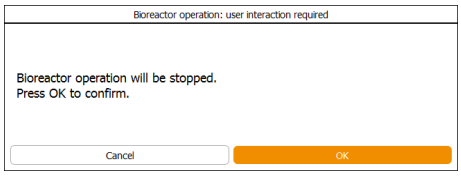
9.2 Stopping the Bioreactor(s)

To stop one running bioreactor (= 1 culture vessel) or all bioreactors, proceed as follows:

Procedure

1. Select the desired bioreactor, e.g. bioreactor *A* (icon to the left) left) or *All* bioreactors (icon to the right) from the selection bar.

2. In main menu *Batch,* press **Stop** or **Stop All**.



A dialogue box for user interaction appears with the instruction to confirm the bioreactor stop (e.g. for one bioreactor, picture to the left).

3. Press **OK**.

The bioreactor(s) is/are stopped. *Stopped after* with display of d/h/min/s below **Start** in main menu *Batch* of each stopped bioreactor indicates after how much running time the bioreactor was stopped.

4. If necessary, shut down the system via **Shutdown** in main menu *System* and switch off the device(s) at the power switch (see separate operating manual for the device).