New Brunswick
an eppendorf company

New Brunswick Single-Use Bioreactor CelliGen® BLU

Operating manual

M1374-0050

Revision B

eppendorf

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Revision B
M1374-0050

Table of contents

1 Operating instructions

1.1 Using this manual

- Carefully read this operating manual before using the device for the first time.
- Also observe the operating manual enclosed with the accessories.
- The operating manual should be considered as part of the product and stored in a location that is easily accessible.
- When passing the device on to third parties, be sure to include this operating manual.
- If this manual is lost, please request another one. The current version can be found on our website http://www.nbsc.com.

1.2 Danger symbols and danger levels

1.2.1 Hazard symbols

	**Hazard point**		**Burns**
	**Electric shock**		**Material damage**
	**Explosion**		**Heavy loads**
	**Inhalation**		

1.2.2 Degrees of danger

The following degree levels are used in safety messages throughout this manual. Acquaint yourself with each item and the potential risk if you disregard the safety message.

DANGER	*Will* lead to severe injuries or death.
WARNING	*May* lead to severe injuries or death.
CAUTION	May lead to light to moderate injuries.
NOTICE	May lead to material damage.

1.3 Symbols used

Example	Meaning
▸	You are requested to perform an action.
1. 2.	Perform these actions in the sequence described.
•	List.
	References useful information.

2 Safety

2.1 Intended use

CelliGen® BLU is a versatile benchtop bioreactor that provides a fully equipped system in one compact package, with its Reactor Process Control (RPC) software in cell culture mode and a 15-inch color touchscreen monitor as the user interface. It can be employed for batch, fed batch, or continuous culture with control of 3- or 4-gas mixing, pH, dissolved oxygen (DO), agitation, temperature, pump feed, volume, and additional analog/digital inputs and outputs.

2.2 Warnings for intended use

Before using the fermentor or bioreactor, read the operating manual and observe the following general safety instructions:

2.2.1 Personal injury and damage to device

WARNING!

Risk of explosion!

- Use gases in this equipment only within the range between their lower explosion limit (LEL) and their upper explosion limit (UEL).
- If your process requires or produces gases, be sure to verify their LEL and UEL concentration range (available online or ask your gas supplier).

CAUTION!

Risk of damage to personnel and/or equipment!

- This equipment must be operated as described in this manual.
- Please read the entire Operating Manual before attempting to use this equipment. If operational guidelines are not followed, equipment damage and personal injury can occur.
- Do not use this equipment in a hazardous atmosphere or with hazardous materials for which the equipment was not designed.

3 Product description

3.1 System

CelliGen® BLU is a versatile benchtop bioreactor that provides a fully equipped system in one compact package, with its Reactor Process Control (RPC) software in cell culture mode and a 15-inch color touchscreen monitor as the user interface. It can be employed for batch, fed batch, or continuous culture with control of 3- or 4-gas mixing, pH, dissolved oxygen (DO), agitation, temperature, pump feed, volume, and additional analog/digital inputs and outputs.

3.2 Vessels

The CelliGen BLU cell culture vessels are single-use stirred tank bioreactors designed for the growth of mammalian cells, insect cultures, and many other cultures.

Each 5.0- , 14.0- or 50.0-liter preassembled vessel consists of a vessel body, headplate, pitched blade impeller with shaft or packed-bed impeller (5.0L vessel only), and a retaining ring which supports all the internal tubing. Ports are provided in the headplate for the following purposes: addition (3 ports); a thermowell for a resistance temperature detector (RTD); a sparger; an overlay; a harvest tube; a sampler; an exhaust tube; and dissolved oxygen (DO) and pH sensors. There is also a threaded PG 13.5 port, which can be used to insert 12 mm probes; this port comes plugged. All ports and tubing come pre-installed in the vessel. The magnetic drive coupling is also located on the headplate.

Each vessel comes pre-sterilized with all tubing and filters already attached. The tubing used for addition, sampling and harvesting lines can be safely welded in a tube welder.

3.3 Agitation system

A non-disposable, removable agitation motor located on top of the bearing housing on the headplate is connected to the agitation shaft with a magnetic coupling. The magnetic coupling on the headplate has a notch to ensure correct and easy orientation as the motor is installed.

The motor can provide a speed range from 25 to 200 rpm for the 5 L and 14 L vessels and from 25 to 150 rpm for the 50 L vessel. The process control software ensures agitation speed accuracy throughout the speed range.

Default P&I (proportional and integral) values are preset at the factory. We strongly recommend that you maintain the factory-set parameters.

NOTICE!

Risk of equipment damage!

- Agitation speed limits are defined by the software. We highly recommend that you do not try to bypass those limits.

3.4 Temperature control

The culture temperature setpoint is controlled within the range of 5 °C above ambient temperature to 40 °C by the process control software. The media temperature is sensed by a Pt100 Resistance Temperature Detector (RTD) submerged in the thermowell. Temperature will be maintained or adjusted by ambient cooling and heating through the use of a silicone heat blanket.

Default P&I (proportional and integral) values are preset at the factory. We strongly recommend that you maintain the factory-set parameters.

3.5 Aeration

Aeration is controlled by inputting values through the touchscreen on the control cabinet. Gas can be introduced by means of microsparger or macrosparger and/or overlay port.

Up to four gases, including air, nitrogen, carbon dioxide and oxygen, can be introduced into the media or headspace. The flow rates for both the sparge and the overlay are controlled automatically by thermal mass flow controllers. The TMFCs are regulated automatically according to demand within the system or manually by the user entering values into the touchscreen.

Generally, air and oxygen are used for DO control and carbon dioxide is used to help maintain pH. Nitrogen can also be used as a means of lowering DO.

NOTICE!

Risk of equipment damage by overpressurization!

- Check all user-entered setpoints for gas flow: maximum combined gas flow for both the sparge and overlay must not exceed 7.5 SLPM.

- For further information on cascading and gas mixing, (see *Cascade control on p. 55)* and (see *Gas mixing for PH and DO control on p. 58)*.

Default P&I (proportional and integral) values are preset at the factory. We strongly recommend that you maintain the factory-set parameters.

3.6 Pumps

Three fixed speed peristaltic pumps are provided as standard on the right front of the control cabinet. All three pumps rotate counter-clockwise and their design facilitates very easy loading (see *Load pump tubing on p. 69)*. Pump 1 is set to 14 rpm and Pumps 2 and 3 are set to 109 rpm.

- For more information on selecting setpoints, calibrating flow rates and selecting pulse periods, (see *About pumps on p. 69)*.
- For information about optional stacked pumps, (see *Appendix A: Stackable pumps on p. 106)*.

3.7 pH control

pH can be measured using either a non-invasive pH probe with optical sensor or a gel-filled probe. When using the pH probe with optical sensor, pH is controlled in the range of 6.00 - 8.00. Control is maintained by a P&I (proportional and integral) controller which operates peristaltic pumps, assigned to add base or to use of gas(es) for this purpose. The user can also select a deadband value to control pH within the user-assigned range: no base (or gas) will be added when the pH value falls within the deadband tolerance above or below the setpoint.

NOTICE!

Risk of damage to pH sensor!

- Do not expose the pH sensor within the vessel to direct light or to any liquid with less than 100 mM ionic strength, as these may adversely affect the performance of the sensor.

If you elect to insert a gel-filled pH probe using the threaded sensor port, pH can be controlled within the range of 2.0 - 12.0.

If you are using a gel-filled pH probe, it must be sterilized prior to use and inserted under a hood or by using other sterile methods.

Cell culture pH control is typically done by the addition of base by means of a peristaltic pump or by sparging in CO_2 to lower the pH.

Default P&I (proportional and integral) values are preset at the factory. We strongly recommend that you maintain the factory-set parameters.

3.8 DO control

DO is controlled and measured in the range of 0 - 200% by means of a non-invasive, non-disposable polarographic DO probe. It is sensed by the DO electrode and control is maintained by the P&I controller by adjusting the gas mixture that is injected into the vessel.

Default P&I (proportional and integral) values are preset at the factory. We strongly recommend that you maintain the factory-set parameters.

3.9 Exhaust system

The exhaust gases pass into the exhaust tube where the gases are heated up by the exhaust heat blanket; any moisture present there is raised above the dewpoint and can easily pass through the filter. The remaining air passes through the 0.2 µm exhaust filter.

CAUTION!

Risk of explosion!

- NEVER block the exhaust to pressurize the vessel (see *Vessel assembly on p. 18)*.

Pressing the Exhaust Heater button at the top right of the control screens will turn the exhaust heater on or off.

The exhaust heater should always be on when gas is flowing into the vessel.

3.10 Sampling system

This system consists of a needle-free connector attached to a sampling tube that extends to the lower portion of the vessel. Both the needle-free connector and the syringe use Luer-style connections. Samples can be taken by aseptically attaching a needle-free syringe to the connector and drawing a sample (see *Sampling the vessel on p. 95)*.

3.11 Overlay system

The overlay system allows gas to be inserted directly into the headspace of the vessel through a port located on the headplate. Overlays can be selected as manual flow with a Rotameter or as automatic flow via thermal mass flow controller (TMFC). Like the sparge system, the overlay gas mixture can be composed of up to four gases and its composition can be controlled automatically or manually (see *Gas overlay mixing on p. 60)*.

3.12 Scale (optional)

An optional load cell scale can be added to your system, to display the weight (volume) of your culture vessel or feed vessel. Cascades and feeds can be set up to pump in or pump out liquid automatically based on the scale's process loop information.

3.13 Bag hanger

A bag hanger is provided so that disposable addition, harvest and/or sample bags can easily be suspended for use in your process. The hanger has three hooks which allow you to hang up to three bags at the right side of the controller (see *Install the bag hanger on p. 28)*.

3.14 Recommended accessories and supplies

Before you begin to assemble your CelliGen BLU, it would be prudent to verify that you have all of the following accessories and supplies readily at hand:

- Rubber gloves
- Flexible tubing
- Plastic tubing connectors
- A tie gun
- Needle-free syringes
- Media
- Antifoam agent
- Addition bottles

A user's kit is available from New Brunswick with many of the commonly required items (including a selection of tubing, clamps, and connectors). Speak to your sales representative for more information.

3.15 Supervisory software

In addition to the built-in Reactor Process Control (RPC) software that you interface with through the touchscreen, your CelliGen BLU system can be remotely controlled from a PC via New Brunswick's BioCommand® optional Modbus supervisory software. Consult your New Brunswick representative for details.

4 Installation

4.1 Physical location

NOTICE!

Possible risk of contamination!

- Do not open your pre-sterilized vessel package until you are ready to use it.

- Place the CelliGen BLU bioreactor on a smooth, level and sturdy surface where utilities are readily available.
- For weights and dimensions, (see *Specifications on p. 99)*.
- Ensure that the surface can bear the weight of the bioreactor plus vessel contents and any applicable ancilliary equipment.
- Also ensure that there is enough space around the back and the front of the CelliGen BLU for proper operation and access.
- Allow at least 4 inches of clearance behind the cabinet for heat dissipation.

4.2 Environment

The CelliGen BLU bioreactor operates properly under the following conditions:

- Ambient temperature range 15°C to 30°C
- Relative humidity up to 80% non-condensing

4.3 Install the control cabinet

- Level the horizontal surface of the control cabinet base with four leveling glides if necessary.
- Connect the mains/power cord to the rear of the control cabinet. At a later time, once the system is completely assembled and all connections have been made, you will plug the mains/power cord into a suitable mains/electrical outlet.

4.4 Install the touchscreen

NOTICE!

Risk of damage to equipment!

- Before making electrical connections, verify that the mains/power supply voltage matches the voltage and the electrical requirements marked on the electrical specification plate (located on the rear panel of the cabinet) and on the control schematics supplied with the system.

- Align the monitor with the mounting rack on the cabinet, and use the four screws provided with the monitor to securely fasten it to the rack. For location (see Fig. 1 on p. 14) and for installation (see Fig. 2 on p. 15). The mounting rack swivels for easy access.

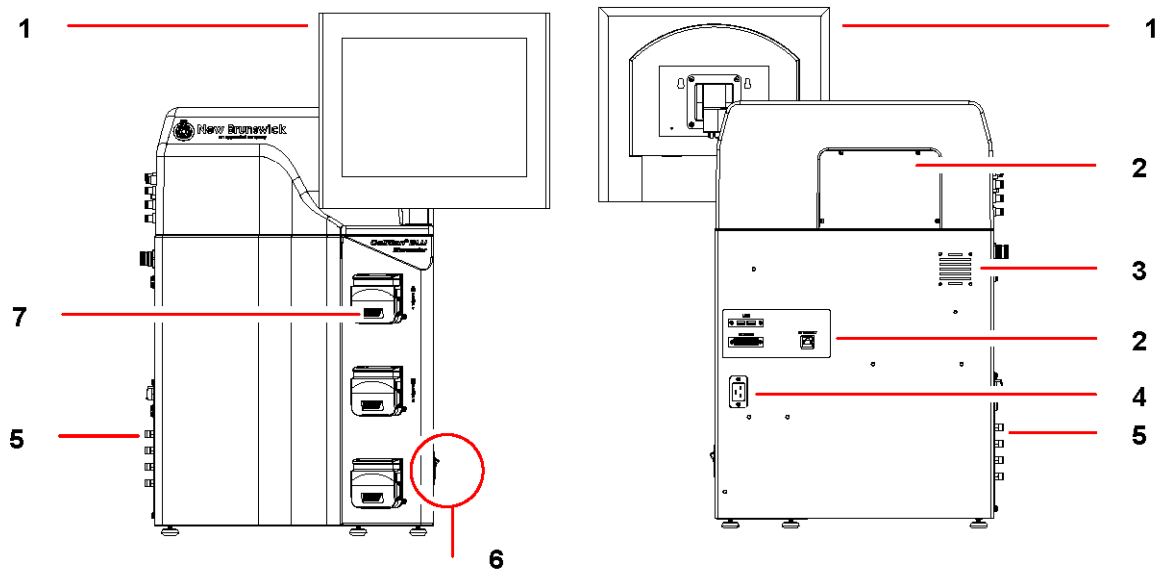

Fig. 1: Front and Rear Views of Control Cabinet

1 Touchscreen	**2 Auxiliary connections**
3 Heat vent	**4 Mains/Power cord connection**
5 Service connections	**6 Mains/Power switch (ON/OFF)**
7 Pumps	

- connect the cabinet's mains/power cord plug
- connect the com port connector

- Connect the VGA monitor connector to the bottom of the touchscreen monitor

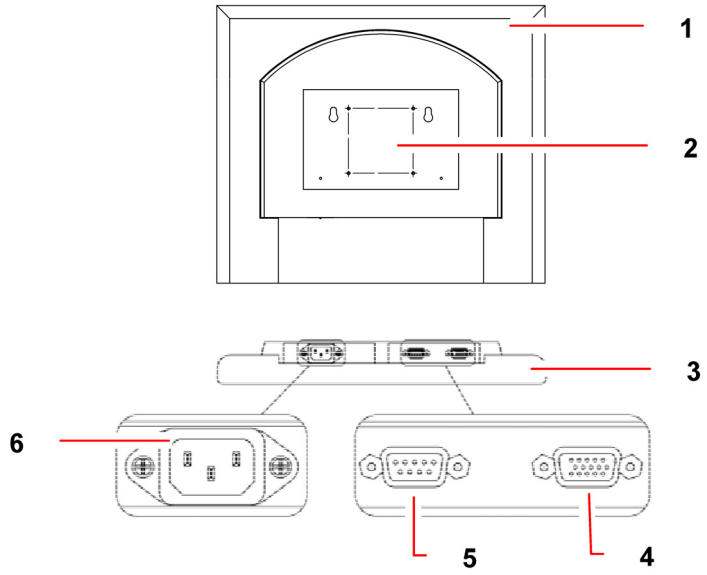

Fig. 2: Touchscreen-to-Control Cabinet Connections

1 Touchscreen (rear view)	**2 Attach the monitor to the control cabinet mounting rack with the 4 screws provided, using these 4 holes.**
3 Touchscreen (bottom view)	**4 VGA monitor connector**
5 COM port connector	**6 Mains/Power cord plug**

4.5 Utilities

CAUTION!

Risk of explosion!

- Use gases in this equipment only within the range between their lower explosion limit (LEL) and their upper explosion limit (UEL).
- If your process requires or produces gases, be sure to verify their LEL and UEL concentration range (available online or ask your gas supplier).

CAUTION!

Risk of explosion! Risk of equipment damage!

- No gas pressure should rise above 6 PSIG.
- Do not use this equipment in a hazardous atmosphere or with hazardous materials for which the equipment was not designed.
- All gases supplied should be medical grade.

The control cabinet assembly must be properly connected to gases and mains/electrical power. All gas connections are located on the lefthand side of the cabinet (see Fig. 3 on p. 16). The mains/power connection is located on the back of the cabinet (see Fig. 1 on p. 14).

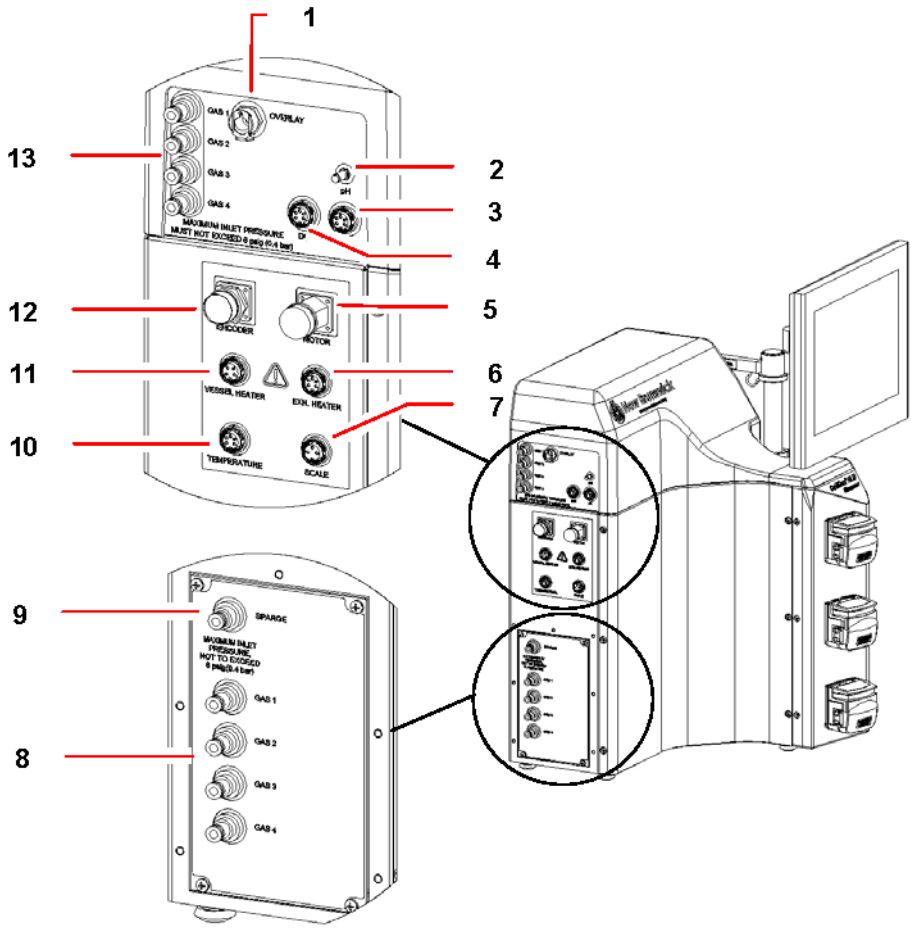

Fig. 3: Control Cabinet Service Connections

1 Outlet to Overlay port on headplate	**2 pH optical probe cable connection**
3 Gel-filled pH probe cable connection	**4 Polarographic DO probe cable connection**
5 Motor cable (female plug) connection	**6 Exhaust heater connection**
7 Scale connector (optional)	**8 Inlets for sparge gases**
9 Sparge outlet connection	**10 RTD temperature probe connection**
11 Vessel heat blanket connection	**12 Motor cable (male plug) connection**
13 Inlets for overlay gases	

Using standard plant practices and respecting all applicable codes, connect services to the appropriate connections (see Tab. on p. 17) (see *Electrical requirements on p. 17)* and (see *Gas connections on p. 17)*.

Tab. 1: Service Connections

Service/Utility	Requirement	Connection
Electrical	100 - 120 VAC, 50/60 Hz., Single Phase, 15 Amp (fluctuations not to exceed ±10%)	100 - 120 VAC 1ph field wired to 15 Amp disconnect in panel
	200 - 240 VAC, 50/60 Hz., Single Phase, 15 Amp (fluctuations not to exceed ±10%)	200 - 240 VAC 1ph field wired to 15 Amp disconnect in panel
Process Air	5 - 6 PSIG	Push on
Oxygen	5 - 6 PSIG	Push on
Nitrogen	5 - 6 PSIG	Push on
Carbon Dioxide	5 - 6 PSIG	Push on

4.5.1 Electrical requirements

100 - 120 Volts	50/60 Hertz	15 Amp
200 - 240 Volts	50/60 Hertz	15 Amp

WARNING!

High voltage.

- Always make sure this equipment is properly earthed/grounded.

The electrical requirements vary depending on the part number that has been ordered. Model, Part Number and Electrical Requirements for each bioreactor appear on a metal label affixed to the rear of the system just above the connection for the mains/power cord.

WARNING!

High voltage.

- Always make sure this equipment is properly earthed/grounded.

NOTICE!

Risk of equipment damage!

- Before making electrical connections, verify that the supply voltage matches the voltage and the mains/power requirements marked on the electrical specification plate (located on the rear panel of the cabinet) and the control schematics supplied with the system.

4.5.2 Gas connections

Gas inlets for both the sparger and the overlay are located on the left side of the control cabinet (see Fig. 3 on p. 16). There are push-in connectors for air, nitrogen, oxygen and carbon dioxide. These connectors accept rigid walled gas tubing, which is supplied with the bioreactor.

It is very important to match the gases to the inlets (see Fig. 3 on p. 16), item 8 and 13, as follows (see Tab. on p. 18):

Tab. 2: Identifying Gas Inputs

Input Label	Gas to Connect
Gas 1	Air
Gas 2	Oxygen
Gas 3	Nitrogen
Gas 4	Carbon Dioxide

Risk of personal injury!

- Do not use this equipment in a hazardous atmosphere or with hazardous materials for which the equipment was not designed.
- All gases supplied should be medical grade.
- No gas pressure should rise above 6 PSIG (0.4 bar).
- Never leave a gas inlet open; if no tubing will be connected, keep the inlet plugged.

- All gas supplies should be pre-regulated.
- The scale of the regulator gauge for gases going into the bioreactor should be such that one can regulate pressure 0 - 10 PSIG (0 - 0.69 bar).

4.6 Vessel assembly

Possible risk of contamination!

- Do not open any port in the vessel headplate until ready for use. Prolonged exposure to light will adversely affect the pH sensor.
- Never place the vessel in direct sunlight or in a brightly lit location.
- Always keep the vessel wrapped with the heat blanket to avoid premature decay of the pH sensor.

4.6.1 Unpacking the vessel

Because the CelliGen BLU vessel is shipped sterile, it is important to carefully follow the directions below:

1. If you are using an optional scale, place it next to the controller where the vessel will stand.
2. Inspect the outer box for damage.
3. Check the label on the box to make sure that the product has not exceeded its expiration period.
4. Open the lid of the box, then remove the cardboard insert by pulling directly up on the cut-out handles.

The outer wrapper is not only a secondary sterile boundary, it is also opaque to protect the pH sensor from light. Do not proceed to Step 5 until you are ready to use the vessel.

5. Remove the vessel in its protective opaque outer wrapper. Do not open the wrapper yet. Inspect the wrapper for damage.
6. Carefully tear open the bag at the top. Do not use sharp blades of any sort.
7. Carefully slide the vessel out of the protective wrapper, keeping the dome in place to hold all the tubing.
8. Place the vessel next to your control station in the rounded cutout, and install the heater blanket (see *Heat blanket and exhaust tube heat blanket on p. 22)* to protect the sensor from ambient light.

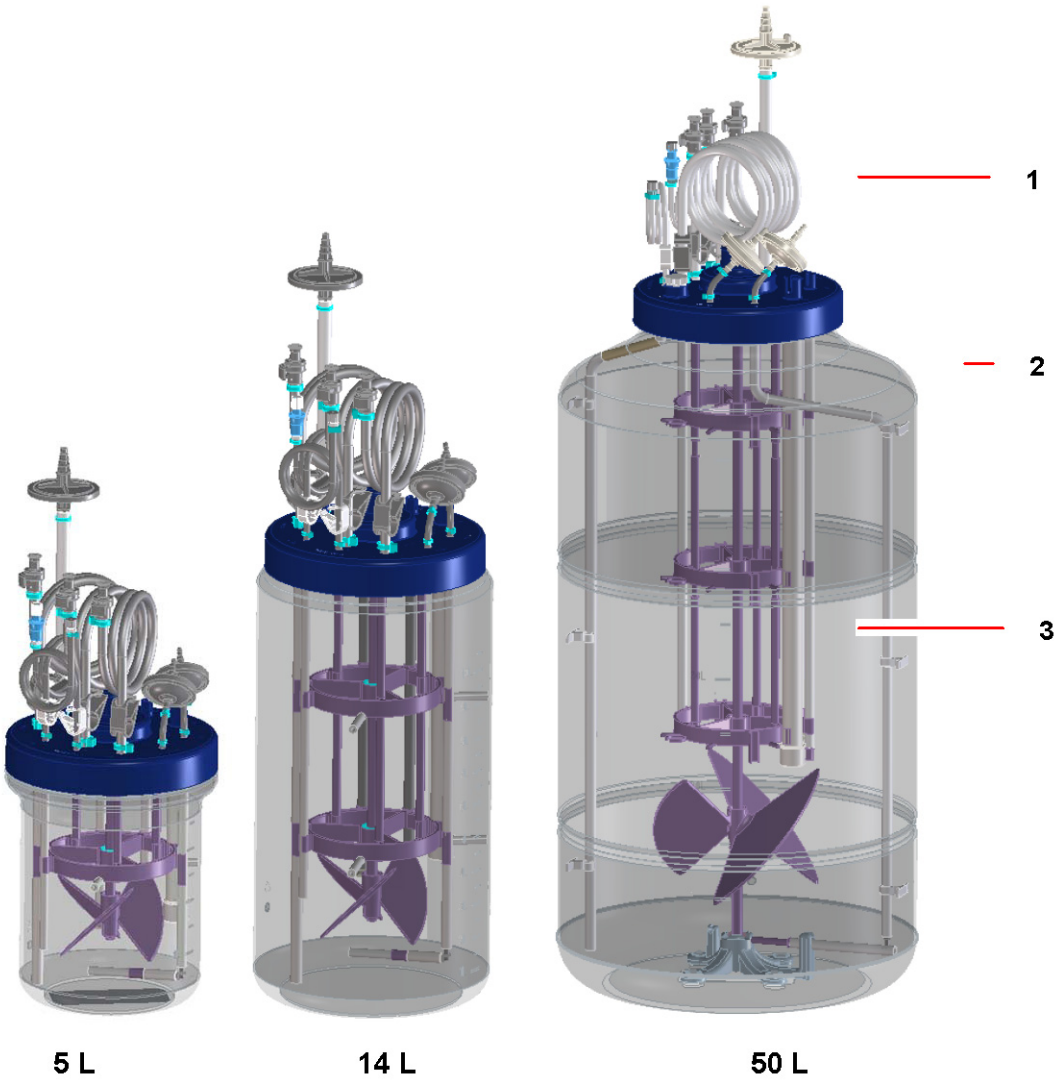

Fig. 4: Vessel Assembly

1 Headplate and tubing assemblies	**2 Vessel**
3 Internal components	

9. Remove the plastic dome and remove all cable ties from the tubing attached to the vessel.
10. If you are using the optional scale, place the vessel on it now.

4.6.2 Headplate penetrations

The illustrations in this section show the port penetrations on the vessel headplate. The ports are the same on all vessels; they are also labeled on the headplate itself.

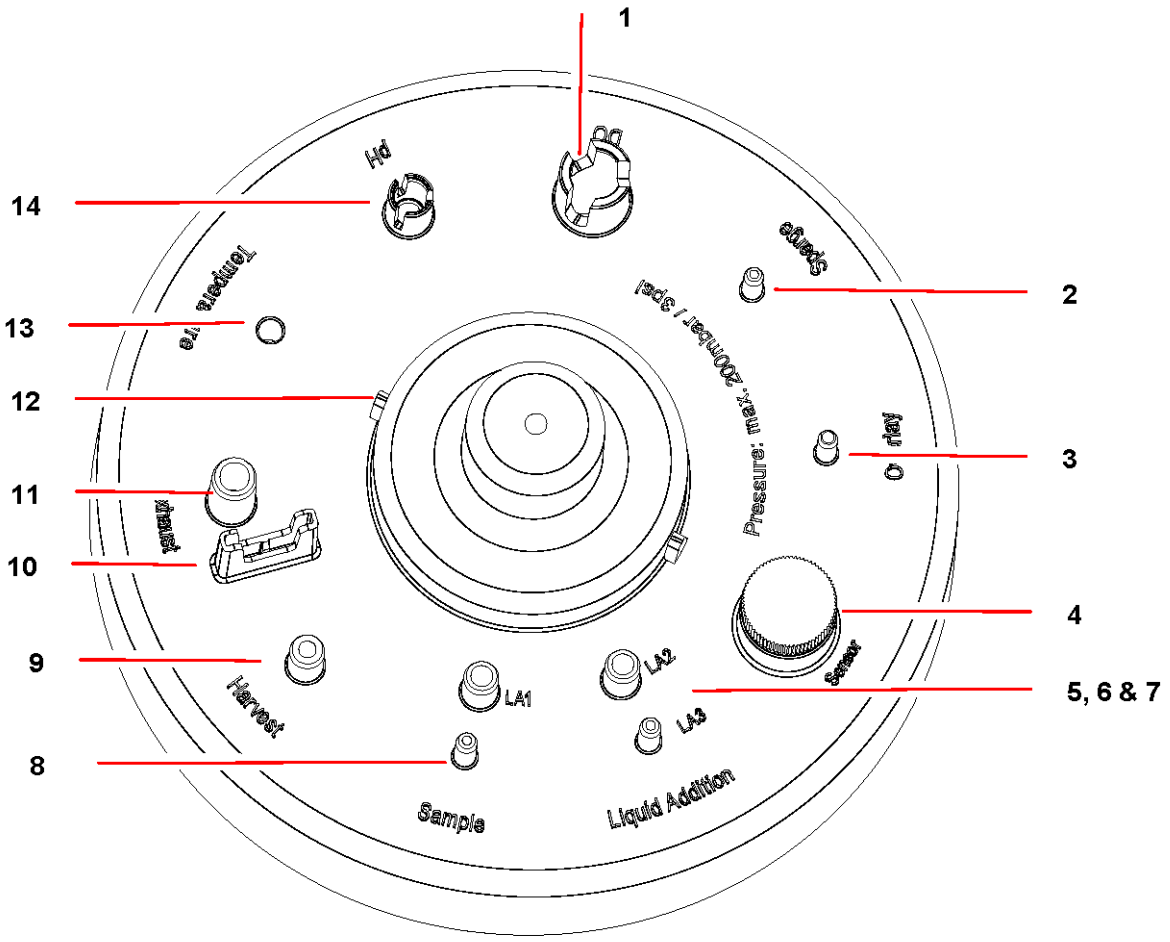

Fig. 5: Headplate Arrangement (shown without tubes and connectors)

1 DO port	**2 Sparge port**
3 Overlay port	**4 Threaded PG 13.5 sensor port***
5, 6, 7Liquid Addition ports 1, 2 and 3	**8 Sample port**
9 Harvest port	**10 Exhaust heater support**
11 Exhaust port	**12 Motor coupling****
13 Temperature port for RTD and thermowell	**14 pH port**

*Plugged as standard, **Note ridges for proper alignment

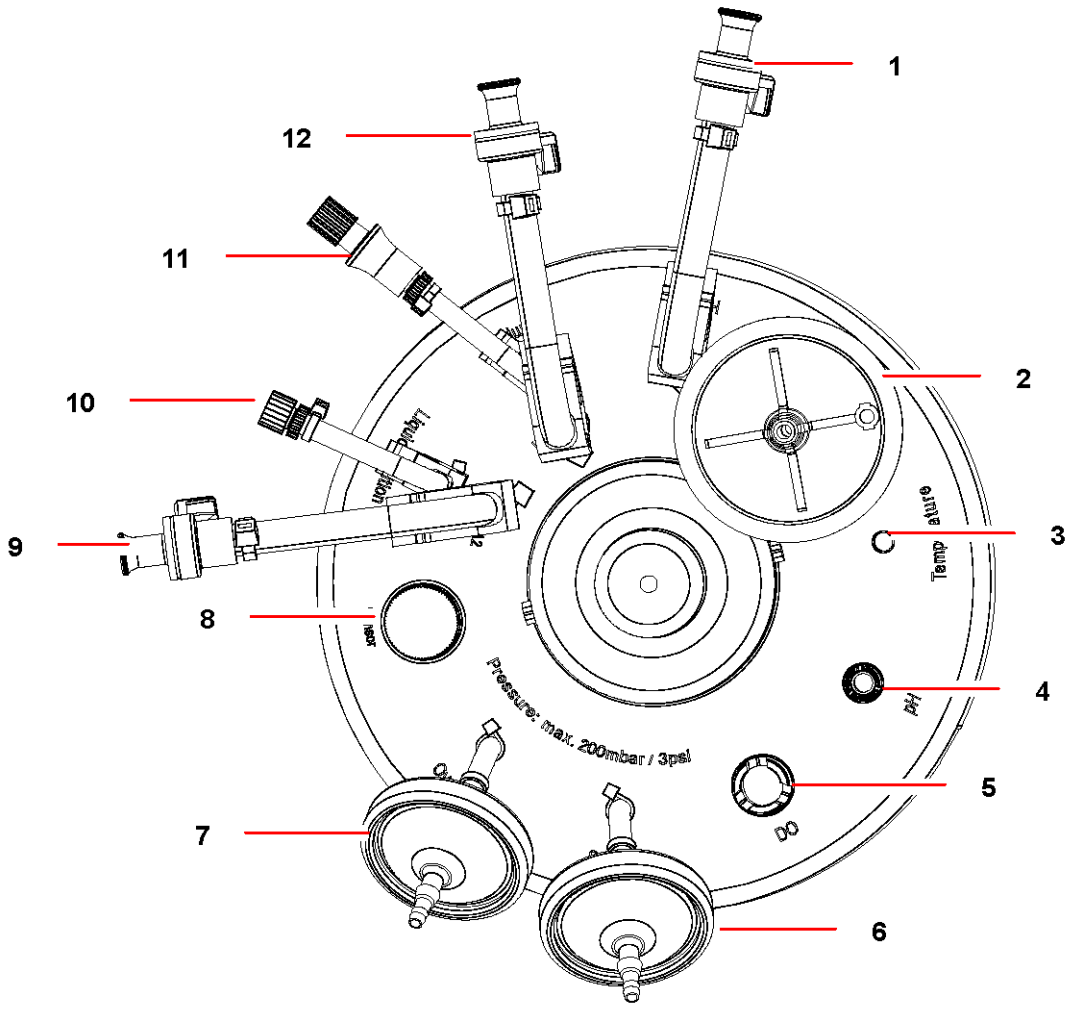

Fig. 6: Headplate Arrangement (shown with tubes and connectors)

1 1/4-inch CPC quick-connect for harvest	**2 0.2 µm exhaust filter**
3 Thermowell port for RTD	**4 Port for optical pH probe**
5 Port for polargraphic DO probe	**6 0.2 µm sparge filter**
7 0.2 µm overlay filterm overlay filter	**8 PG 13.5 threaded port**
9 1/4-inch CPC quick-connect for Addition 2	**10 1/4-inch CPC quick-connect for Addition 3**
11 Needle-free connector for sampling	**12 1/8-inch Luer-style connect for Addition 1**

The following (see Tab. on p. 22) summarizes the type, length and size (inner and outer diameter) of all the vessel headplate tubing and their connections.

Tab. 3: Headplate Tubing and Connections

Use	Tubing Type	Length	Size	Connection/Filter
Addition 1	C-FLEX®	500 mm (20 in)	3.18 mm ID x 6.4 mm OD (1/8 in ID x 1/4 in OD)	3.18 mm (1/8 in) Luer-style connect
Addition 2	C-FLEX®	700 mm (28 in)	6.4 mm ID x 9.6 mm OD (1/4 in ID x 3/8 in OD)	6.4 mm (1/4 in) CPC quick-connect
Addition 3	C-FLEX®	700 mm (28 in)	6.4 mm ID x 9.6 mm OD (1/4 in ID x 3/8 in OD)	6.4 mm (1/4 in) CPC quick-connect
Sample	C-FLEX®	500 mm (20 in)	3.18 mm ID x 6.4 mm OD (1/8 in ID x 1/4 in OD)	needle-free connector
Harvest	C-FLEX®	700 mm (28 in)	6.4mm ID x 9.6 mm OD (1/4 in ID x 3/8 in OD)	6.4 mm (1/4 in) CPC quick-connect
Exhaust	Silicone (platinum-cured)	200mm (8 in)	9.5mm ID x 12.7 mm OD (3/8 in ID x 1/2 in OD)	0.2 µm filter
Sparge	Silicone (platinum-cured)	50mm (2 in)	1.59mm ID x 3.18 mm OD (1/16 in ID x 1/8 in OD)	0.2 µm filter
Overlay	Silicone (platinum-cured)	50mm (2 in)	1.59mm ID x 3.18 mm OD (1/16 in ID x 1/8 in OD)	0.2 µm filter

4.6.3 Heat blanket and exhaust tube heat blanket

NOTICE!

Risk of equipment damage!

- Never turn on the heat blanket or exhaust tube heat blanket without first plugging in the RTD and inserting it into the thermowell inside the vessel (see *Install the temperature (RTD) probe on p. 26)*.

1. As soon as you unpack the vessel from its protective covering, wrap it with the heat blanket provided, securing it with the Velcro straps.
2. Be sure to position the hole in the blanket away from the pH sensor tube to minimize its exposure to light.
3. Attach the exhaust tube heater by wrapping it around the exhaust tube and bracing it with the support rod.

The exhaust heater should always be on when gas is flowing into the vessel.

4.6.4 Internal components

The vessel comes completely assembled and sealed for sterility.

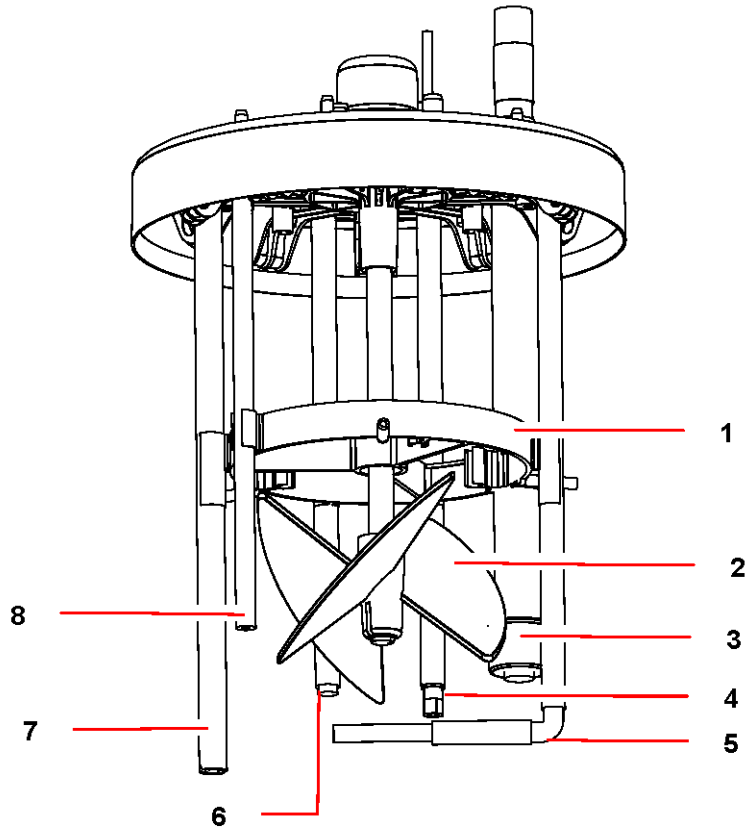

Fig. 7: Internal Vessel Components

1 **Retaining ring (for support)**	2 **Pitched blade impeller**
3 **DO tube with silicone cap**	4 **pH tube**
5 **Porous microsparge or tube macrosparge, depending on configuration selected**	6 **RTD thermowell**
7 **Harvest tube**	8 **Sample tube**

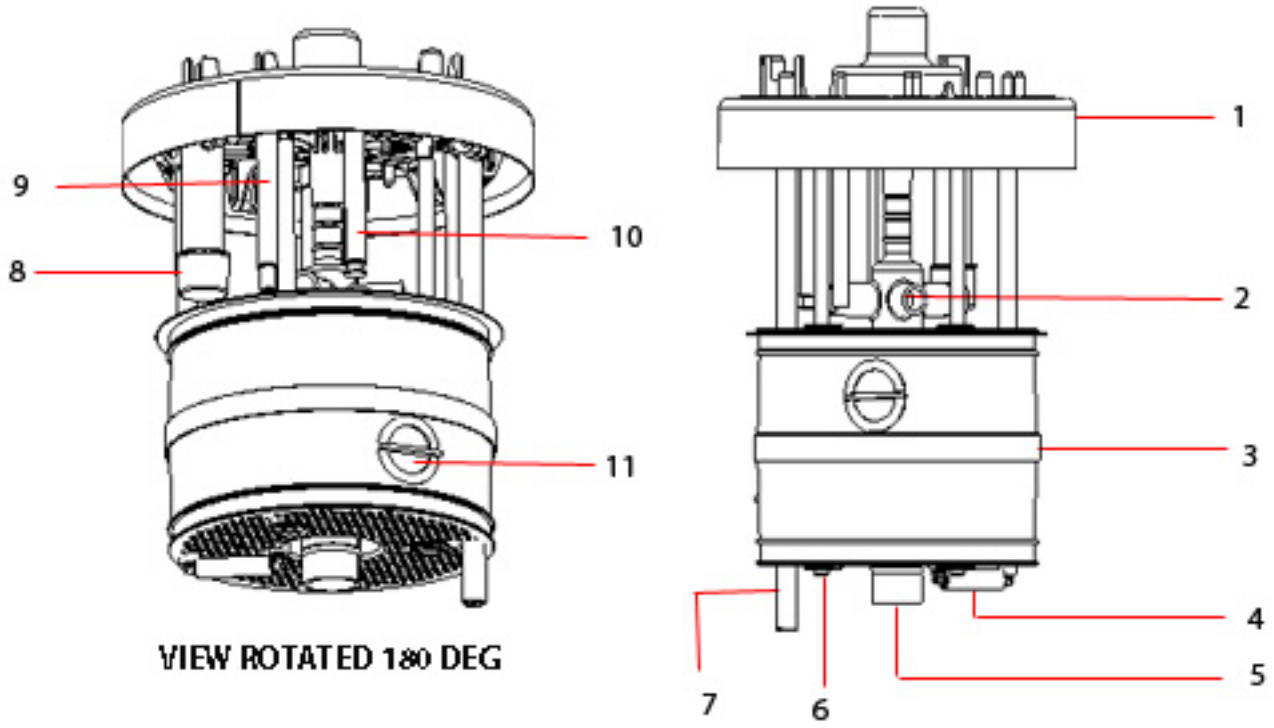

Fig. 8: Packed Bed Basket Vessel

1 Headplate	**2 Cell lift impellar**
3 Packed bed basket	**4 Sparge**
5 Impeller draft tube	**6 Support rod**
7 Harvest tube	**8 DO probe**
9 pH probe	**10 RTD temperature probe**
11 Plug	

4.6.5 Inspect the optical pH probe

Inspect the pH probe for possible shipping damage. When the probe is plugged in and the control cabinet is powered on, a purple light should pulse from the tip of the probe approximately every 30 seconds.

If you are using a gel-filled pH probe, (see *Install the gel-filled pH probe into the PG 13.5 port on p. 25)* to install the probe under a hood.

4.6.6 Install the optical pH probe

1. Make sure the probe cable is not connected to the control cabinet. To protect the sensor from excessive use, attach the cable just prior to calibration (see *pH calibration on p. 45)*.
2. Gently insert the probe into the pH headplate port.

The pH port is fluted and the fit is snug, so gently turn the probe as you press it into the port to avoid breakage. When the probe is fully inserted, it becomes difficult to remove: this ensures that the probe remains secure during the culture run.

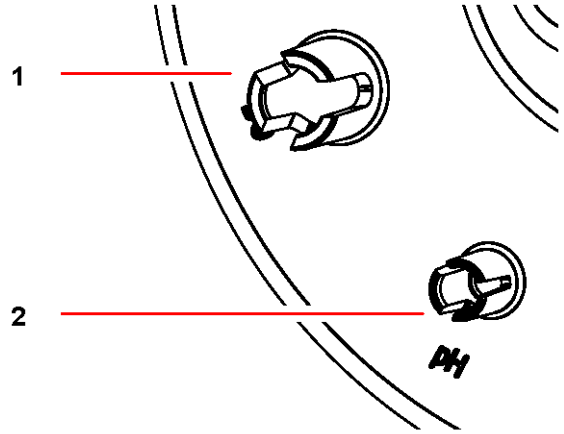

Fig. 9: pH and DO Headplate Ports (close-up)

1 DO port	**2 pH port**

4.6.7 Install the gel-filled pH probe into the PG 13.5 port

Be sure to calibrate the pH probe before installing it in the vessel.

Be sure to install the probe under a hood.

1. Clean and sterilize the probe.
2. Following standard aseptic practice, unscrew and remove the plug from the spare PG 13.5 headplate port labeled “Sensor”, then carefully thread the probe into the port.
3. Plug the pH probe cable into the designated pH connector on the control cabinet (see Fig. 3 on p. 16).

4.6.8 Inspect the DO probe

1. Inspect the probe for possible shipping damage.
2. Immediately report any damage you may observe to the New Brunswick Scientific Service Department.
3. Unscrew the protective cap from the electrode end and check the electrotype level. Fill it if necessary. The membrane is delicate and care must be exercised to prevent accidental damage.

Never rest the probe on its membrane.

4.6.9 Install the DO probe

The DO tube is designed for a snug fit at the top. When the probe is fully inserted, it becomes slightly difficult to remove: this ensures that the probe remains secure during the culture run.

NOTICE!

Risk of damage to DO sensor!

- Never put excessive pressure on the probe.
- Stop pushing when you feel resistance against the silicone DO port cap at the bottom of the DO tube.

1. Wear protective gloves to protect yourself in case of accidental breakage.
2. Gently insert the probe into the DO headplate port and slide it to the bottom of the DO tube.

4.6.10 Install the temperature (RTD) probe

1. Insert the RTD temperature probe into its headplate port, making sure the probe extends all the way to the bottom.
2. Attach the RTD cable to the Temperature connector on the control cabinet (see Fig. 3 on p. 16).

Water or glycerol is not required for proper probe operation.

4.6.11 Install motor assembly

NOTICE!

Risk of damage to the motor circuit board!

- Never plug the motor into the controller while the controller is powered on.
- Turn the controller off, then connect the two motor cables.

1. Position the motor assembly on top of the coupling, using the locating notch to orient it properly.
2. Remove the caps from the Encoder (female) connector and Motor (male) connector on the control cabinet (see Fig. 3 on p. 16).
3. Connect the motor cables to their respective connectors.

4.7 Mains/Power switch

NOTICE!

Risk of damage to the equipment!

- Before turning on the mains/power switch, make sure that the mains/power cord is properly connected to the control cabinet and plugged into a suitable mains/power outlet.

The mains/power switch is located on the lower righthand side of the control cabinet (see Fig. 1 on p. 14), Front View.

4.8 Connect gases

- Ensure that all gas lines (air, oxygen, etc.) are routed to the appropriate ports and secured at both ends with plastic ties.

CAUTION!

Risk of explosion: damage to equipment and possible harm to personnel!

- NEVER over-pressurize a culture vessel!
- Always use eye protection, and exercise caution in the vicinity of culture vessels. If the vessel exhaust becomes blocked, pressure can build up, possibly shattering the vessel and endangering personnel.
- Before opening the airflow valve(s), visually confirm that the vessel exhaust is not blocked by kinked tubing, clamps or a wet filter.
- After opening the airflow valve(s), verify by feel that air is flowing freely from the exhaust. If not, immediately close the valve(s) or turn off the air/gas supplies.
- Never intentionally block the exhaust to raise vessel pressure.
- Use the minimum air/gas pressure that will provide adequate airflow for the application.
- Never exceed the maximum pressure specified in this manual.

4.9 Optional BioCommand software

If you are using New Brunswick supervisory software be sure to consult your BioCommand user's manual for installation and start-up instructions in addition to the general instructions provided below.

A 25-pin RS-232/-422 Modbus com port is provided on the rear panel of the control cabinet (see Fig. 6 on p. 21) to connect the CelliGen BLU to a supervisory host computer.

Communications to BioCommand software are via an optional RS-232 interface cable:

1. Connect the 25-pin end of the RS-232 cable to the Modbus port, and ensure that the connection is secure.
2. Hand tighten the thumbscrews.
3. Refer to the BioCommand Operating Manual for instructions on connecting the RS-232 interface cable to the supervisory host computer.

4.10 Inputs/Outputs for ancillary devices

Additional analog input and output ports are available on the control cabinet rear panel for the connection of analog ancillary devices such as additional pumps, gas analyzers and glucose analyzers. After the inputs are connected to the control cabinet, the collected information will be viewed and controlled via the touchscreen display.

Three of these additional analog input and output ports have dip switches to allow selection of either 4 - 20 MA or 0 - 5 V. The other four input and output ports are 0 - 5 V dedicated.

Two USB serial ports are available on the control cabinet rear panel for the connection of serial ancillary devices such as scales for vessel and addition bottles. You can connect a box with eight serial (RS-232) inputs and outputs to one USB port to allow you to connect and control up to eight scales or other ancillary equipment.

The following (see Fig. 10 on p. 28) will acquaint you with these inputs and outputs.

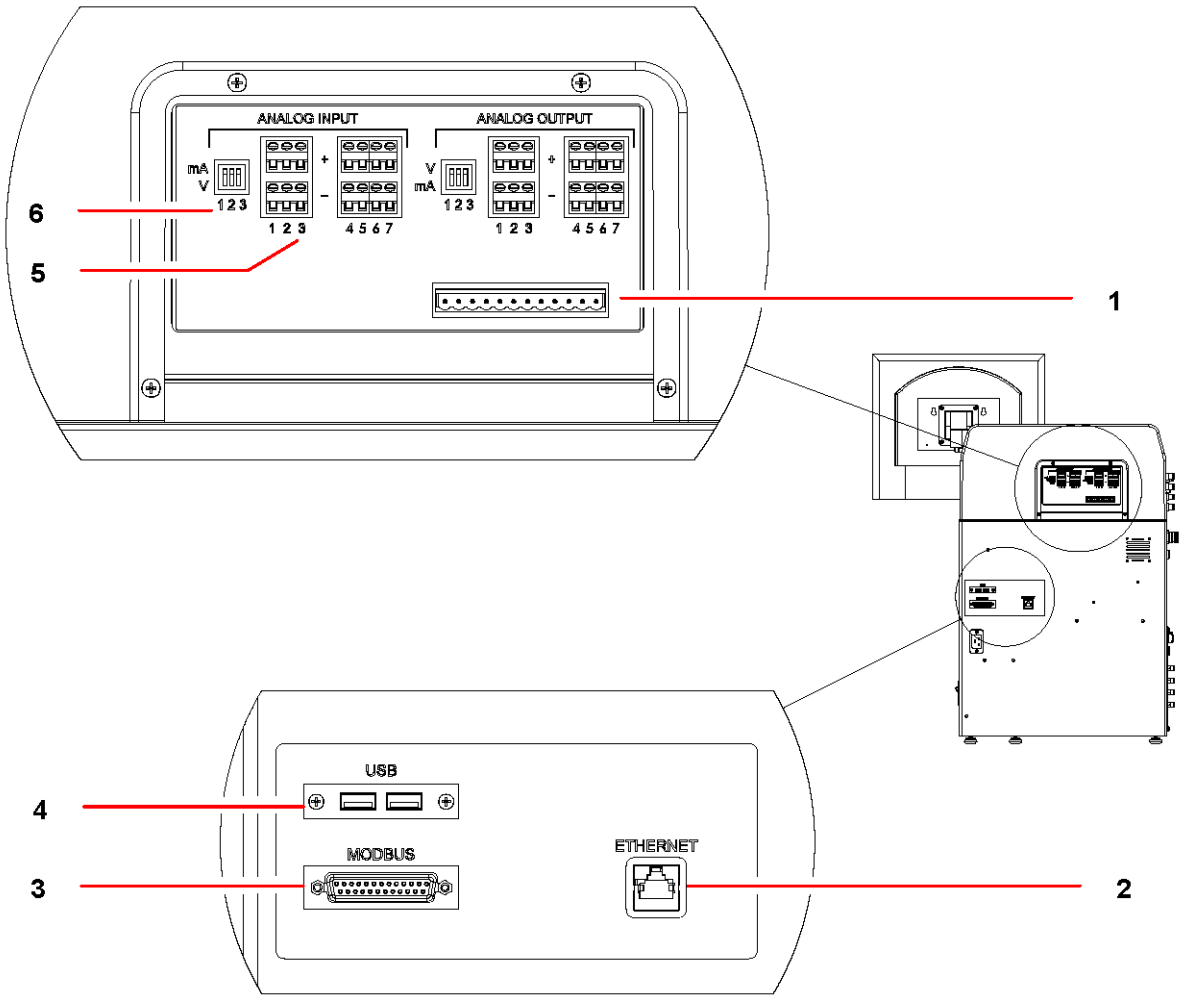

Fig. 10: Inputs and Outputs for Ancillary Equipment

1 Capped as standard (not used at this time)	**2 Ethernet port provided for network connectivity**
3 The MODBUS connection is provided for the use of New Brunswick BioCommand.	**4 USB connections are provided for updates or data export.**
5 These switches 1 - 3 can be set to 4 - 30 mA or 0 - 5 V; switches 4-7 are for 0 - 5 V only.	**6 Dip switches 1 - 3, to toggle from 4 - 20 mA (up) to 0 - 5 V (down) for analog input (and output)**

4.11 Install a scale

If you are using an optional load cell scale, it should already be placed under the vessel and connected to the controller (see *Inputs/Outputs for ancillary devices on p. 27)*.

- Set up a control loop for the scale (see *Adding loops on p. 35)*.

4.12 Install the bag hanger

If you plan to use the bag hanger provided with the system, install it, as shown below, on the two hinge pins located on the righthand side of the controller:

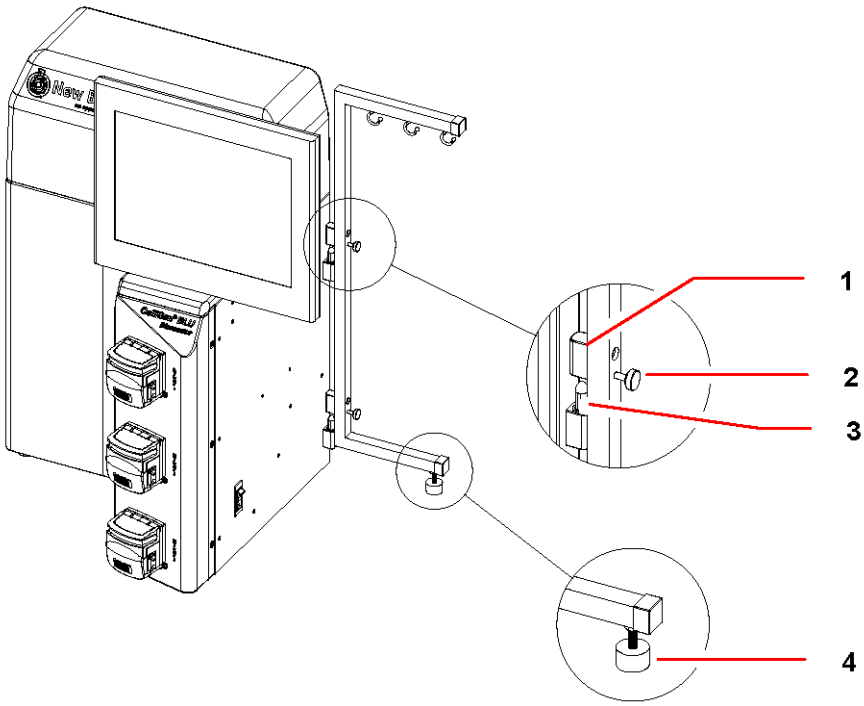

Fig. 11: Bag Hanger

1 Bracket hinge	**2 Thumbscrew**
3 Hinge pin on controller	**4 Adjustable foot**

NOTICE!

Risk of damage to the equipment!

- Do not allow the combined weight of the bags and their contents to exceed 15 kg (33 lb).

1. With the three hooks at the top of the bracket and the adjustable foot at the bottom, orient the long side of the bracket against the side of the controller, sliding its two hinges onto the pins that are mounted on the controller.
2. The bracket swings freely on the hinges unless you choose to fix it in place at the desired angle by tightening its two thumbscrews against the controller.
3. Be sure to tighten the adjustable foot to secure the bracket on the benchtop before you add any contents to the bag(s) you hang there.
4. As needed, feed the tubing from the bag(s) into the dedicated pump(s) and aseptically attach the tubing to the appropriate port connection (addition, harvest or sampler).

5 Operating controls and function

5.1 Touchscreen

Your primary interface with the CelliGen BLU is the touchscreen on the control cabinet:

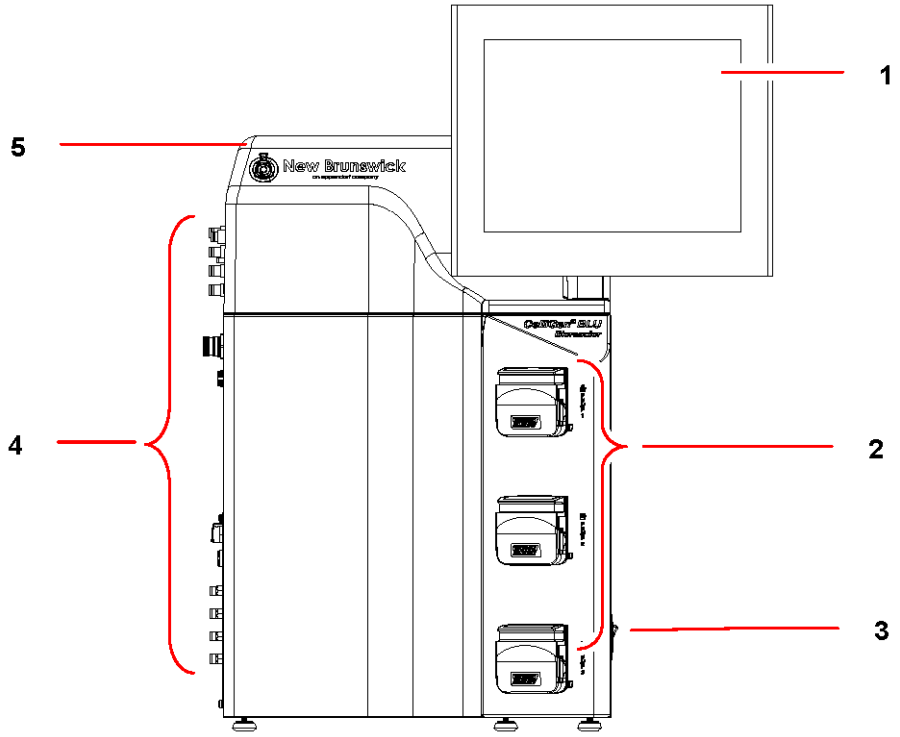

Fig. 12: Touchscreen

1 Touchscreen display	**2 Pumps**
3 ON/OFF mains/power switch	**4 Service Connections**
5 Control cabinet	

5.2 Display screens

The Start-Up screen, which tells you which operating software version is installed in your CelliGen BLU, is first screen you see each time you turn on the mains/power.

This screen remains in view for a few seconds, then it is replaced by the SUMMARY screen.

5.2.1 Summary screen

The SUMMARY screen (see Fig. 13 on p. 31) is command central; it puts as many as 32 loops at your fingertips.

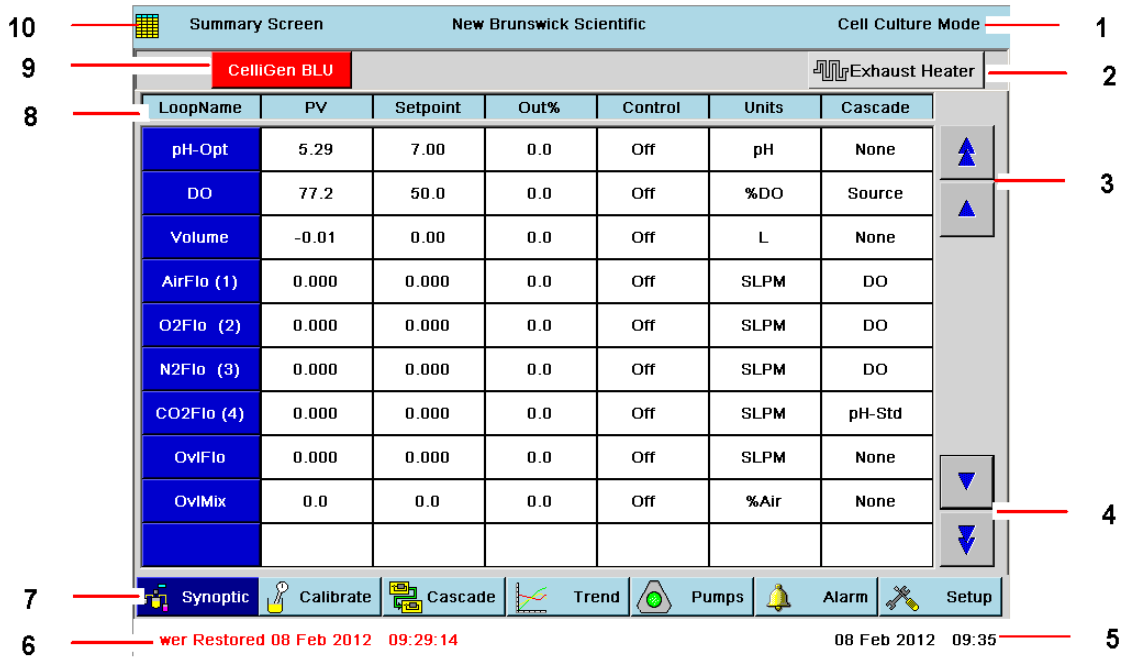

Fig. 13: Sample SUMMARY Screen

1	**Operating Mode (factory-set)**	2	**Exhaust Heater button**
3	**Scroll Up buttons**	4	**Scroll Down buttons**
5	**Current Date and Time**	6	**Any ALARMS will appear in this space.**
7	**Screen Access buttons. NOTICE: The dark blue button usually represents the screen being displayed. Here it shows a new screen, SYNOPTIC, that is accessible from this screen.**	8	**Your CelliGen BLU comes with pre-assigned loop names. As you add more, use the Scroll Down buttons to see them.**
9	**Unit Tab (user-definable). This tab is normally blue; if it is red, an alarm condition has occurred.**	10	**Screen Name and Icon**

The following (see Tab. on p. 32) identifies the other interactive features of the SUMMARY screen:

Tab. 4: SUMMARY Screen Features

Parameter	Description
LoopName	The system comes with standard factory-assigned control loops (e.g., Agit[ation], Temp[erature], pH, DO, etc.) for the bioreactor. There are also unassigned loops available, to be named and set up by the user when adding external equipment, for a maximum total of 32 loops.
PV	Process Variable: here the display reflects the current value for each loop.
Setpoint	The current setpoint (automatically generated or user-set) for each loop. See also Section 15.2 for recommended setpoints.
Out%	The current percent output for each loop. This is an automatic control function to maintain current readings within the setpoint tolerance range.
Control Mode	Depending on the loop, the control mode may be Off, Auto, Manual, On, 3 Gas or 4 Gas.
Unit (of measure)	This is the unit of measure used for the PV and Setpoint.
Cascade	If any cascades have been programmed, they will be displayed here: if the word Source is displayed, the loop is the source of a cascade; if the name of another loop is displayed (e.g., DO in the Gasflo row), that loop is the cascade source (DO is cascaded to Gasflo).
Summary (1)	This screen is command central; it shows all your loops, their PV, setpoints and the control mode they are set to.

Synoptic (1)	This screen is a graphical alternative to the SUMMARY screen. It shows your loops, their current readings and their setpoints. It also displays the current state of the fixed speed pumps, level probes and process valves.
Calibration	This screen allows you to calibrate the DO probe, the pH probe, vessel volume, and any user-defined loop(s) which have been added.
Cascade	A cascade is a control function that uses the output of one loop to influence the action and output of one or more other loop(s). This screen allows you to set up cascades, to view current settings, and to make changes to those settings.
Trend	This screen allows you to set the parameters for plotting trend graphs and to view the graphs that track the activity of the selected loops over a certain period of time.
Pumps	This screen gives you access to the Pump Gauges screen, where the three pump gauges are displayed, providing both current readings and the opportunity to change pump settings.
Alarms	In this screen you can turn alarms on and off, read the alarm history and acknowledge any alarm.
Setup	This screen allows you to load and save recipes and to make changes to your system settings, hardware setup, security settings and controller setup.
Exhaust Heater	Press this button to turn the exhaust heater on or off when it is connected to the control station. The button is green when the heater is on.
Scroll Up	Press this button to scroll upwards, one loop at a time.
Scroll Down	Press this button to scroll downwards, one loop at a time.

(1) The far left navigation button at the bottom of all main screens is a toggle between the SUMMARY and the SYNOPTIC screens. When viewing one, the button will be labeled for the other. Upon leaving either for one of the other screens, the default selection shown on the button will be the most recently visited of the two. That is, if you leave the SUMMARY screen to view the TREND screen, for example, the far left button will be labeled SUMMARY.

(2) It is very important to be sure the exhaust heater is on when you are actively growing cells, to reduce the risk of clogging the exhaust filter.

5.2.2 Synoptic screen

- Press the far left SYNOPTIC button from any main screen to open the SYNOPTIC screen (see Fig. 14 on p. 34).
- If the far left button says SUMMARY, press it to open the SUMMARY screen. The button will now be labeled SYNOPTIC; press it again.

This screen provides a visual representation of all the loops, their settings and current process values—the sample screen below may not be exactly like the screen you see; it depends on your system's options. This screen provides all the functionality of the SUMMARY screen with the exception of the ability to add loops.

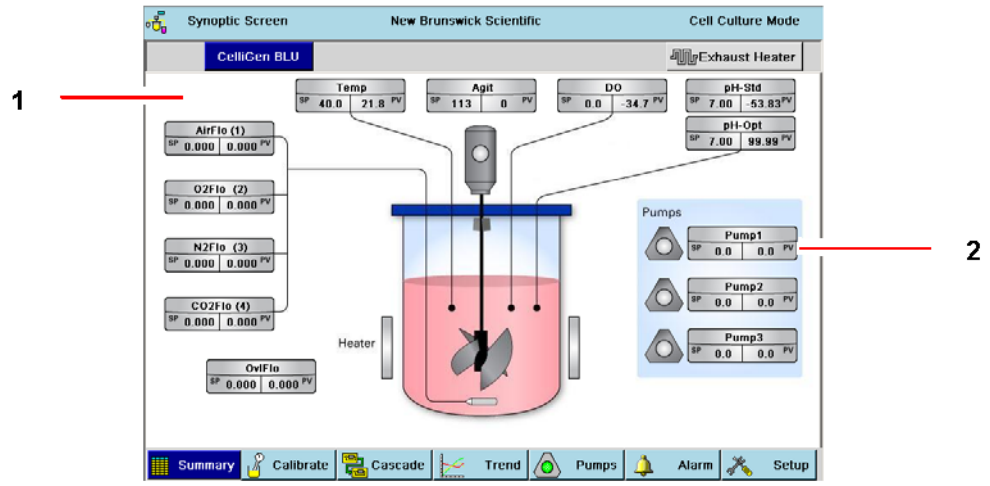

Fig. 14: Sample Synoptic Screen

1 Loops	**2 Pumps**

Each loop gauge indicates setpoint (SP) and process variable (PV). Its title color indicates the loop's status: Grey = OFF, Green = ON and Blue = MANUAL.

- Touch the loop gauge in this screen to open the full loop gauge screen (see *Gauge screens on p. 34)*.

Each pump gauge indicates setpoint (SP) and process variable (PV). Pump icon and gauge title color indicates that pump's status: Grey = OFF and Green = ON.

5.2.3 Gauge screens

Every loop has its own gauge screen. To access it:

- Touch the screen inside the appropriate blue box in the LoopName column in the SUMMARY screen. Your touch will open that loop's GAUGE screen (see Fig. 15 on p. 34).

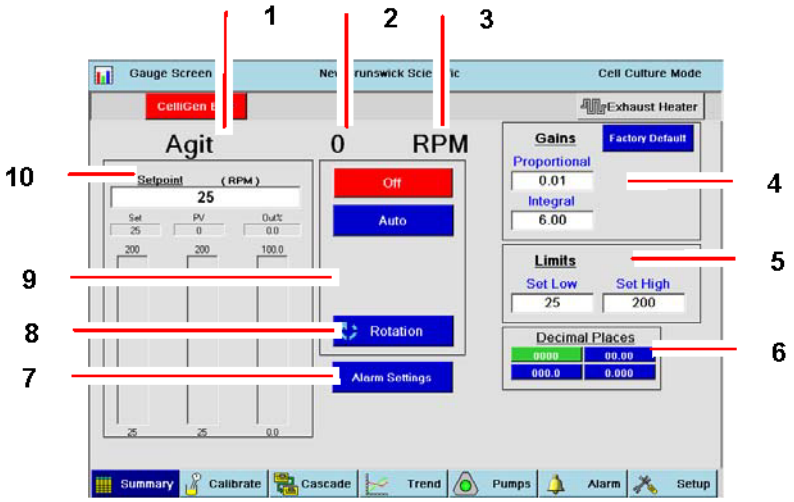

Fig. 15: Sample GAUGE Screen

1 Loop Name	**2 Process Variable (present value)**
3 Units: the action of this loop, Agitation, is measured in rpm.	**4 P&I values; some GAUGE screens also have a Deadband here**

5 Limits: Here you adjust the high and low settings for this specific loop. When adjusted, the scaling for the gauge (on the left of the screen) will also be adjusted to reflect the high and low limits selected.	**6 Decimal Places: Press the appropriate button to display values with 0, 1, 2 or 3 decimal places.**
7 Alarm Settings: pressing this button opens the Alarm setup screen for this loop.	**8 Rotation: pressing this button reverses the rotation of the pitched blade impeller**
9 Control Mode	**10 Setpoint (and units of measurement)**

Pressing inside any edit box in the GAUGE screen opens a numeric touchpad, used to input values.

5.2.4 Adding loops

The CelliGen BLU comes to you with standard factory-assigned loops and the possibility to add more loops, which are related to external auxiliary equipment, added via standard analog and optional serial (RS-232) inputs/ outputs located on the rear panel.

To add a new loop:

1. Scroll down in the SUMMARY screen beyond the last pre-assigned loop, and press on a blank LoopName box.

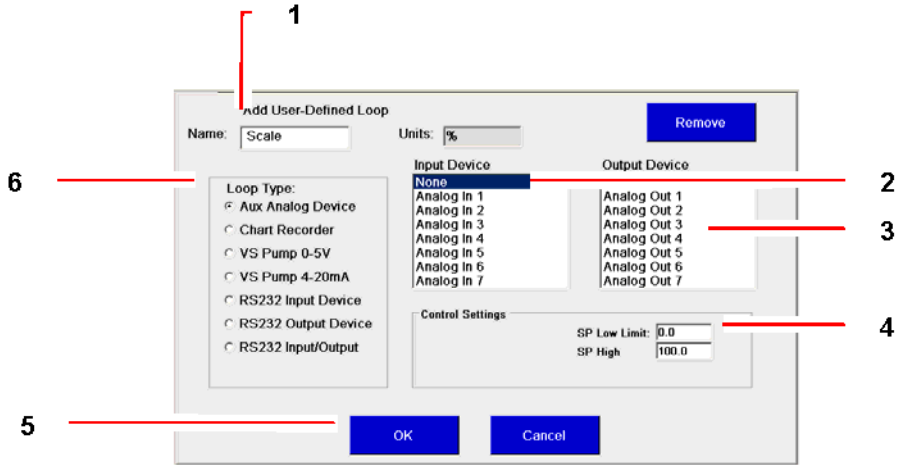

Fig. 16: Add User-Defined Loop Screen

1 Name edit box	**2 Input Device list**
3 Output Device list	**4 Control Settings**
5 OK button	**6 Loop Type options**

The Add User-Defined Loop screen will open (see Fig. 16 on p. 35).

2. Press inside the Name edit box and use the LoopName Touchpad (see Fig. 17 on p. 36) to name the loop.
3. Press the appropriate Loop Type option button.

   The corresponding Unit of measurement will automatically appear in the Units box (% in this sample screen).
4. Press the appropriate Input Device designation.
5. Press the appropriate Output Device designation.
6. Input the desired Control Settings (Setpoint low and high limits).

7. After making all of your selections, press the OK button to save them.

Options are not available (grey) if the system does not detect their presence.

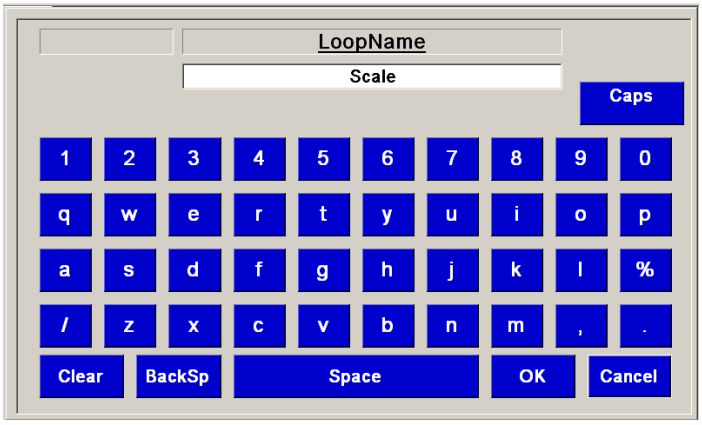

Fig. 17: LoopName Touchpad

To use the LoopName touchpad:

- Press Caps Lock to shift to CAPITAL letters. Press it again to shift back to lower case.
- Press Cancel to return to the Gauge screen without saving work done with the touchpad.
- Press OK to return to the Gauge screen, saving the work done with the touchpad.
- Press BackSp to backspace, cancelling one character at a time.
- Press Clear to clear the LoopName edit box in this touchpad, allowing you to begin again.

5.2.5 Deleting loops

Only user-added loops can be deleted. If you wish to delete a loop:

1. In the SUMMARY screen press the LoopName box for the loop you wish to delete.
   The loop's GAUGE screen will open.
2. If this is a pump control loop, skip to Step 4. If this is not a pump control loop, press the User Settings button (see Fig. 18 on p. 36).

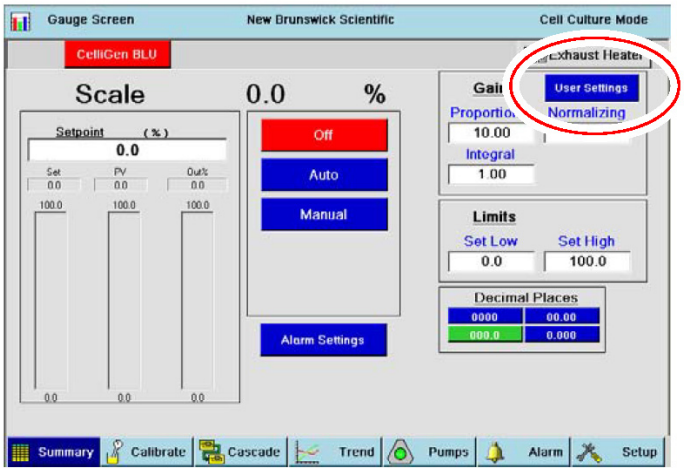

Fig. 18: Deleting a Control Loop

3. In the Add User-Defined Loop screen, press the Remove button in the upper righthand corner.

4. If the loop is a pump: only optional pumps have a Settings button that provides access to their Remove button.

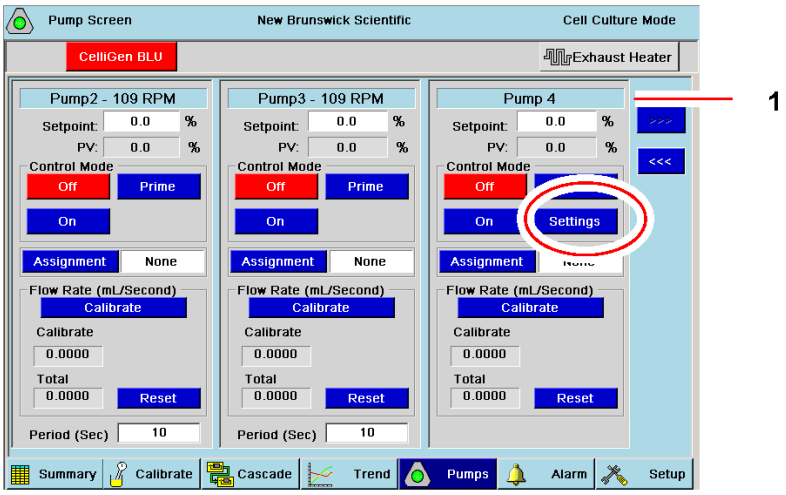

Fig. 19: Deleting a Pump Control Loop

1	**Pump 4 is a user-added pump loop.**

5. Press the Settings button to open the screen where you can press the Remove button to delete the pump loop. If there is no Settings button in the pump gauge (see Pump1 and Pump 2 for example), that pump's control loop cannot be deleted.

When you return to the SUMMARY screen, the loop will be deleted.

5.2.6 Selecting loop control modes

Control modes vary according to the loop and process mode. There are also operating modes for all of the pumps (see *Pump control mode on p. 70)*. To change operating modes for any of the displayed loops, in the SUMMARY screen:

1. Press either the LoopName or the Control Mode box in the row for the appropriate loop to open that loop's GAUGE screen:

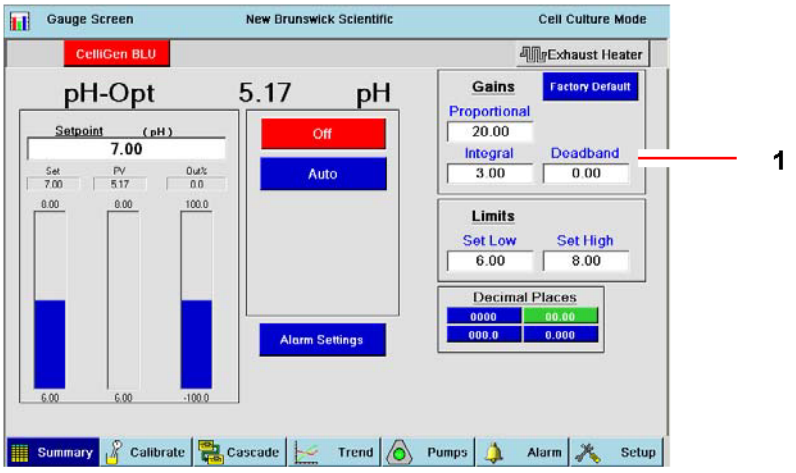

Fig. 20: Sample GAUGE Screen

1	**Deadband is a user-definable pH value within which, above or below the setpoint, no response will be triggered.**

2. Press the button (Off or Auto in the sample screen) that corresponds to the desired Operating Mode. Other GAUGE screens may include Manual, 3-Gas, 4-Gas and/or Cascade/Manual modes.
3. To save the new operating mode and return to the SUMMARY screen, press the SUMMARY button.

The below Sections introduce you to the other main screens accessible by pressing the blue navigation buttons at the bottom of the screens.

5.2.7 Calibration screen

This screen is used to calibrate the pH probes, DO probes and vessel volume, as well as any user-defined loops added to the system.

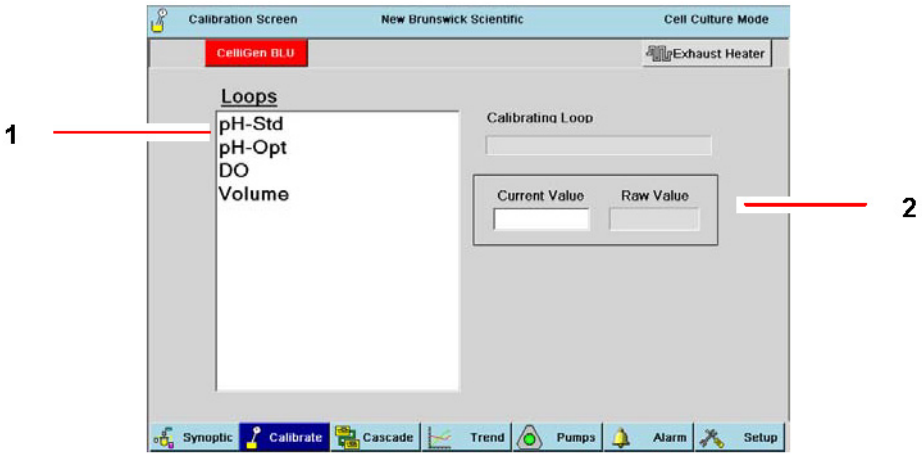

Fig. 21: Calibration Screen

1 Loops available for calibration	2 Input boxes

- For details on probe calibration, (pH probe, optical or standard gel-filled) (see *pH calibration on p. 45)* and (DO probe) (see *DO probe calibration: setting zero on p. 47)*.
- For details on volume calibration, (see *Scale/Volume calibration on p. 49)*.

5.2.8 Cascade screen

A cascade is a control function that uses the output of one loop to influence the action and output of one or more other loop(s). This screen allows the user to set up cascades, to view current cascade settings and to change those settings.

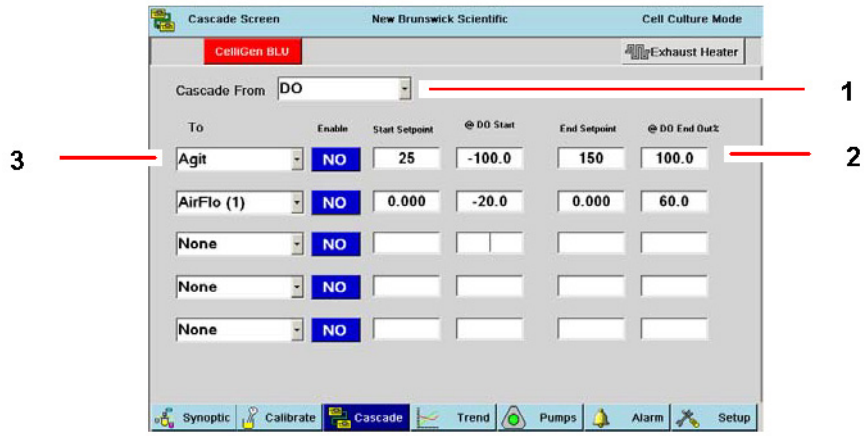

Fig. 22: Cascade Screen

1 Loop being cascaded from	**2 User-definable variables**
3 Loop(s) being cascaded to	

1. For details on setting cascades, (see *Creating a cascade on p. 56)*.

5.2.9 Trend screen

This screen allows the user to set the parameters for plotting trend graphs and to view the graphs that track the activity of up to 8 selected loops during an entire process run. The data can be exported through the USB port in Excel format to a PC.

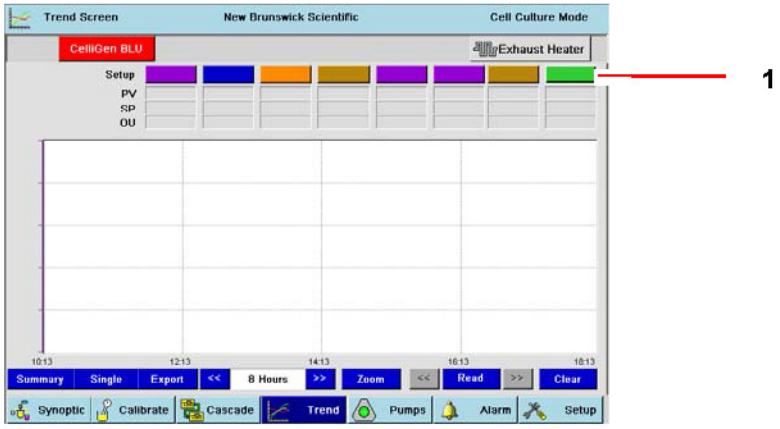

Fig. 23: Trend Screen

1 The user will assign a tracking color to each loop.

- For details on using the TREND screen, (see *Plotting trends on p. 63)*.

5.2.10 Pumps screen

This screen allows the user to access the pump gauges screens, where the three standard pumps (plus any optional pumps) are displayed, providing both current readings and the opportunity to change pump settings.

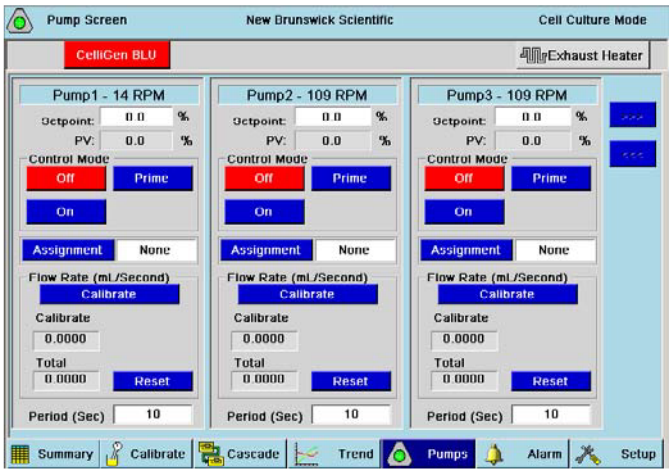

Fig. 24: Pumps Screen

- For details on using the PUMPS screen, (see *Pump assignment on p. 52)*.

5.2.11 Alarms screen

This screen allows the user to turn alarms on and off, to read the alarm history and to acknowledge any alarm while it is active.

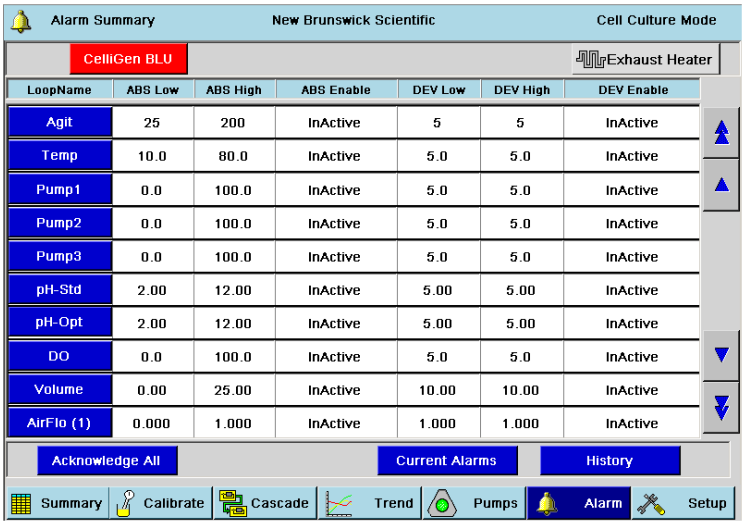

Fig. 25: Alarms Screen

- For details on using the ALARMS screen, (see *About alarms on p. 77)*.

5.2.12 Setup screen

This master SETUP screen is actually comprised of four screens, accessed by tabs, which are used to set up the controller, recipe management, system settings and hardware for the CelliGen BLU system.

This section will introduce you to those screens and their features. For details on using the SETUP screen, including a fifth tab that may be present (see *Using the setup screen on p. 82)*.

When you press the SETUP button, the screen that opens is actually the first tab, the CONTROLLER SETUP screen:

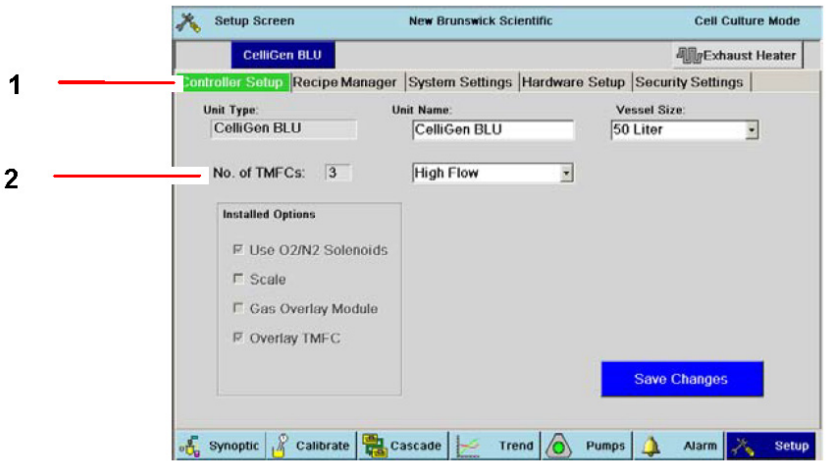

Fig. 26: Controller Setup Screen

1 Controller Setup TAB	**2 The number of TMFCs is factory-set at 3.**

Details regarding the selection of a Unit Name, Vessel Size and TMFC gas flow range (High Flow or Low Flow) are provided (see *Controller setup on p. 82)*.

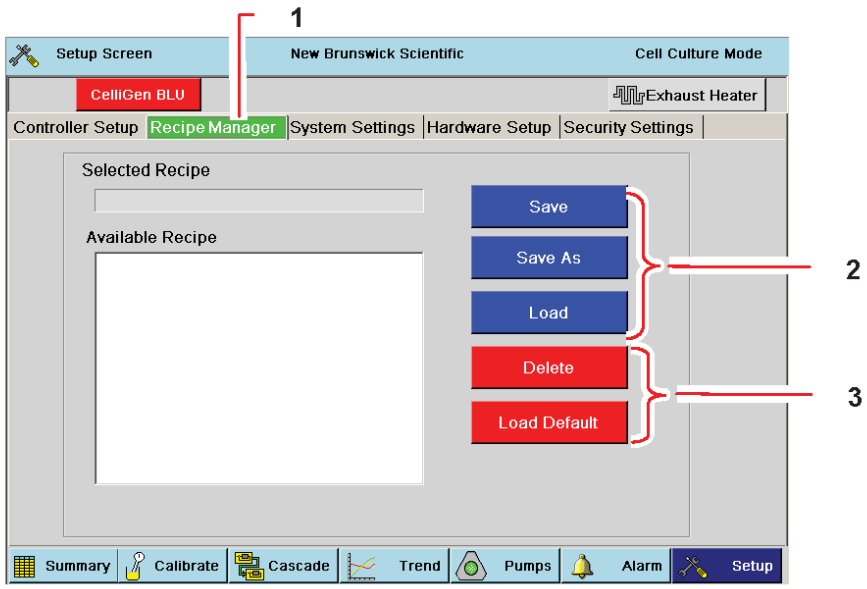

Fig. 27: Recipe Manager Screen

1 Use the Recipe Manager screen to save and load up to 10 recipes.	**2 Recipes can be saved and loaded using these top three buttons.**
3 The Delete button removes the currently selected recipe; the Load Default button restores factory settings.	

A recipe consists of all setpoints, controller settings, control modes, calibration data and cascades set on a system.

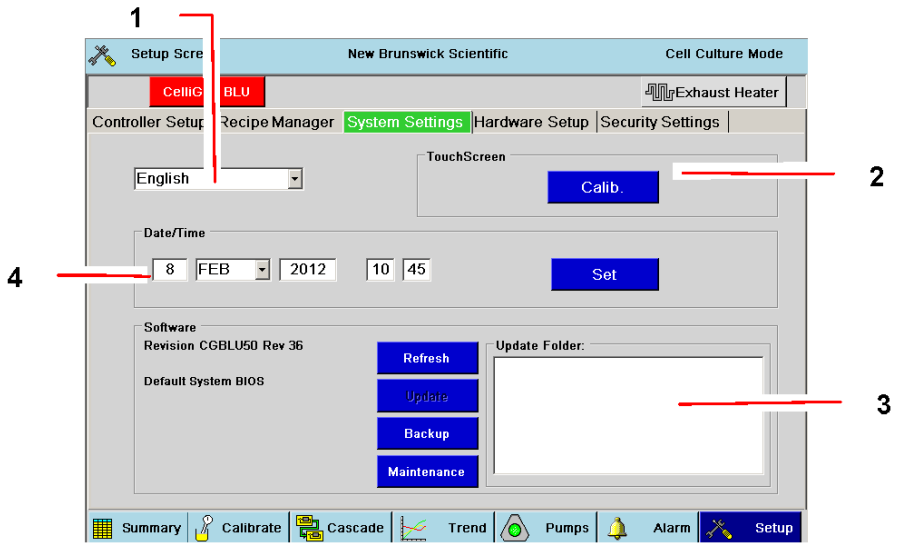

Fig. 28: System Settings Screen

1 English is the default language. When other choices (Français, Deutsch, Español) become available, the user will select the language here.	**2 Use this pane to calibrate the touchscreen.**
3 Use this pane to view the Software/Firmware version installed, and to update software via the USB port.	**4 Use this pane to change Date and Time.**

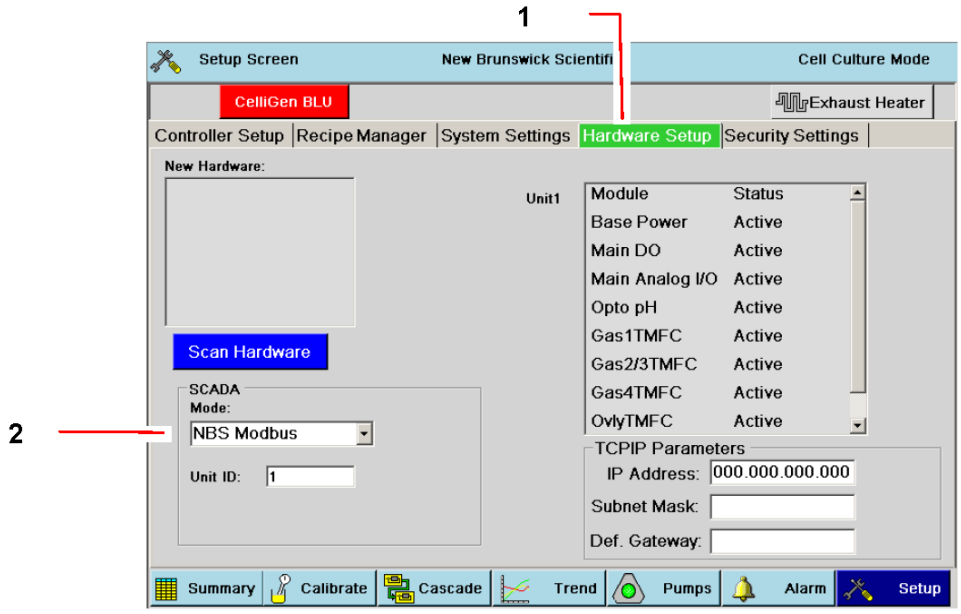

Fig. 29: Hardware Setup Screen

1 Use the Hardware Setup screen to view hardware installed in the system and to set Unit IDs for software.	**2 Use this pane to choose software connections.**

5.3 Analog inputs/outputs and RS-232/-422 computer interface

As shown below, an RS-232/-422 com port has been provided; there is a 25-pin “D” connector located on the lower rear panel of the control cabinet. It is labeled Modbus

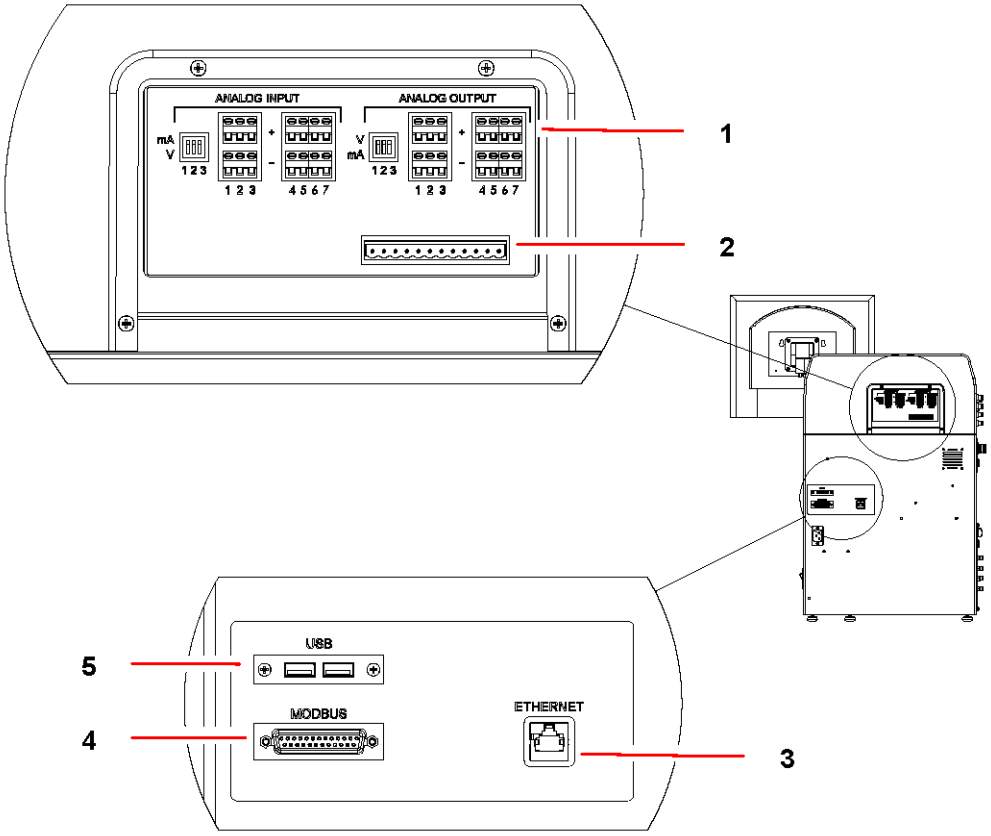

Fig. 30: Control Cabinet Rear Panel

1 Analog Inputs and Outputs are easily accessible*	**2 Capped as standard: not in use at this time**
3 Ethernet port provided for network connectivity	**4 Modbus port, for use with New Brunswick BioCommand supervisory software**
5 2 USB ports, for software updates, diagnostics and TREND screen data downloads	

* A stainless steel cover may need to be unscrewed and removed to gain access.

A New Brunswick BioCommand advanced supervisory software program is available which will enable the operator to interface with a computer that has a Windows® 2000 (or higher) operating system. With this software, you will be able to establish or change the setpoints for temperature, pH, DO, agitation speed and pump flow rate. You will also be able to read and log the process values of any parameters (temp, pH, DO, air flow, pump flow rate, levels and agitation) that are monitored. The data can also be stored, plotted and, afterwards, transferred to other commonly available programs, to be manipulated and analyzed in various ways.

The following (see Tab. on p. 44) identifies the pin designations for this 25-pin RS-232/-422 connector:

Tab. 5: Modbus Com Port Pin Designation

Pin Number	Signal	Comments
1, 4-6, 8-11, 14-20, 22-23	NC	not assigned
2	TXD	RS-232 Data Output from bioreactor
3	RXD	RS-232 Data Input to bioreactor
7	GND	Earth/Ground reference for all signals
12	IRXD+	RS-422 paired data input to bioreactor
24	IRXD-	
13	ITXD+	RS-422 paired data output from bioreactor
25	ITXD-	
21	IOS	Open selects RS-232 Earthed/ Grounded selects RS-422

Unless otherwise requested, the baud rate is factory-selected at 19200 (Modbus) and the connector is configured as an RS-232 port: i.e., no jumper between pin # 7 and pin # 21. The factory-set address for the machine is 8.

6 Preparation and calibrations

6.1 pH calibration

The pH probe provided as standard with this system is a reusable optical probe, which works in conjunction with a disposable fluorescent pH sensor; the light that blinks at the tip of the probe when it is plugged in to the control cabinet is not dangerous to your vision. An optional gel-filled pH probe is also available.

To ensure proper calibration of the sensor and to compensate for any discrepancy, you will need an accurate external pH meter.

1. Press the Calib. Button at the bottom of the SUMMARY screen to open the CALIBRATION screen:

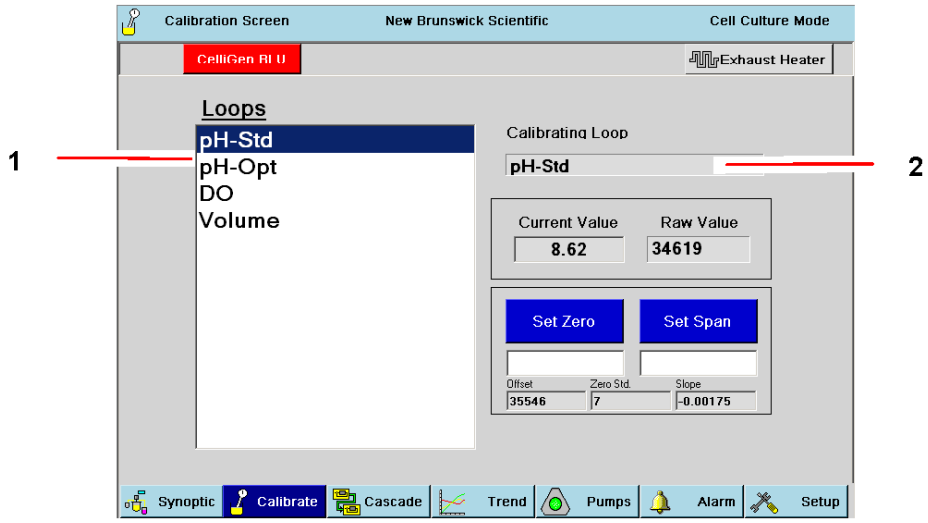

Fig. 31: Calibration Screen

1 Loops pane	2 Calibrating loop box

2. Press pH-Opt in the Loops pane (or pH-Std if you are using a gel-filled probe), and your selection will appear in the Calibrating Loop box.

---

pH-Opt means “optical” which is standard with the CelliGen BLU. pH-Std means industry “standard” gel-filled pH prove, which is optional on the CelliGen BLU.

When pH-Opt is selected in the Loops pane, a new Probe Data button appears.

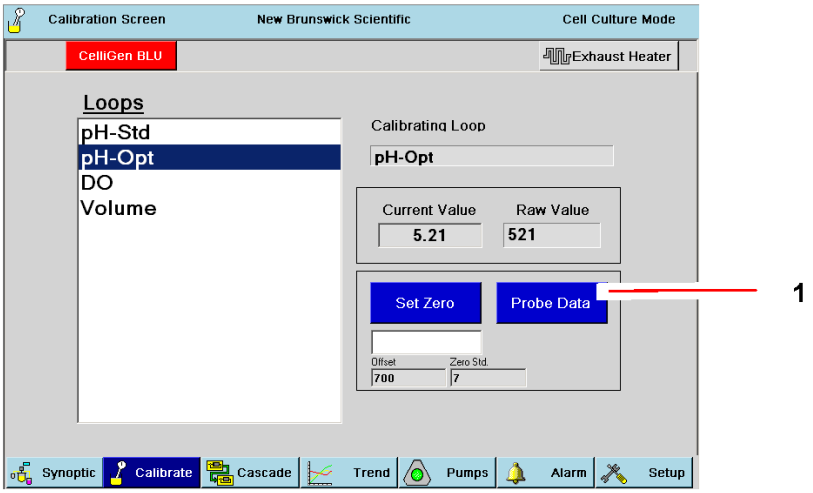

Fig. 32: Selecting the pH-Opt Loop

3. If you have selected pH-Std, skip to Step 6. If you have selected pH-Opt, press the Probe Data button to open the PROBE DATA screen:

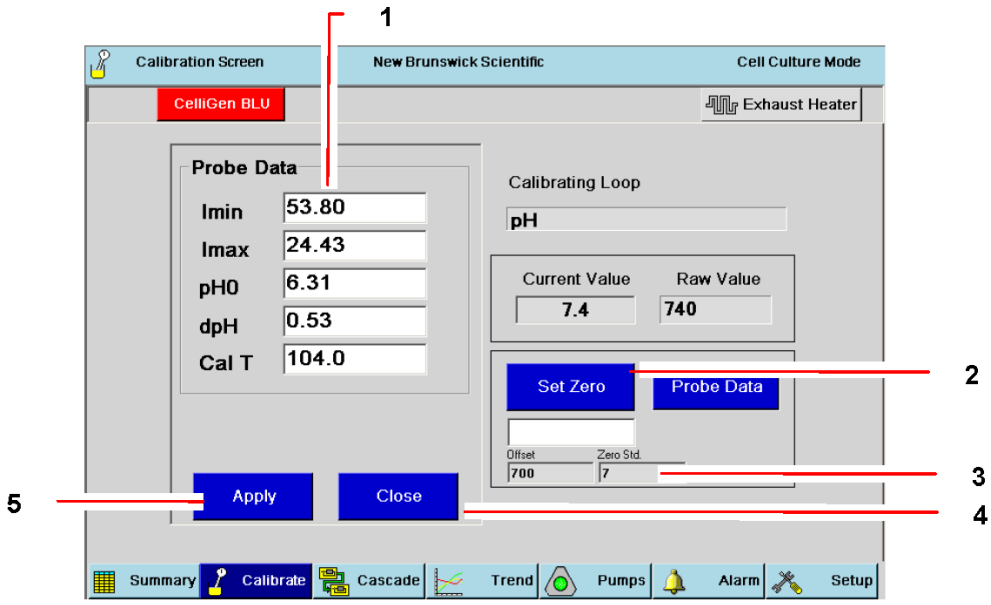

Fig. 33: Probe Data Screen

1 Probe Data edit boxes	**2 Set Zero button**
3 Set Zero edit box	**4 Close button**
5 Apply button	

4. As marked on the label on the bottom of your vessel (and also on the vessel box and on the lightproof vessel wrapper), enter the Imin, Imax, pH0, dpH and Cal T values in their respective edit boxes of the PROBE DATA screen by pressing the box, using the popup touchpad to type the number, then pressing the touchpad OK button.
5. When all values have been entered, press the Apply button.

6. Take a sample of media (see *Sampling the vessel on p. 95)* and measure the pH using the external meter.
7. Press inside the edit box below the Set Zero button and, using the popup touchpad, enter the value of measured pH from Step 6. Press the OK touchpad button to save the value.
8. Press the Set Zero button.
9. Press the Close button.

It may take as long as 20 minutes from the time the vessel is filled with media for the pH sensor to become saturated and begin to provide readings. If, however, it takes longer there may be an air bubble trapped on the sensor. Tap the vessel lightly and/or jiggle the pH sensor tube to dislodge it. See also Section xx regarding use of the pH probe bubble breaker.

A Raw Value indication of 9999 means that the values you have entered are incorrect or that the pH probe is either not connected or not functioning properly.

You can expect to see a very slight drift (~0.02 pH units per day) in your pH value due to the inherent properties of optical pH sensors.

1. We recommend that you recalibrate the probe every 3 - 5 days.
2. To recalibrate, take an offline measurement, enter that value into the Set Zero edit box and press the Set Zero button.

6.2 Use of pH probe “bubble breaker”

Delays in pH signal response, such as a Raw Value of 0 in the CALIBRATION screen, may be caused by air bubble attachment, which prevents saturation of the pH sensor spot. In the event of air bubble attachment, if tapping the vessel and/or jiggling the pH sensor tube does not dislodge the bubble, use the bubble breaker provided with your CelliGen BLU:

1. Remove the pH probe/transmitter.
2. Insert the bubble breaker into the pH sensor tube until its plastic top makes contact with the end of the tube.
3. Apply moderate downward pressure.
4. Repeat steps 2 and 3 until you see the bubble detach from the tube.
5. Remove the bubble breaker.
6. Reinstall the pH probe/transmitter in the pH sensor tube.
7. Verify that the controller is reporting a Raw Value for the optical pH loop. It may take up to 20 minutes for the probe to become fully saturated and begin to provide readings.

6.3 DO probe polarization

If the probe has been disconnected from a voltage source (either the system’s O2 amplifier or a separate polarizing module) for longer than 5 minutes, re- polarize it.

NOTICE!

Risk of damage to system!

- Never attempt to operate the system if the DO probe is not installed with its cable connected to the control cabinet.

To polarize the DO probe:

1. Connect the probe to the operating O2 amplifier (or polarizing module).
2. Allow six hours for polarization prior to calibrating the probe.

6.4 DO probe calibration: setting zero

There are two methods to obtain zero for calibrating the DO probe. Review both methods and use the one you prefer:

Method 1:

1. Remove the DO cable from the DO electrode.
2. Go to the CALIBRATION screen and select DO.
3. Enter 0 in the Set Zero edit box, then press Set Zero.
4. Reconnect the DO cable to the DO electrode.

If you use Method 1, make sure the probe is not disconnected for more than two minutes.

Method 2:

Nitrogen is needed for Method 2. There is an N2 gas inlet on the control cabinet for this purpose. Make sure that your nitrogen source is connected to this inlet.

1. Connect the DO cable to the DO electrode and the control cabinet.
2. Go to the CALIBRATION screen and select DO.
3. Press the N2 (3) ON button. If your system has 3 or 4 TMFCs, however, this button will not be present. In this case, manually turn the N2 loop on from the SUMMARY screen and set it to the maximum setting (depending on vessel size and flow controller).
4. Set Agitation to at least 50 rpm.
5. In approximately 10-30 minutes, the current value reading will stabilize.
6. Press the Set Zero edit box, use the touchpad to enter 0, press the OK button, then press the Set Zero button.
7. Press N2 (3) OFF (or, if in Step 3 you manually turned the N2 loop on, now manually shut off the nitrogen flow to the vessel).

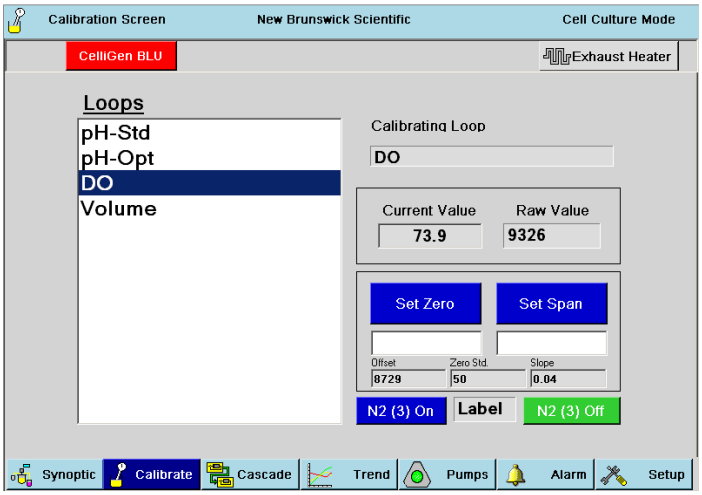

Fig. 34: Calibrating DO

6.5 DO probe calibration: setting span

1. In the AGIT GAUGE screen, set the AGIT speed to 50 rpm.
2. Set the AGIT mode to AUTO.
3. Sparge air into the media (at a rate of 0.01 VVM for microsparge or 0.1 VVM for macrosparge) until the display is stable for approximately 10 minutes (this may take up to 30 minutes total).
4. In the CALIBRATION screen, select DO
5. Enter 100 in the Set Span edit box, then press the Set Span button.

6.6 Scale/Volume calibration

If you do not have the optional scale, skip this section.

Before connecting the scale to the controller, be sure to pull off the plastic clips that immobilized the scale for shipping.

The scale is calibrated using a two-point calibration method:

1. Make sure the scale is properly connected to the control station. It is also a good idea to add a User-Defined Loop for the Scale (see *Adding loops on p. 35)*.
2. Press the Calib. button to open the CALIBRATION screen, then press Volume in the Loops pane.
3. Place a graduated cylinder or Ehrlenmeyer flask on the scale and allow the reading to settle.

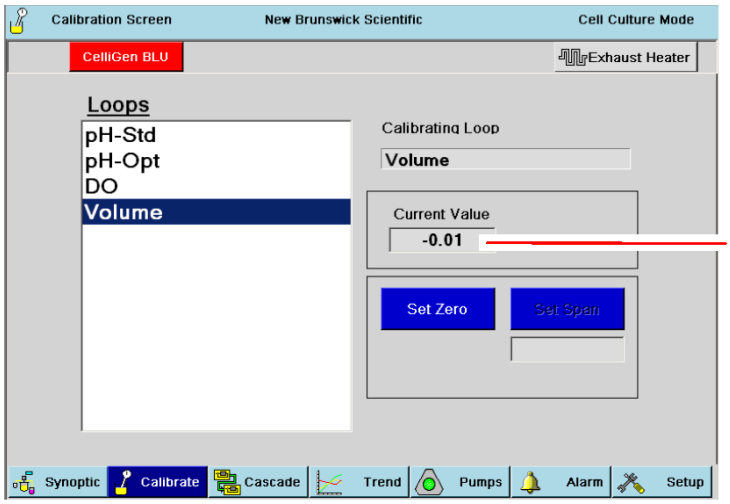

Fig. 35: Setting Zero for Scale/Volume Calibration

1	**Current Value arbitrary reading**

4. Allow the Current Value time to settle.
5. Press the Set Zero button.
6. Fill the cylinder or flask to a known quantity of water (e.g., 1.0 liter).

7. Enter the liquid volume in the Set Span edit box.

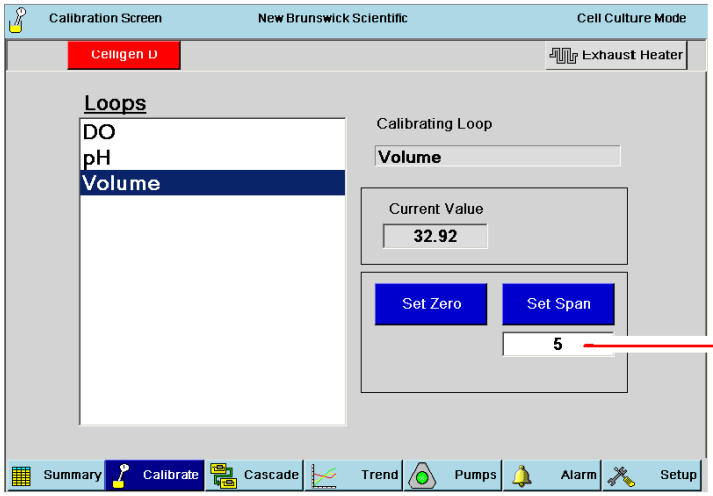

Fig. 36: Setting Span for Scale/Volume Calibration

1	**Set Span edit box**

8. Place the filled container on the scale, then press the Set Span button.
9. Remove the container from the scale and place the complete CelliGen BLU vessel assembly (with motor, heat blanket and exhaust heater but without media) on the scale. Press the Set Zero button.

The scale is now calibrated and will measure the weight of liquid added or removed from the vessel.

7 Getting started

7.1 Control modes

A control mode is the logic by which a controller generates the desired control signal. The operator has a choice of control modes, the most common of which are ON, OFF, AUTO and MANUAL.

In cascaded control, one sensor influences an actuator that is normally associated with a different sensor. The onscreen control mode choice will be the name of the loop chosen to have influence on the actuator.

7.2 Setting P & I values

P & I values are numbers that determine how the bioreactor responds to changing growth conditions and new setpoints. These are listed in each loop's GAUGE screen.

You may need to modify P & I values to suit your particular process. To do so:

- press inside the Proportional and Integral edit boxes, each time entering the desired value using the popup touchpad.

If you change P & I values, you can return to the original settings at any time by pressing the Factory Default button.

7.3 Loop setpoints

The setpoint is the value you want each loop to attain. When the loop control mode is AUTO, the bioreactor will automatically make appropriate adjustments to maintain the value at the setpoint.

7.3.1 Entering setpoints

To enter a setpoint for any loop, follow these steps:

1. Touch either the LoopName box or the Setpoint box for the desired loop on the SUMMARY screen. In this example, we have selected AGIT.
2. In the loop GAUGE screen (see Fig. 37 on p. 51), press inside the Setpoint box to open the touchpad.

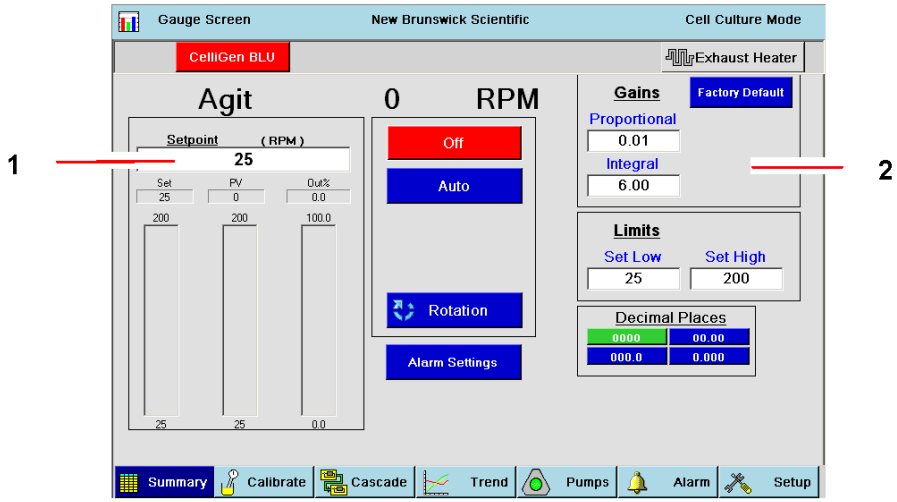

Fig. 37: Sample GAUGE Screen

1 Setpoint edit box	**2 P&I Values: adjusting these values will determine how your system responds to changes in your culture.**

3. Use the touchpad number keys to enter the desired Setpoint. At any time before Step 4, you may use the white Clear button to empty the Setpoint edit box.

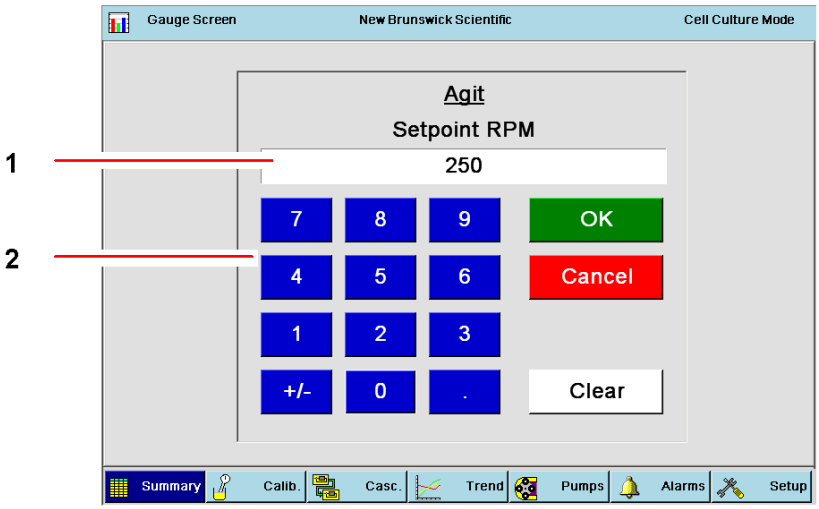

Fig. 38: Setpoint Touchpad

1 Note that Agitation cannot be set higher than 200 rpm; the system will default to 200 if you try to input a higher number.	**2 Number keys**

4. Press the OK button to save the setpoint and to return to the GAUGE screen, or press the Cancel button to return without saving the setpoint

7.3.2 Modifying setpoints

This process is the same as entering setpoints.

- For instructions, (see *Entering setpoints on p. 51)*.

7.4 Cascade system

Cascading brings several systems together to work jointly for the achievement of your goal. An example of how this works would be controlling pH by using a cascade from a pump: as the pH alters from the setpoint, the program would cause the pump to turn on and off to compensate.

- For details about setting cascades, (see *Cascade control on p. 55)*.

7.5 Pump assignment

The user has the ability to assign each pump present in the system.

To assign a pump:

1. From any screen, press the PUMPS button at the bottom to open the PUMPS GAUGE screen:

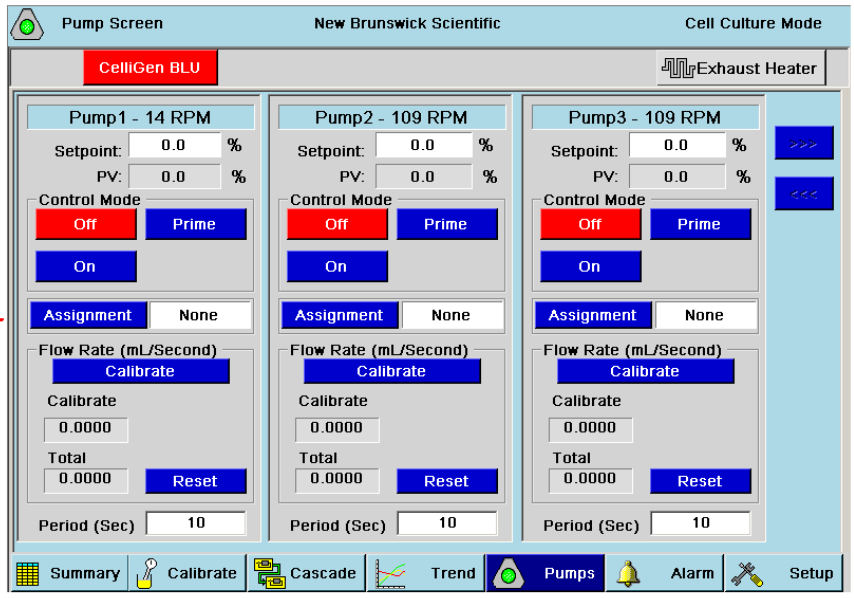

Fig. 39: Pumps Screen

1 **Assignment button**

2. Press the Assignment button to show the Pump Assignment pane for that pump. Our example is for Pump1.
3. Press the button that corresponds to your choice of assignment for the pump:

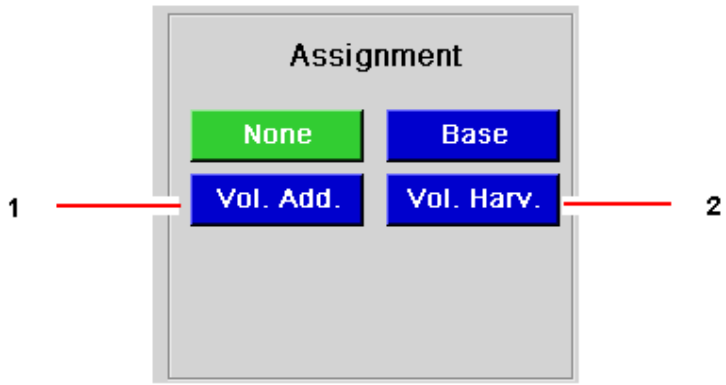

Fig. 40: Pump Assignment Pane

1 **Vol. Add. = Volume Addition (see Section 8.7.1)**	2 **Vol. Harv. = Volume Harvest (see Section 8.7.2)**

4. Repeat Steps 2 and 3 for any other pump(s) to be assigned.
5. Press the Summary screen access button to save the pump assignment(s) and to return to the SUMMARY screen.

7.6 Pump calibration

For pump flow rates, (see *Pump flow rate and calibration methods on p. 71)*. However, more accurate flow rates through the various lines may be established by pre-calibrating the pumps, using the PUMPS screen (see *Pump flow rate and calibration methods on p. 71)*. This screen controls all pump parameters for the three standard fixed speed pumps supplied with the control cabinet and for any additional pumps added through the available analog input and output connections.

Using the PUMPS screen, you can view total pump flow rate in ml/second, set the pump's cycle time, and assign each pump to one of four functions (None, Base, Vol Add and Vol Harv; these last two are explained (see *Using optional scales to program pumps on p. 54)*.

To assure the most accurate flow rate, calibrate the pump (see *Pump flow rate and calibration methods on p. 71)* each time you change tubing.

7.7 Using optional scales to program pumps

7.7.1 Setting a feed pump to add liquid

A feed pump can be set to add liquid whenever the optional load cell/scale informs the pump that an addition is needed to maintain level.

1. Open the PUMPS screen.
2. Select the feed pump you wish to pump liquid from your addition system (see *Install liquid addition systems on p. 74)* into the vessel, and press that pump's ASSIGNMENT button to open the PUMP ASSIGNMENT pane.

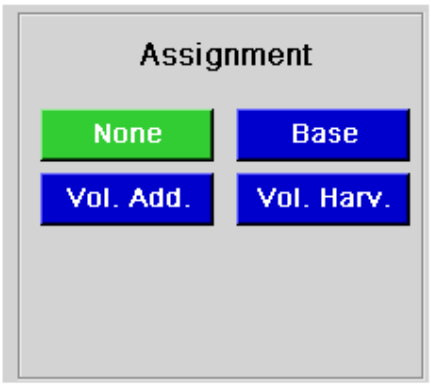

Fig. 41: Pump Assignment Pane

3. Press the Vol. Add. Button.
4. Press the Summary screen access button to save the pump assignment and to return to the SUMMARY screen.

7.7.2 Setting a pump to harvest vessel contents

A pump can be set to harvest liquid when the scale informs the pump that the harvest setpoint has been reached.

1. Open the PUMPS screen.
2. Select the pump you wish to harvest contents from your vessel (after aseptically setting up your harvest system), and press that pump's Assignment button to open the PUMP ASSIGNMENT pane (see Fig. 41 on p. 54).
3. Press the Vol. Harv. button, then press Summary to save the pump assignment and to return to the SUMMARY screen.

8 Cascade control

8.1 General cascade control

Cascades are control schemes in which the Output % of one process control loop influences the setpoint of one or more other loops. In other words, it uses feedback from one parameter to influence others. In New Brunswick Scientific's CelliGen BLU bioreactors, the output % value is mathematically determined by evaluating the error between measured present values and desired setpoints, and integrating these values into a PID-based control algorithm.

The CelliGen BLU's RPC controller allows cascading from any loop to as many as five other loops. DO and pH are the most commonly cascaded-from loops; oxygen, air and nitrogen commonly receive the cascade from DO, and CO_2 and Base pump usually receive the cascade from pH.

When more than one loop is configured as the recipient of a cascaded loop, they may respond in parallel, at the same time, or in series, one after the other, depending on how the cascade has been set up. Cascades set up to run in series generally give more predictable control responses. Sometimes a small region of overlap, where two loop setpoints vary simultaneously, is used to smooth the transition from one loop to another.

NOTICE!

Risk of equipment damage by overpressurization!

- Check all user-entered setpoints for gas flow: maximum combined gas flow for both the sparge and overlay must not exceed 7.5 SLPM.

To enable cascades:

- gas loops must be in Manual/Cascade mode, which can be selected from the GAUGE screens,
- and all other loops involved in the cascades must be set to Auto or, in the case of pumps, set to ON.
- When Manual/Cascade mode is selected, the controller automatically populates default cascade values for the gases being used, but make sure all loops involved in the cascades are set to Manual/Cascade mode.
- Each cascade must be enabled (see *Creating a cascade on p. 56)*.

The default cascade values can be overwritten, and customer values can be entered using the procedures outlined in this section.

8.2 Creating a cascade

Below (see Fig. 42 on p. 56) shows the headers from the CASCADE screen (set to “Cascade From DO”), with an explanation of the settings those headers represent:

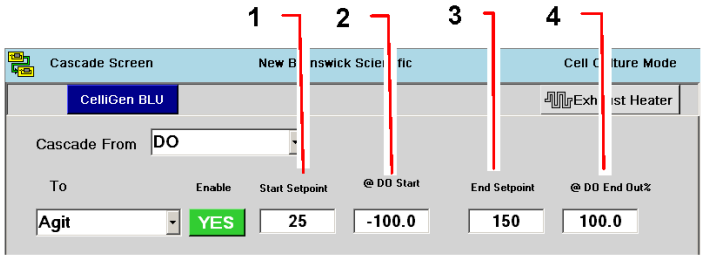

Fig. 42: Cascade Screen

1 Start Setpoint is the loop value the user defines for the system to be at when initial DO Start Out% is reached. Typically this value will be close to the normal operating setpoint.	**2 @DO Start Out% represents the DO output % value where the user wants the cascade to begin. When this output % is reached, the setpoint of the Cascade To loop will change to the value entered as Start Setpoint. The current DO output % can be found on the SUMMARY screen at the intersection of the Output% column and the DO loop row. This value is calculated by using the integrated PI values. It is essentially a mathematical calculation of setpoint “error” from PV (current process value), “error” meaning any readings that are above or below the programmed setpoint. As the “error” discrepancy increases, or as the duration of such a discrepancy remaining static increases, the Output% also increases.**
3 End Setpoint is the loop value the user defines as the maximum allowable value when the DO End Out% is reached. Typically this value will also be the same as the system’s maximum allowable setpoint for the loop.	**4 @DO End Out% represents the DO output % where the user wants the cascade to stop. This value can be set to any integer from 0 to 100% as long as it is greater than the Start Out%. The greater it is than the Start Out%, the smoother the increase in setpoints.**

It is important to remember that cascades are based on the loop (whether DO or pH) Out% value posted in the SUMMARY screen. These numbers are the basis for all cascades involving that loop. See the examples below for more explanation.

It can be a very beneficial exercise to watch how the values on the SUMMARY screen change to reflect differences between the present value (PV), the setpoint, and the DO output percentage (Out%).

When the PV is greater than the setpoint, the system will be generating a negative Out% because the controller senses a need to decrease DO:

LoopName	PV	Setpoint	Out%	Control Mode	Units	Casc.
DO	74.8	35.0	38.6	Auto	%DO	Source

When the PV is less than the setpoint, the system will be generating a positive Out%, because the controller senses a need to increase DO:

LoopName	PV	Setpoint	Out%	Control Mode	Units	Casc.
DO	25.2	35.0	51.6	Auto	%DO	Source

When the PV equals the setpoint, the Out% should be approximately 0, as the controller senses no need to make adjustments to DO:

LoopName	PV	Setpoint	Out%	Control Mode	Units	Casc.
DO	35.2	35.0	0.0	Auto	%DO	Source

To create a cascade:

1. Press the CASCADE button to open the CASCADE screen (see below).
2. Use the Cascade From edit box dropdown menu button to select the “Cascade From” loop.

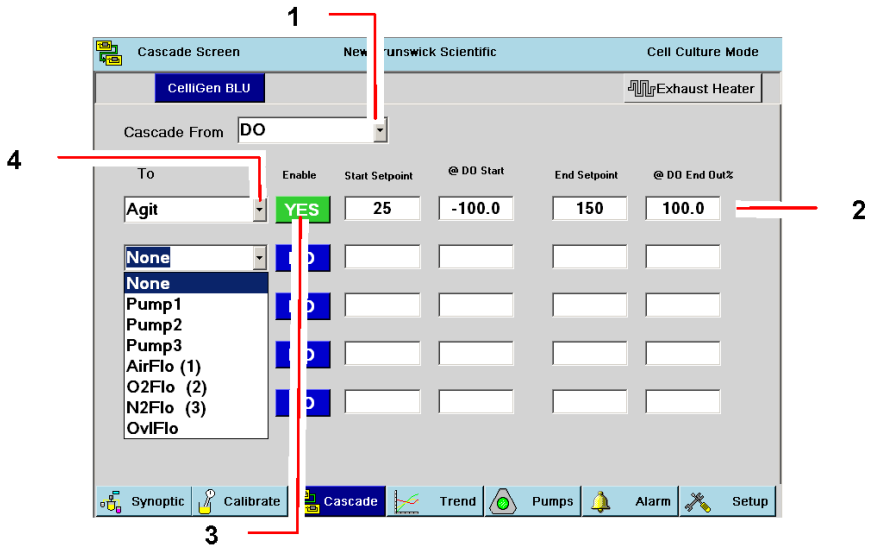

Fig. 43: Cascade Screen

1 Cascade From edit box dropdown menu button	**2 Cascade To loop setting boxes**
3 Enable button	**4 Cascade To edit box dropdown menu button**

3. Use the first To edit box dropdown menu button to select the first “Cascade To” loop.
4. Set the Start Setpoint, @DO Start Output%, End Setpoint and @DO End Output% values one by one by pressing the edit box, entering the desired value on the touchpad and pressing the OK button.
5. Enable the cascade by pressing its Enable button to change it from NO to YES.

9 Gas mixing for PH and DO control

9.1 General

CelliGen BLU systems come equipped with 3 thermal mass flow controllers (TMFC) and one overlay with or without a TMFC.

These TMFCs can be configured as either High Flow (0.04 – 7.5 SLPM) or Low Flow (0.002 – 1.0 SLPM). A switch between these configurations is possible using the Controller Setup screen (see *Selecting gas flow range on p. 84)*.

Your system is capable of operating in either 3-gas or 4-gas control mode. 3-gas uses air and O_2 to regulate DO and CO_2 to regulate pH; 3-gas mode does not include N_2. 4-gas mode uses air and O_2 as well as N_2 for the control of DO and CO_2 to control pH.

Depending on how your system is configured, you may find that the high limit for CO_2 is below the high limit of its associated flow controller. This limit is imposed to prevent oxygen starvation while adjusting pH with CO_2.

NOTICE!

Risk of equipment damage by overpressurization!

- Check all user-entered setpoints for gas flow: maximum combined gas flow for both the sparge and overlay must not exceed 7.5 SLPM.

9.2 Gas control

Your CelliGen BLU controller is configured with three TMFCs but is capable of 3-gas or 4-gas mixing as there is a solenoid valve between O_2 and N_2. These two gases cannot be used at the same time because they use the same TMFC.

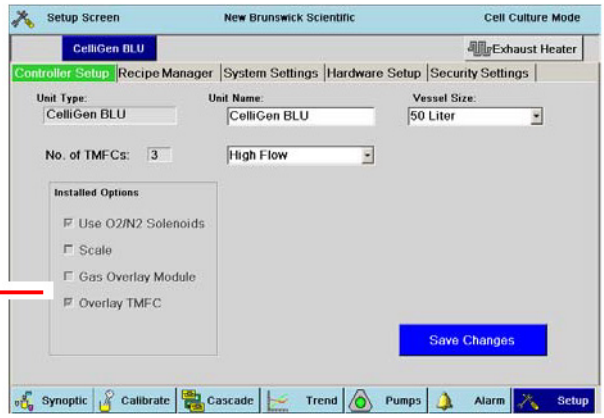

Fig. 44: Controller Setup Screen

1	**See Section 10.2 for details on the Gas Overlay.**

In the various gas GAUGE screens, you will have access to Manual/Cascade, 3-Gas Auto and 4-Gas Auto control modes.

The gas process loops you will find in the SUMMARY screen are labeled AirFlo (1), O2Flo (2), N2Flo (3) or CO2Flo (4). Their numbers 1-4 correspond to the gas connections on the cabinet.

With three TMFCs, when you set any gas gauge to Manual/Cascade, Air, O2 and CO2 setpoints can either be manually entered in their individual gas gauge screens or they can be controlled by cascades:

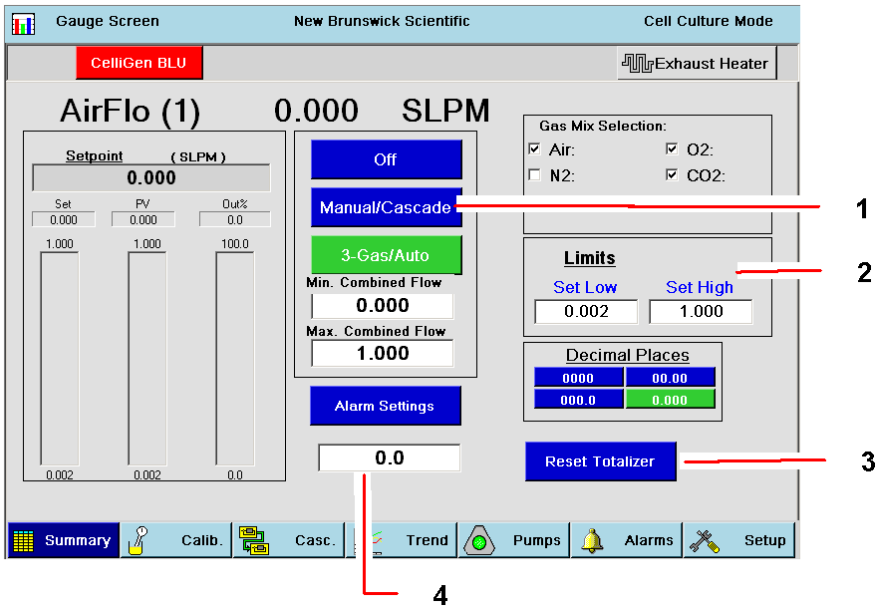

Fig. 45: AirFlo (1) Gauge in Manual/Cascade Mode

1 Manual/Cascade mode has been selected; the button is green.	**2 NOTICE: Gas flow limits are displayed in CCM or SLPM, not percentages.**
3 Use the Reset Totalizer button at any time to return to 0.0 and begin counting again.	**4 The Totalizer feature tracks and displays the accumulated flow for the associated loop; here it measures accumulated air flow.**

To reduce the risk of clogging in microsparge vessels, minimum gas flow should not be set below +2 CCM.

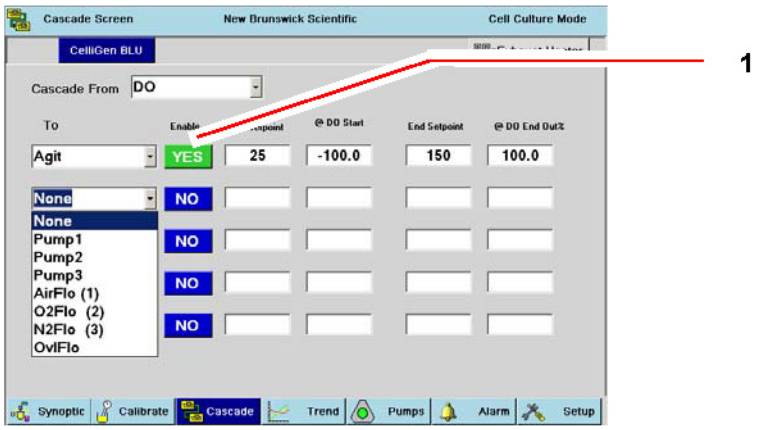

Fig. 46: Sample Cascade Screen

1 Press each loop's Enable button to activate automatic cascade control.

Cascade values are automatically controlled, but first you must activate them by selecting each loop's Enable button in the CASCADE screen.

Default Out % values are presented as starting points. Loop setpoints will need to be entered by the user.

When you set the system to the 3-Gas/Auto control mode, the controller automatically adjusts the flow ratio of Air, O_2 and CO_2 based on the demands of pH and DO. The Minimum and Maximum Combined Flow fields allow limits to be set to the total gas flow to prevent too much gas being injected while also maintaining a total positive flow.

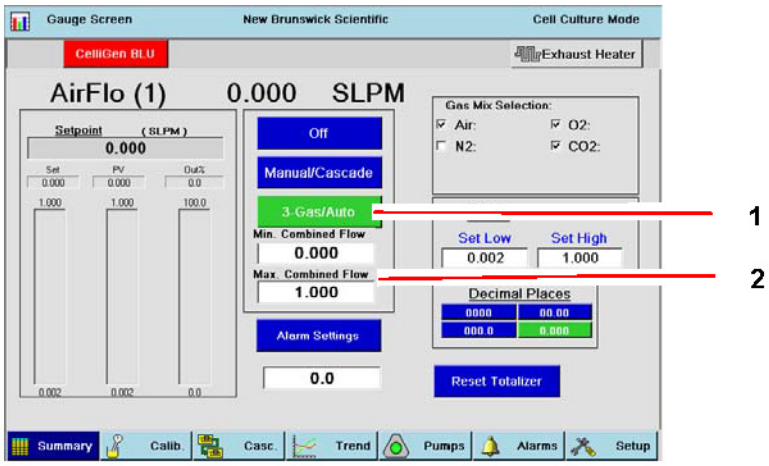

Fig. 47: AirFlo (1) Gauge in 3-Gas/Auto Mode

1 3-Gas/Auto mode has been selected; the button is green.	**2 NOTE that these fields are not for GasFlo Cascade; they are for Minimum and Maximum Combined Flow settings, as explained in the text above this figure.**

To reduce the risk of clogging in microsparge vessels, minimum gas flow should not be set below +2 CCM.

9.3 Gas overlay mixing

As shown in the screen below, when the Gas Overlay is set to Automatic Flow Control, two additional process loops will be present in the SUMMARY screen: OvlMix (Gas Overlay Mix) and OvlFlo (Overlay Gas Flow).

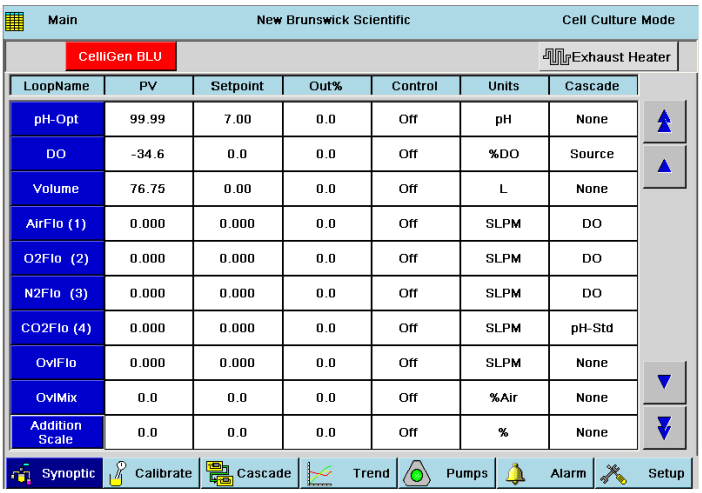

Fig. 48: Summary Screen with Overlay Loops

If no TMFC is present, only the OvlMix process loop will be available and the flow must be controlled manually by means of a Rotameter.

1. Open the OvlMix loop gauge screen, as shown below, to set the parameters for the Gas Overlay:

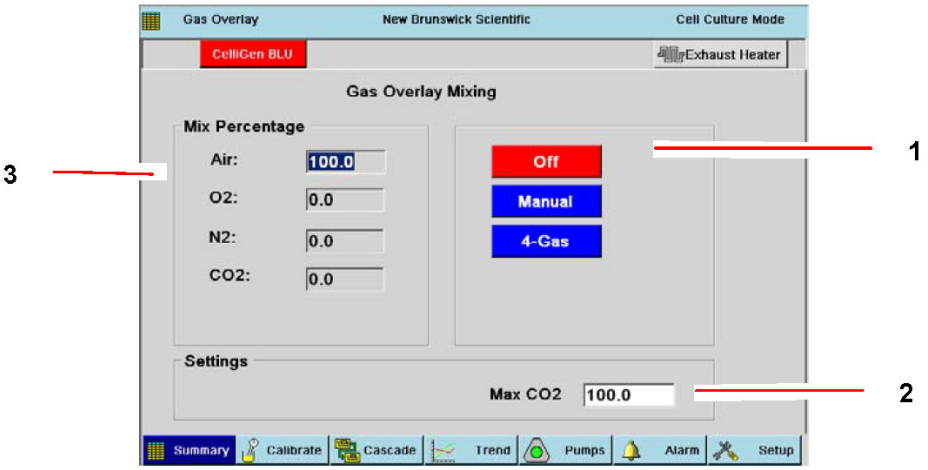

Fig. 49: OvlMix Gauge Screen

1 Operating Mode buttons	**2 Max CO2 edit box**
3 Mix Percentage edit boxes	

2. Press the button that represents your choice for the Gas Overlay operating mode (see Tab. on p. 62).

There is no 3-Gas mix option for gas overlay.

3. If you have selected Manual mode, use the Mix Percentage edit boxes to set the percentage for O2, N2 and CO2 as desired; the system will automatically set Air so that all gases total 100%.
4. If desired, use the Max CO2 edit box to set a maximum CO2 percentage. This is for 4-Gas mode only.

Tab. 6: Gas Overlay Operating Modes

Operating Mode	Description
Off	Press this button to turn the Gas Overlay off.
Manual	Press this button to program the mix percentage of each gas yourself.
4-Gas	Press this button to leave automatic gas mixing to the controller. This selection disables user input to the Mix Percentage pane.

10 Plotting trends

10.1 General

Opening the TREND screen allows you to plot and display a graph of ongoing culture data, viewing from 30 minutes to 144 hours of input. Up to 8 loops can be plotted on the graph, each in its own distinctive user-selected color. The graph and data are only available while the bioreactor is running.

Data cannot be stored in the controller, but can be saved to a USB storage device in MS Excel® format. The controller can also be connected to New Brunswick BioCommand® on a PC for supplemental data storage and archiving (see *Analog inputs/outputs and RS-232/-422 computer interface on p. 42)*.

10.2 Creating a trend graph

1. From any screen, press the TREND button to open the TREND screen:

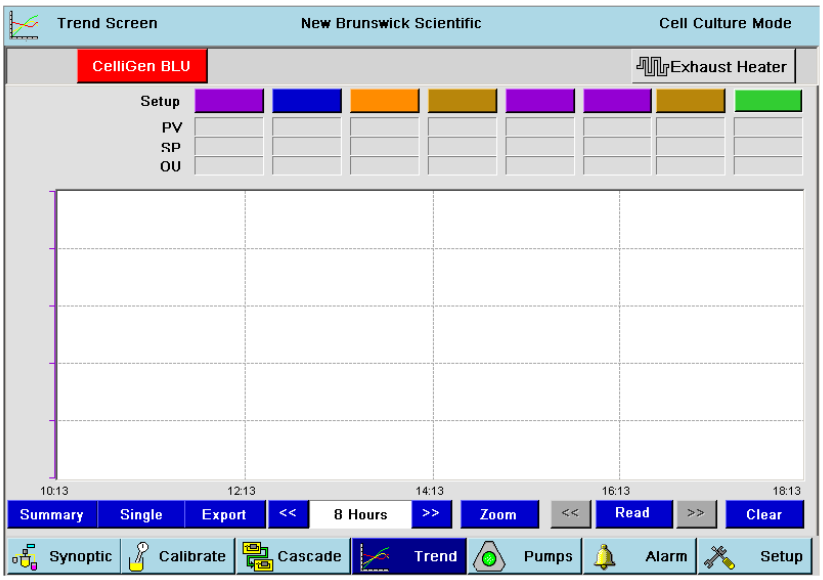

Fig. 50: Trend Screen

2. To select the first loop you wish to display, press the first (far left) Setup button, which is red.
3. In the Trend Setup screen that opens (see Fig. 51 on p. 64), select the loop from the list in the Loops pane.

   The program will automatically place it in the red box.

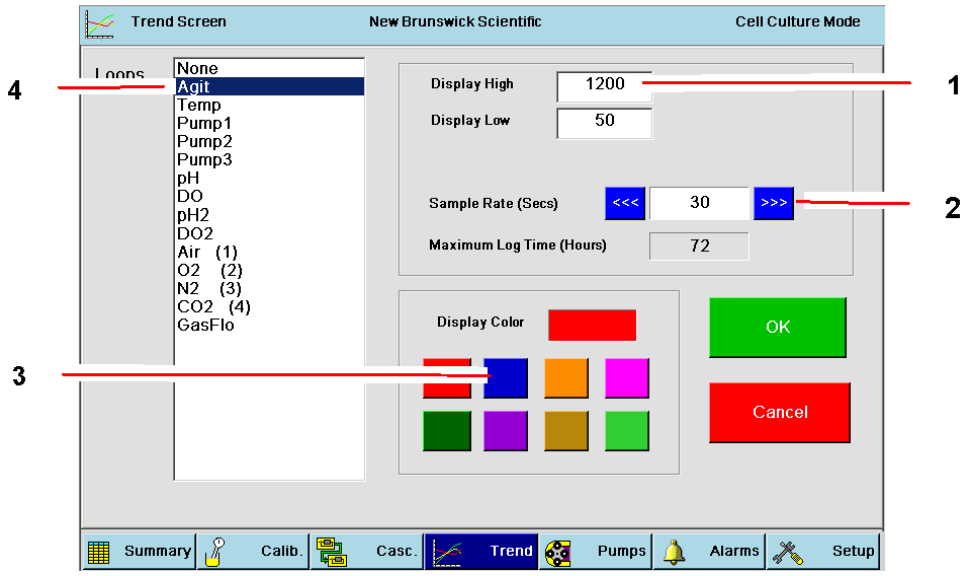

Fig. 51: Trend Setup Screen

1 Display High and Display Low edit boxes	**2 Data sampling rate interval**
3 Display Color pane	**4 Loops pane**

4. If you wish to change the color of this loop, press the colored button in the Display Color pane that corresponds to your choice.
5. Press the Display High box to enter (using the touchpad) the high limit for the Y axis, then use the Display Low edit box to set the low limit.
6. Set the Sample Rate (the desire data sampling interval) by pressing the ramp up >>> or ramp down <<< button to select 5, 15, 30 or 60 seconds.
7. Press OK to save your choice and return to the TREND screen, or Cancel to return to the TREND screen without saving any changes.
8. Repeat Steps 2 – 7, selecting a different color for each loop, up to a maximum total of 8 loops.

9. A sample trend graph is shown below (see Fig. 52 on p. 65) and (see Tab. on p. 66) to acquaint yourself with the Trend Graph buttons at the bottom of the graph.

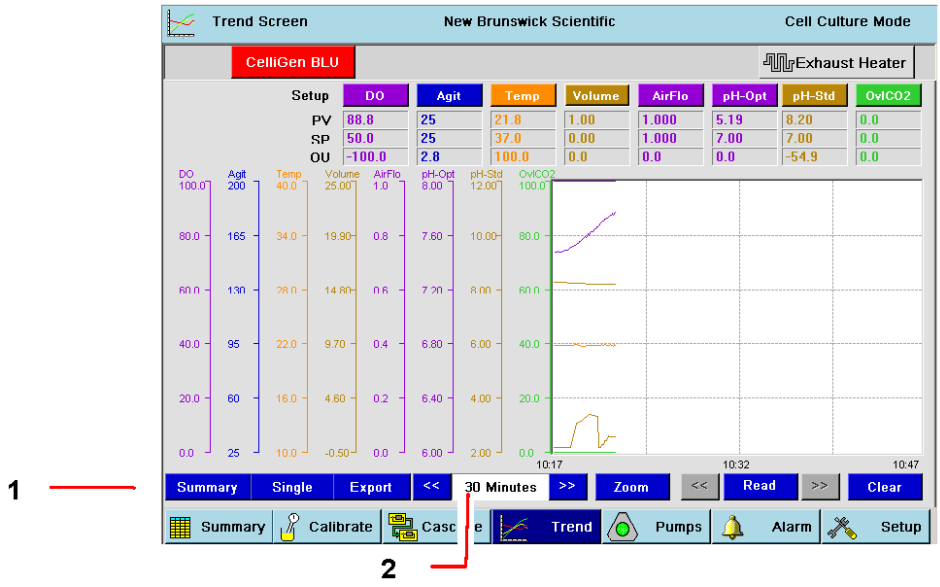

Fig. 52: Trend Graph

1 Trend Graph buttons (see Table 7 for more information)	**2 Timespan Indicator**

Tab. 7: Trend Graph Buttons

Button/Feature	Description
Summary	Press this button to cycle through three summary display modes: all eight loops at once, loops 1-4, and loops 5-8.
Single	Press this button to display the graph for one loop at a time, in the order (left to right) they are displayed in the colored buttons at the top of the screen.
Export	Press this button to export a text file containing all of the Trend data.For detailed instructions, (see *Using the Export button on p. 66)*.
<<< Ramp Down	Press this button to select a lower Timespan or to move the Read Line toward the left of the screen.
[Timespan Indicator]	Using the Ramp Down or Ramp up button on either side of this edit box, select the timespan to display onscreen. Preset increments range from 30 Minutes to 144 Hours.
>>> Ramp Up	Press this button to select a higher Timespan or to move the Read Line toward the right of the screen.
Zoom	Press this button to open an interactive mode where you can zoom in on a section of interest on one plot. The button turns red when you touch it, indicating you are in Zoom mode.For detailed instructions, (see *Using the Zoom button on p. 67)*.
Read Line	Press this button to open an interactive mode where you can move a vertical (cross-sectional) line across the graph to aid in determining a particular reading.For detailed instructions, (see *Using the Read line on p. 68)*.
Clear	Press this button to clear all plots and data from the graph.

10.2.1 Using the Export button

To export Trend data as a text file to a USB external memory device for use with a PC program (e.g., Microsoft Excel®):

1. Install the USB external memory device into one of the USB connections on the back of the Control Cabinet.
2. Open the TREND screen and push the Export button.
3. In the screen that opens, select the USB external memory device from the list of available drives.

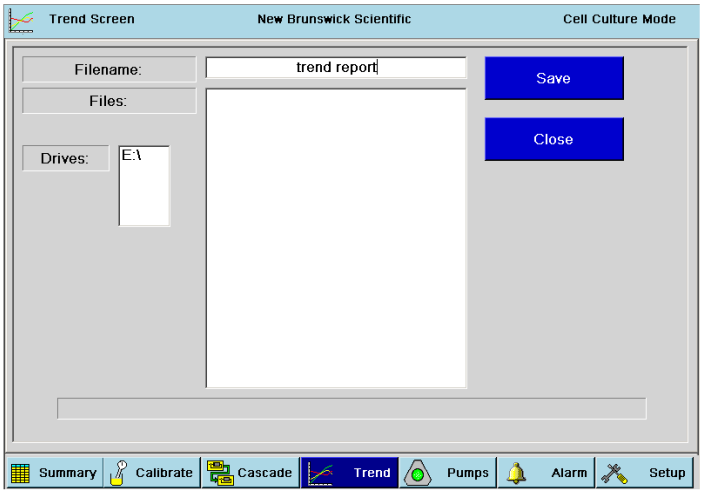

Fig. 53: Exporting Trend Data

4. Touch the empty FileName box. Using the touchpad that appears, enter the desired file name (“trend report” in the sample screen shown), then press the OK button.
5. Press the Save button to save the file to the USB external memory device.
6. Remove the USB external memory device and use it to download the data to your PC.

10.2.2 Using the Zoom button

To zoom in on a particular section of one loop plot:

1. Press the Zoom button at the bottom of the TREND screen. It will turn red to indicate that the zoom mode is active.
2. Press, in succession, two diagonal locations that would frame, left to right, the section of interest:

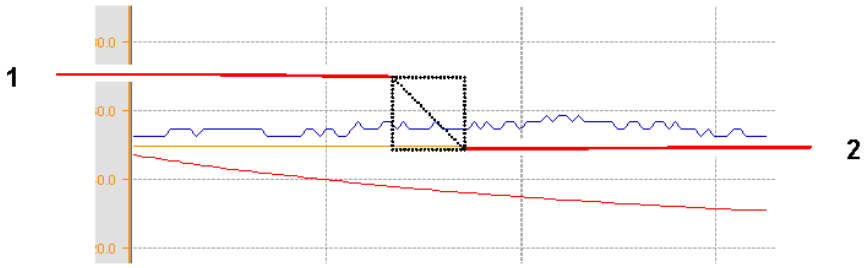

Fig. 54: Selecting Zoom Coordinates

1 Press first here (in the upper left corner of desired quadrant)	**2 Press second here (lower right corner of desired quadrant). NOTICE: the rectangle does not appear onscreen; it is indicated here for reference purposes only.**

3. The Trend view will display the data between the two points selected, and will adjust the time axis to match the elapsed time represented by this close-up.
4. Press the Zoom button again to return to the regular trend graph.

Minimum axis time in zoom mode is 120 seconds. If you wish to use the zoom mode and the read line (see *Using the Read line on p. 68)* at the same time, you must enter Zoom mode first.

10.2.3 Using the Read line

The Read line mode allows you to read PV values from the graph (displayed at the top of the screen) at a position you select. To use the Read line:

1. Press the Read line button at the bottom of the TREND screen. It will turn red to indicate that the read line mode is active, and black vertical line will appear at the current time position on the graph.
2. To move the line to a time of your choosing, press the graph at the desired point. You can also press the Read line <<< or >>> button (both are now red and active) to move the line one click at a time for more precision (see Fig. 55 on p. 68):

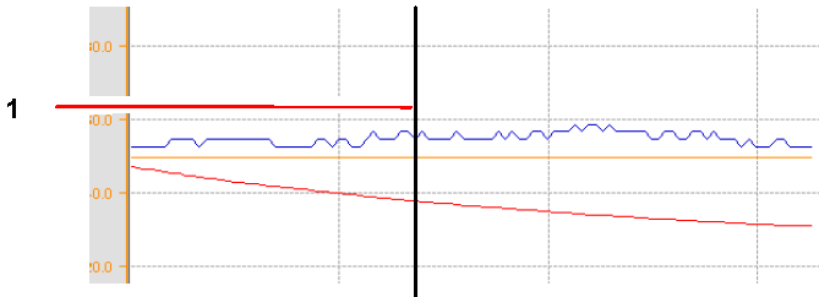

Fig. 55: Selecting a Read Line Location

1	**Press anywhere along the desired vertical axis to locate the read line.**

3. Press the Read Line button again to return to the regular trend graph.

If you wish to use the zoom mode (see *Using the Export button on p. 66)* and the read line at the same time, you must enter Zoom mode first.

11 About pumps

11.1 General

After assigning the pumps (see *Pump assignment on p. 52)*, you will need to select a setpoint and a control mode for each, calibrate their flow rates, and select their pulse periods. This section will walk you through those and other pump-related operations.

There are three peristaltic pumps on the front right of your control cabinet (see Fig. 56 on p. 69). The flow direction is from right to left.

- Remember to set up any optional pumps you may have added to your system ((see *Install an external variable speed pump on p. 73)* to install an external VS pump, and (see *Appendix A: Stackable pumps on p. 106)* about optional stacked pumps).

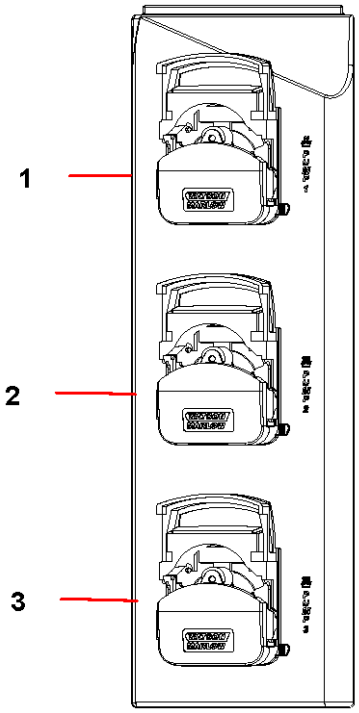

Fig. 56: Standard Pump Array (pumps open)

1 Pump1: 14 rpm	**2 Pump2: 109 rpm**
3 Pump3: 109 rpm	

11.2 Load pump tubing

As shown above, the three standard pumps are located on the front of the control cabinet.

Before you insert tubing into the pump channel, verify that the pump is in the OFF control mode, then follow these steps to properly load tubing into the pump:

1. Pull the upper pump cover upward to gain access to the interior of the pump.
2. Select the desired tubing size (see Tab. on p. 72) and cut a length sufficient to reach from the inlet source, through the pump, and to the outlet recipient, allowing a few extra inches.
3. Noting that the pumps run in a counter-clockwise direction, place the tubing snugly across the pump channel.
4. Close the upper pump cover by pulling it back down until it clicks into place.
5. Use the pump wheel on the right side (facing the pump) to set the channel to the diameter of your tubing.

6. Press and hold the pump mode Prime button or change the pump mode to ON at 100% setpoint and ensure that the pump operates smoothly.

A novel optional feature of these CelliGen BLU pumps is that you can add another identical pump onto the front of one of the pumps in the array (see *Appendix A: Stackable pumps on p. 106)*.

For details on pump assignment, (see *Pump assignment on p. 52)*.

11.3 Pump setpoint

To enter a setpoint for any pump:

1. Open the PUMPS screen. Gauges for Pumps 1-3 are displayed in this screen (see Fig. 57 on p. 70). If you have one or more additional pumps, press the >>> button to continue past Pump 3. If you have a stacked pump, it will be governed by settings for its base pump.

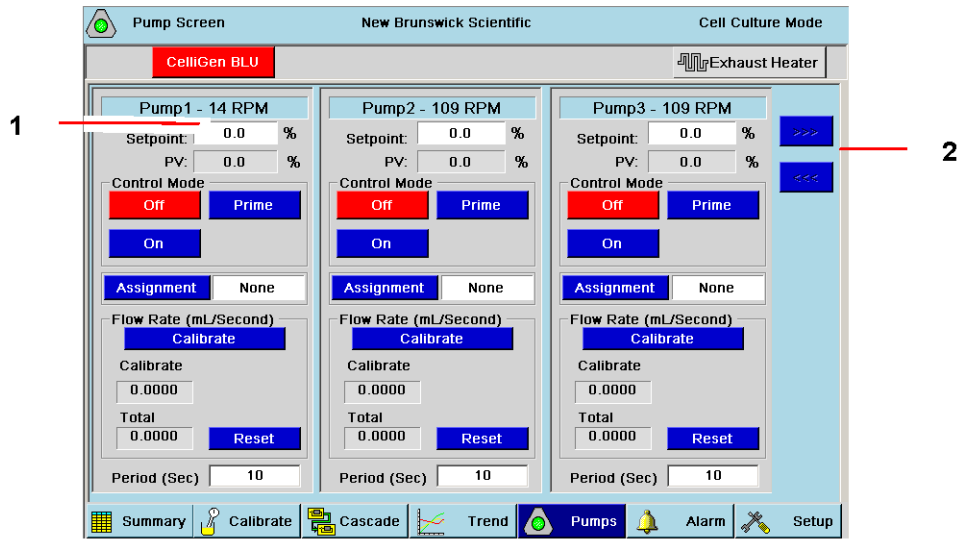

Fig. 57: Setting Pump Setpoint

1 Setpoint edit box	**2 If optional pumps are installed on your system, these ramp up (>>>) and ramp down (<<<) buttons will be active, allowing you to scroll to the next page or back.**

2. Press inside the Setpoint edit box for Pump1.
3. Use the touchpad that pops up to enter the desired setpoint, then press the OK button in the touchpad to save the setpoint and to return to this screen (or press the Cancel button to return to this screen without saving a setpoint).
4. Repeat Steps 2 and 3 for each pump.

11.4 Pump control mode

There are three available control modes for each pump, as explained below (see Tab. on p. 71):

Tab. 8: Pump Control Modes

Control Mode	Description
Off	The pump will receive no input and will not operate.
On	The pump will operate according to the parameters you have set.
Prime	This button toggles the pump on or off manually: as long as you press the button, the pump will run continuously. When you release the button, the pump will stop running.

If pumps are linked to a cascade, this may affect the ability to manually change setpoints and control modes.

To enter select a Control Mode for any pump, press the appropriate button in the Control Mode pane of the PUMPS gauge screen.

11.5 Pump flow rate and calibration methods

The pump will always run at the same speed, but their flow rate depends on the diameter of the tubing you use. Below (see Tab. on p. 72) provides the pump flow rates according to various tubing diameters.

Tab. 9: Flow Rate per Tubing Size

Tubing Wall Thickness	1.6mm (1/16 in)				
Tubing ID: mm (in)	0.8 (1/32)	1.6 (1/16)	3.2 (1/8)	6.4 (1/4)	8.0 (5/16)
14 rpm Flow ml/minute	0.84	3.50	11.90	42.00	56.0
109 rpm Flow ml/minute	6.54	27.25	92.65	327.00	436.0

To calibrate any pump with the tubing you have selected:

1. Load approximately three feet of the tubing into the pump head.
2. Set up a reservoir with water at the input end of the tubing and an empty graduated cylinder, capable of measuring small quantities, at the output end of the tubing.
3. Read this step completely before you do it: with the input end of the tubing in the water reservoir, prime the tubing line by pressing the pump's Prime button, but allow it to run only until liquid starts to flow into the tubing: DO NOT allow the liquid to run into the graduated cylinder yet.
4. If you are not using a scale, skip to Step 5. If you are using a scale, place the graduated cylinder (with the tubing) on the scale and press Zero on the scale.
5. In the Flow Rate pane of the PUMPS screen for that pump, press the Calibrate button to open the Calibration pane (see Fig. 58 on p. 72):

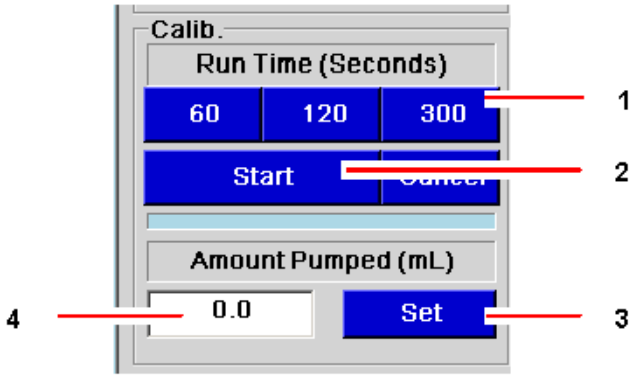

Fig. 58: Calibrating the Pump Flow Rate

1 Run Time selection buttons	**2 Start button**
3 Set button	**4 Amount Pumped edit box**

6. Press your choice of Run Time (60, 120 or 300 seconds); that button will turn green.
7. Press the Start button. The button will turn green and the pump will start running.
8. When the Run Time has elapsed, record the amount (mL) of liquid accumulated in the cylinder, then enter that number (or the number registered on the scale) in the Amount Pumped edit box.
9. Press the Set button to save this data to the PUMPS screen.

Calibration must be performed at operating setpoint.

Each pump and each tubing size will need its own calibration.

The pump is now calibrated. As the pump runs, you will see that the total will increase by this calibration standard.

Periodically adjust the tubing inside the pump heads to avoid excessive wear on and deformation of the tubing over time. Failure to do this may affect pump performance and calibration accuracy.

11.6 Pump period

At the bottom of each pump gauge is the Period (Sec) pane (see Fig. 59 on p. 73):

Fig. 59: Pump Period (Sec)

NOTICE!

Running at a very low percentage renders the totalizer's results inaccurate.

- We recommend the use of smaller tubing to avoid choosing a very low percentage for the pump setpoint.

- Use this edit box, and its associated touchpad, to enter a pump cycle time in seconds. For example, if the pump setpoint is 30%, setting a period of 5 seconds (as illustrated) will cause the pump to run 1.5 seconds, stop for 3.5 seconds, then cycle back on again.

11.7 Install an external variable speed pump

NOTICE!

Risk of damage to equipment!

- When selecting an external pump to operate with your system, please consult with your local sales representative to be sure the model you choose is compatible with your CelliGen BLU.

New Brunswick recommends, and provides for purchase, the Watson Marlow 120U series 0 – 200 rpm variable speed pump for use with your system.

NOTICE!

Risk of damage to system function!

- Be sure to set the dip switches correctly when using either 4 - 20 mA or 0 - 5 V inputs/outputs.

1. Connect the D connector of the pump's 3-wire cable at Interface on the rear panel of the pump. Your pump will be marked 120 V or 230 V, depending on the electric supply you specified when you purchased the pump.

Fig. 60: Variable Speed Pump

1	**Use Interface to connect the cable provided**

2. Locate the Analog Output Connections on the rear of the CelliGen BLU cabinet:

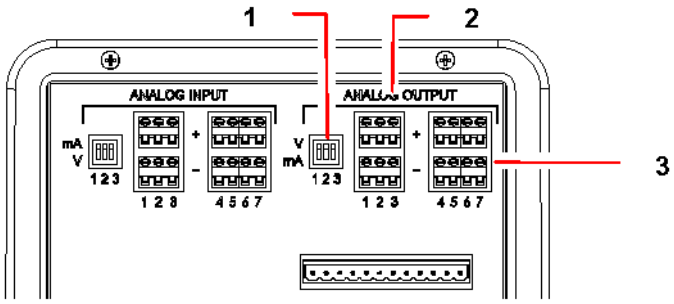

Fig. 61: Rear Panel of CelliGen BLU Cabinet

1 These dip switches are provided to switch connectors 1 - 3 between mA (down) and V (up)	**2 These dip switches (1 - 3) are for mA or V**
3 These dip switches (4 - 7) are for V only.	

3. The preferred connection for pumps is 4 - 20 mA. If you are using a 0 - 5 V connection, skip to step 5. To use 4 - 20 mA, connect the end of the green cable wire to one of the three (1, 2 or 3) negative (-) outputs at the bottom.
4. Connect the end of the white cable wire to the positive (+) output at the top: be sure to use the same number (1, 2 or 3) as you used for the green wire.
5. If, and only if, you are using a 0 - 5 V connection instead of 4 - 20 mA, connect the end of the green wire (return) to one of the four (4, 5, 6 or 7) negative (-) outputs at the bottom and connect the end of the black wire (0 - 5 V input) to the matching positive (+) outputs at the top.
6. Set up the pump control loop using a loop for external equipment (see *Adding loops on p. 35)* and (see Fig. 62 on p. 74).

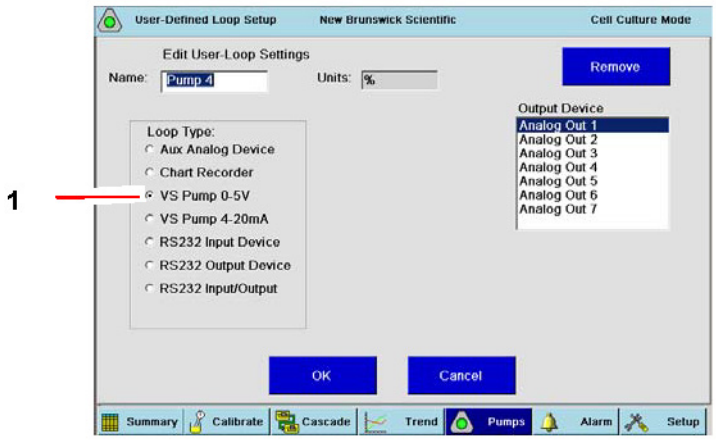

Fig. 62: Add User-Defined Loop Screen

1 Selections for variable speed (0 - 5 V and 4- 2 0 mA) pumps.

After a pump is added, it will appear on the PUMPS screen.

11.8 Install liquid addition systems

The drawing below is a simple depiction of a typical addition system. Depending on the liquids (base, nutrients, media) to be added, your system may be slightly different.

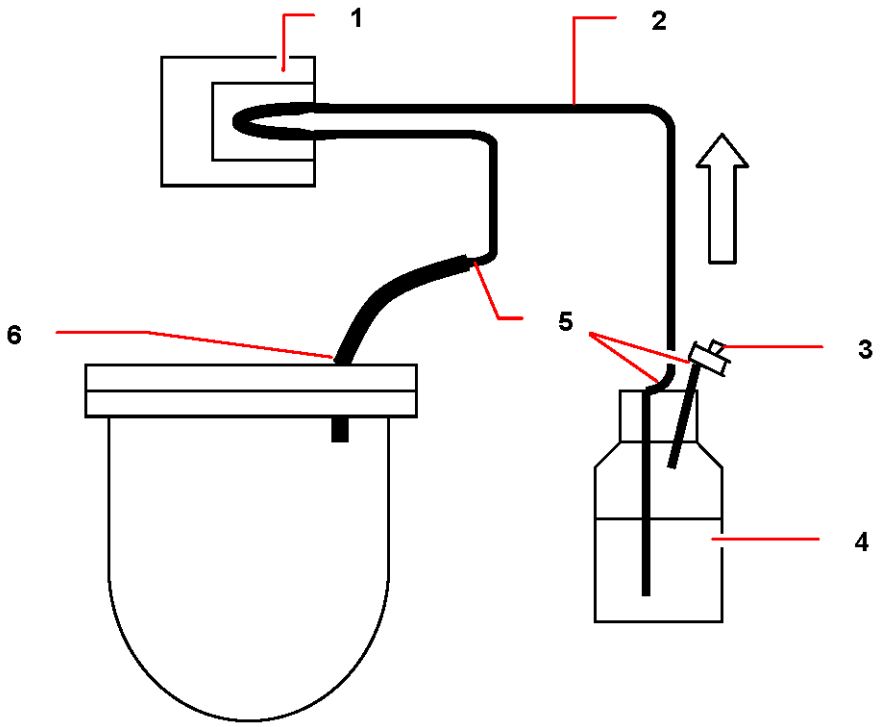

Fig. 63: Typical Liquid Addition System

1 Peristaltic pump	**2 Tubing**
3 Breathing port with sterile filter (0.2 µm)	**4 Addition bottle**
5 Tubing connectors	**6 Access to addition port**

NOTICE!

Risk of damage to system function!

- Proper pH control is critically dependent on tubing size, which should be as small as possible (see Tab. on p. 72).

1. Aseptically install (if applicable) a sterile (0.2 µm) filter in one of the two penetrations on the addition bottle cap.
2. Aseptically connect the tubing to the harvest tube in the addition bottle, securing it with a plastic tie.
3. Clamp the tubing off at the top.
4. Connect the addition bottle to the vessel using a tube welder or quick-connects.
5. Thread the tubing through the selected feed pump.
6. Connect the tubing, securing it with a plastic tie, to the appropriate addition port on the headplate.
7. Remove the clamp.

11.8.1 Addition tubing size

pH can be controlled by automatic additions of liquid base and CO_2. Additions are triggered by the RPC controller, which is constantly comparing current pH value with the pH setpoint and making adjustments as necessary.

The concentration of base, and the inner diameter of the base addition tubing (where it passes through the peristaltic pumps), are critical parameters in the proper operation of a P&I pH control system. If the tubing is too large, excessive doses may be added. The result is that the system will “overcontrol,” alternating in close succession between adding base, then CO_2, providing little or no change in pH reading. A user-selected deadband value is an aid to control pH within the user-assigned range: nothing will be added when the pH value falls within the deadband tolerance above or below the setpoint.

5-normal solutions make a good trade-off between moderate addition volume and good control characteristics. The correct tubing diameter varies a little with process, but inside diameters as small as 0.2 mm sometimes eliminate overcontrol while supplying sufficient liquid during high-demand culture phases.

New Brunswick suggests that you begin with the supplied tubing, which is correct for most applications.

- If the system oscillates, reduce the tubing ID where it passes through the pump.
- Use commonly available step-up/step-down adapters and narrower bore tubing to make the tubing modifications, if required.
- Consult the flow rate/tubing size chart, for further information (see Tab. on p. 72).

12 About alarms

12.1 ABS and DEV alarms

There are two types of alarm modes you can set, Absolute (ABS) and Deviation (DEV):

- An Absolute alarm is triggered when the control loop's Process Variable falls below the absolute Low limit or rises above the absolute High limit that you set.
- A Deviation alarm is triggered when the control loop's Process Variable falls below or rises above the control band that you specify around the loop's setpoint (e.g., a tolerance of 10 rpm above or 5 rpm below the Agitation setpoint).

12.2 Setting alarms

To set alarms:

Tab. 10: Alarms Screen Features

Feature Name	Description
LoopName	Like the CelliGen BLU name box, this box is blue under normal operating conditions, and red when there is an alarm condition. Press a LoopName box to open that control loop's alarm screen.
ABSLow	This column indicates the Absolute low limit you program for control loops. An alarm is triggered if the loop PV falls below this point.
ABSHigh	This column indicates the Absolute high limit you program for control loops. An alarm is triggered if the loop PV rises above this point.
ABSEnable/ABSAudible	This column indicates whether the Absolute alarm limits have been enabled ("Active") or not ("InActive") for visible (ABSEnable) and/or audible (ABSAudible) alarms.
DEVLow	This column indicates any tolerance you have set below the control loops' setpoints.
DEVHigh	This column indicates any tolerance you have set above the control loops' setpoints.
DEVEnable/DEVAudible	This column indicates whether the Deviation alarm limits have been enabled ("Active") or not ("InActive") for visible (DEVEnable) and/or audible (DEVAudible) alarms.
Acknowledge All button	Press this button to acknowledge (and stop) all alarms.
Current Alarms button	Press this button to open a screen that addresses any current alarm condition.
History Button	Press this button to open the historical record of alarms for the current run.
Scroll Up ( ) or Scroll Down ( )	Use this button to scroll upwards or downwards in the table onscreen.
Scroll Back (<)	Use this button to return to a previous screen

1. Press the ALARMS button to open the ALARMS screen (see Tab. on p. 78) and (see Fig. 64 on p. 78).

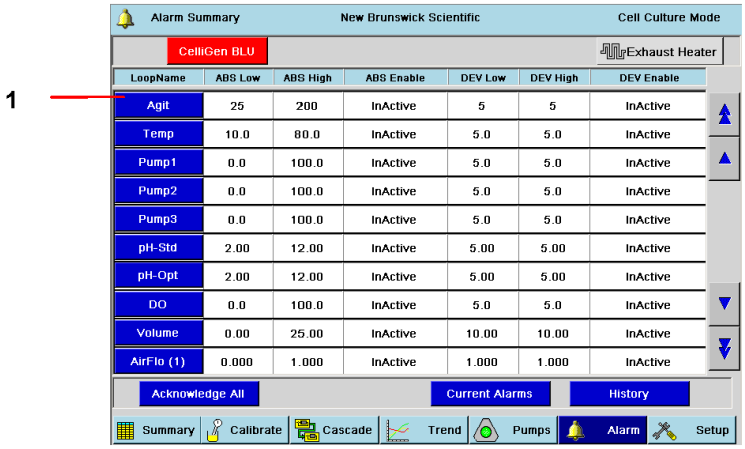

Fig. 64: Alarms Screen

1	**LoopName column**

2. In the LoopName column, press the first loop for which you want to enable an alarm. That loop's individual Alarms Screen will open. For this example we use the pH loop.

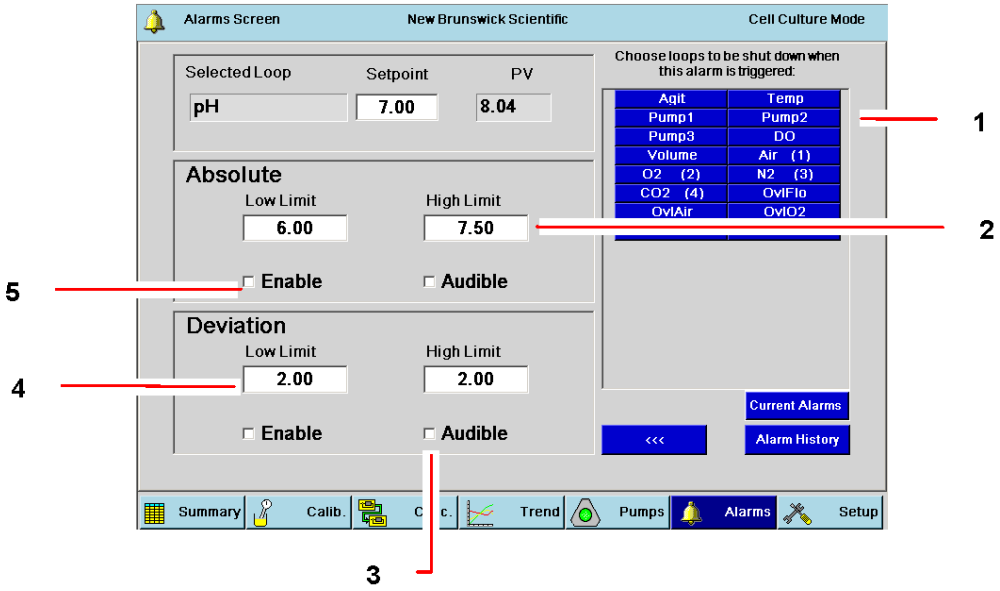

Fig. 65: Sample Loop Alarms Screen (pH)

1 Pressing any of these loop buttons will cause the selected loop(s) to shut down when an alarm is triggered for the loop whose Alarms screen this is (in this case, pH).	**2 Alarm High Limit edit box**
3 Audible alarm checkbox	**4 Alarm Low Limit edit box**
5 Enable alarm checkbox	

3. If you wish to set an Absolute alarm, enter the desired values in the Low Limit and High Limit edit boxes of the Absolute pane (see Fig. 65 on p. 79).
4. Press the Enable checkbox to enable the Visual alarm.
5. Press the Audible checkbox to enable the Audible alarm.
6. If you wish to set a Deviation alarm, use the Deviation pane and follow the same procedure as outlined in Steps 3 – 5.
7. Use the Scroll Back button (<<<) to return to the main Alarms screen and follow these steps for any other alarms you wish to set, or press the Summary button to return to the SUMMARY screen.

12.3 Acknowledging an alarm

When an alarm condition develops, the LoopName box on the SUMMARY screen for the control loop involved will turn from blue to red, as will the CelliGen BLU name box. This is the Visual alarm. A footnote, written in red, will also appear in order to identify the nature of the alarm (e.g., Unit 1—Deviation Low Error).

The Visible alarm will remain onscreen until the alarm condition is rectified. If the Audible alarm is also enabled, beeping will occur until the alarm is acknowledged.

There are three ways to acknowledge alarms: (1) one alarm at a time, (2) all alarms for one control loop at a time, and (3) all alarms for all control loops at a time, for the rare occasion such a condition should arise.

NOTICE!

Risk of damage to system function!

- Acknowledging alarms is NOT a replacement for correcting the condition that triggered the alarm. Diagnose the cause of the alarm condition and rectify the situation to ensure proper operation of your CelliGen BLU.

To acknowledge one alarm at a time:

1. Press the ALARMS screen button to open the ALARMS screen.
2. Press the red LoopName box to open that control loop's ALARMS screen.
3. Press the Current Alarms button to open the Current Alarms Summary screen.
4. Press the Index box for the alarm you wish to acknowledge. It will turn green.
5. Press the Acknowledge button. The alarm will be deleted from the screen.
6. Repeat Steps 4 and 5 for any other alarms recorded for this loop.
7. Press the Scroll Back (<<<) button to return to the ALARMS screen.
8. Repeat Steps 2-7 for any other control loop alarms.

To acknowledge all alarms simultaneously for one control loop:

1. Press the ALARMS screen button to open the ALARMS screen.
2. Press the red LoopName box to open that control loop's ALARMS screen.
3. Press the Current Alarms button to open the Current Alarms Summary screen.
4. Press the Acknowledge All button. All alarms will be deleted from this screen.
5. Press the Scroll Back (<<<) button to return to the ALARMS screen.

To acknowledge all alarms for all control loops at the same time:

1. Press the ALARMS screen button to open the ALARMS screen.
2. Press the Acknowledge All button. All alarms will be deleted from this screen.
3. Press the Scroll Back (<<<) button to return to the ALARMS screen.

12.4 Alarms history

Each time an alarm is triggered, whether Visible and/or Audible, the controller records the event. The controller also records each alarm acknowledgement. You can access the Alarms History screen (1) to consult the data, (2) to save the data to an optional auxiliary PC, and/or (3) to purge the records once the condition has been rectified.

To access the Alarms History screen (see Fig. 66 on p. 81) to consult data:

1. Press the desired control loop's LoopName box in the main ALARMS screen.

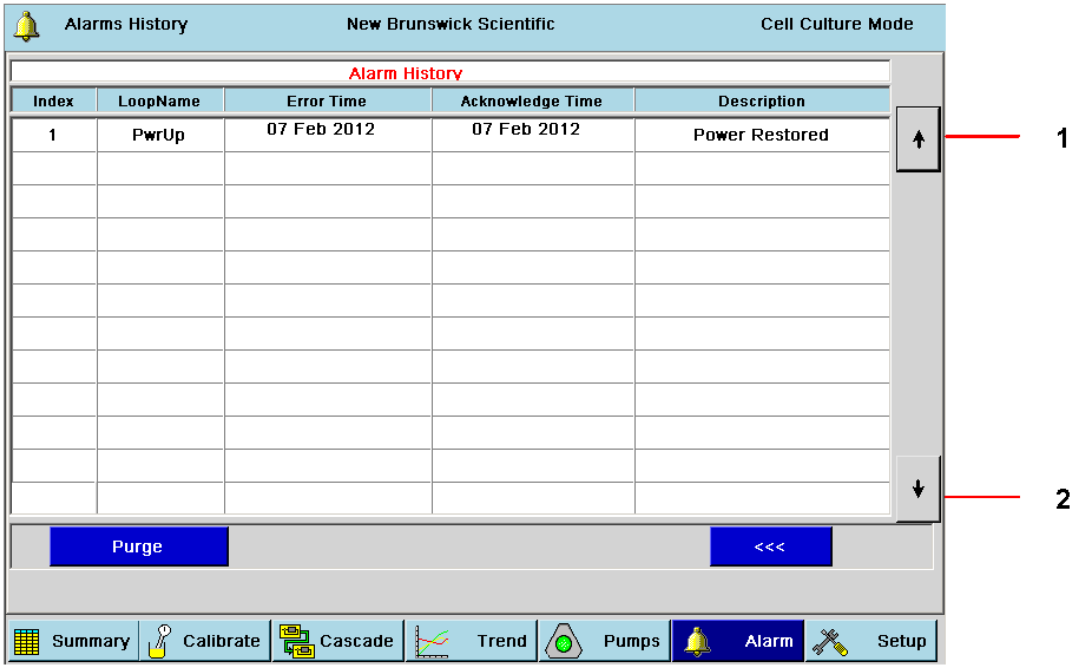

Fig. 66: Sample Alarms History Screen

1 Scroll up button	**2 Scroll down button**

2. In the control loop's Alarms Screen that opens, press the Alarm History button.
3. Press the Scroll Down or Scroll Up button to read through the data.
4. Press the Scroll Back (<<<) button to return to the ALARMS screen.

To access the Alarms History screen to purge the history:

1. Press the desired control loop's LoopName box in the main ALARMS screen.
2. In the control loop's Alarms Screen that opens, press the Alarm History button.
3. Press the Purge button to erase all records.

You cannot delete one record at a time; you can only purge all records simultaneously.

4. Press the Scroll Back (<<<) button to return to the ALARMS screen.

13 Using the setup screen

13.1 General

If you are a user with Supervisor or Administrator status, the SETUP screen has one feature that you will use with frequency, the Recipe Manager (see *Selecting gas flow range on p. 84)*.

You can also use this screen to change Controller Setup (see *Controller setup on p. 82)*, to adjust System Settings (select onscreen language when available, change date and time, update software and calibrate the touchscreen; (see *System settings on p. 86)*), and to check or change the Hardware Setup (see *Hardware setup on p. 88)*.

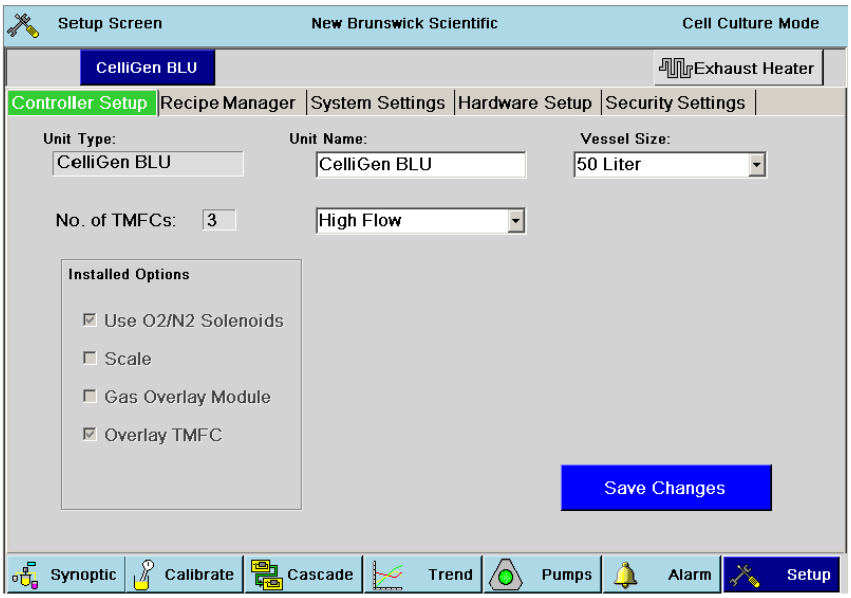

Fig. 67: Setup Screen

- If you need to contact New Brunswick Customer Service about your CelliGen BLU, you may wish to access this screen to check the status of installed equipment, and the firmware version (which you also see briefly in the START-UP screen) by consulting the Hardware Setup screen.

13.2 Controller setup

When you open the SETUP screen, normally the Controller Setup screen will display first.

- If you find any other Setup screen in the display, press the Controller Setup tab to open this screen.

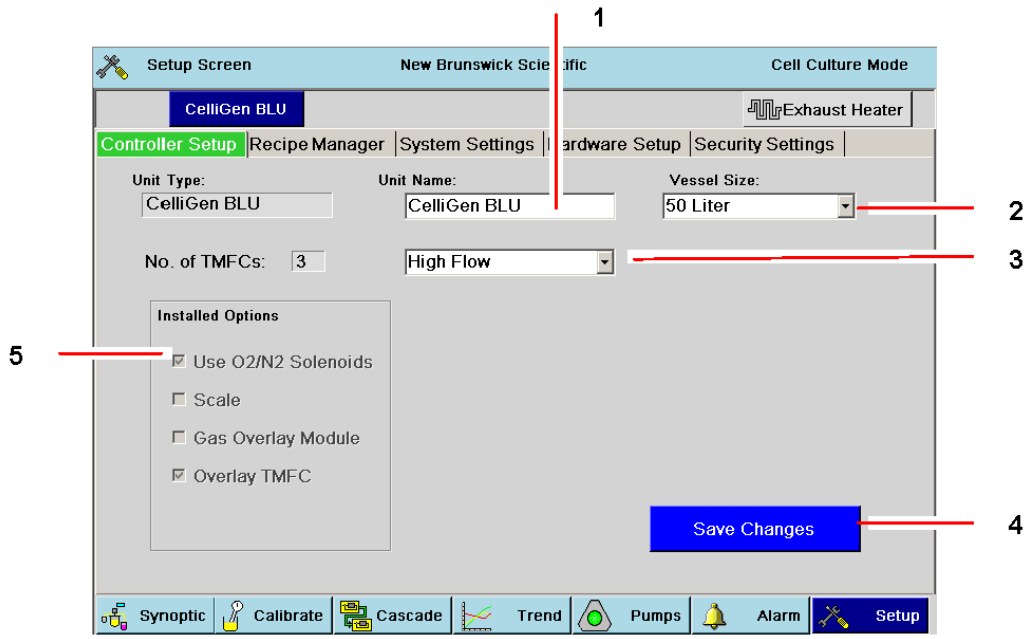

Fig. 68: Controller Setup Screen

1 The assignable Unit Name	**2 The size of the vessel you are using**
3 The flow range of your three TMFCs	**4 Whenever you make a change, be sure to press the Save Changes button**
5 The factory-installed options present on your system	

Some information displayed in this screen is factory-set and cannot be changed: the Unit {equipment] Type, the No. [number] of TMFCs, and the Installed Options.

13.2.1 Assigning a name

1. You can name the bioreactor using the Unit Name touchpad: press inside the edit box to open the touchpad. You may wish to simply name the system by its default designation in the Hardware Setup screen (see *Hardware setup on p. 88)*.
2. The name you write in this box will appear on a colored Name tab on the top menu line, above the Setup tabs.
3. Press the Save Changes button to save the new Unit Name. If you leave this screen and wish to save any change you made, be sure to press the Save Changes button before you move to another screen.

13.2.2 Selecting vessel size

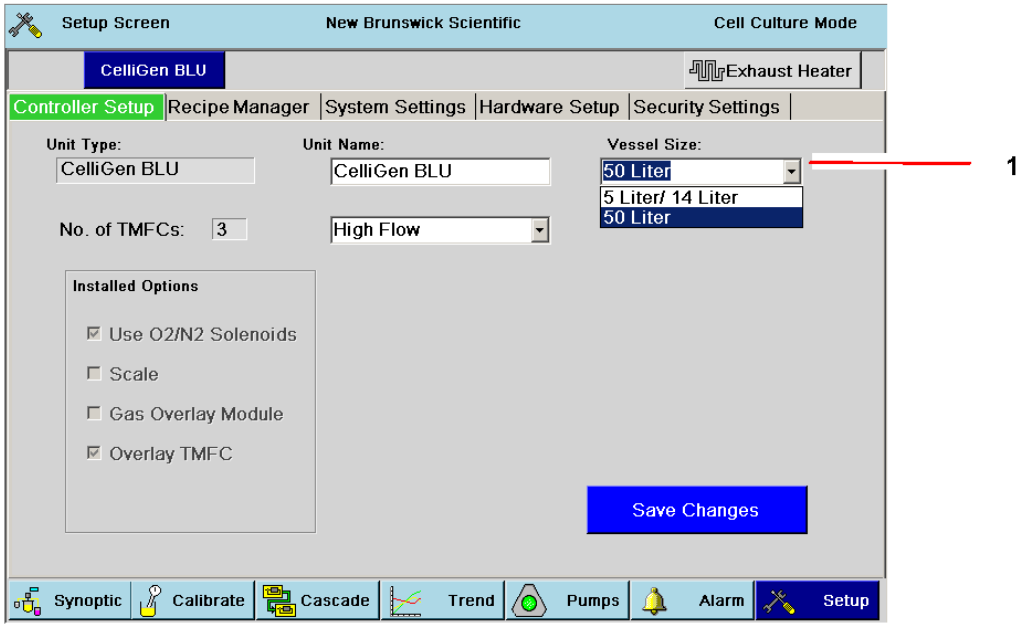

Fig. 69: Selecting Vessel Size

1	**Choice of assignable vessel sizes**

1. Press the Vessel Size down arrow and select the size of the vessel you are using: as shown in the sample screen above, select either 5 Liter/14 Liter or 50 Liter.
2. Press the Save Changes button to save the vessel size. If you leave this screen and wish to save any change you made, be sure to press the Save Changes button before you move to another screen.

13.2.3 Selecting gas flow range

Your CelliGen BLU's three thermal mass flow controllers (TMFCs) can be configured for High Flow (0.04 – 7.5 SLPM) or Low Flow (0.002 – 1.0 SLPM) in the Controller Setup screen.

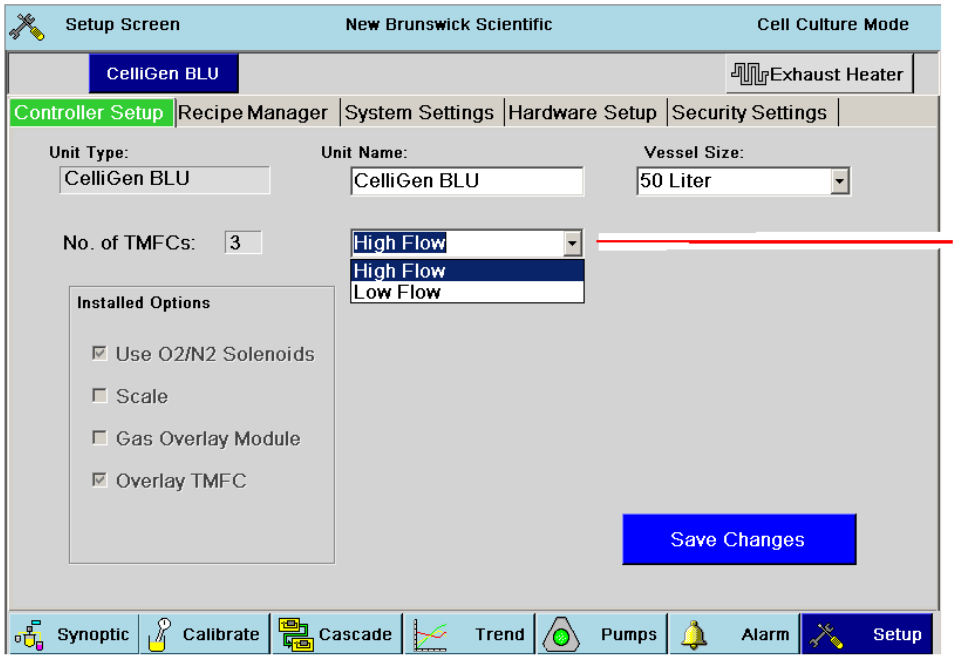

Fig. 70: Selecting Flow Range

1	**Choice of assignable gas flow ranges**

1. To change the factory-set TMFC flow range, press the High Flow / Low Flow down arrow and select the other choice available. In the sample screen above, High Flow is selected.
2. Press the Save Changes button to save your selection. If you leave this screen and wish to save any change you made, be sure to press the Save Changes button before you move to another screen.

13.3 Recipe manager

- Press the second tab in the SETUP screen to open the Recipe Manager screen.
- Use this feature to access, rename, save, load and delete recipe files for your cell culture runs.

Recipes consist of all user-definable variables available on the CONTROL screens. When a recipe is saved, all the current settings on the controller (including but not limited to setpoints, control modes, alarms, P&I values, and cascades) are saved to the controller's memory.

You can save this data with a unique name using the Save As button, or overwrite an existing recipe using the Save button:

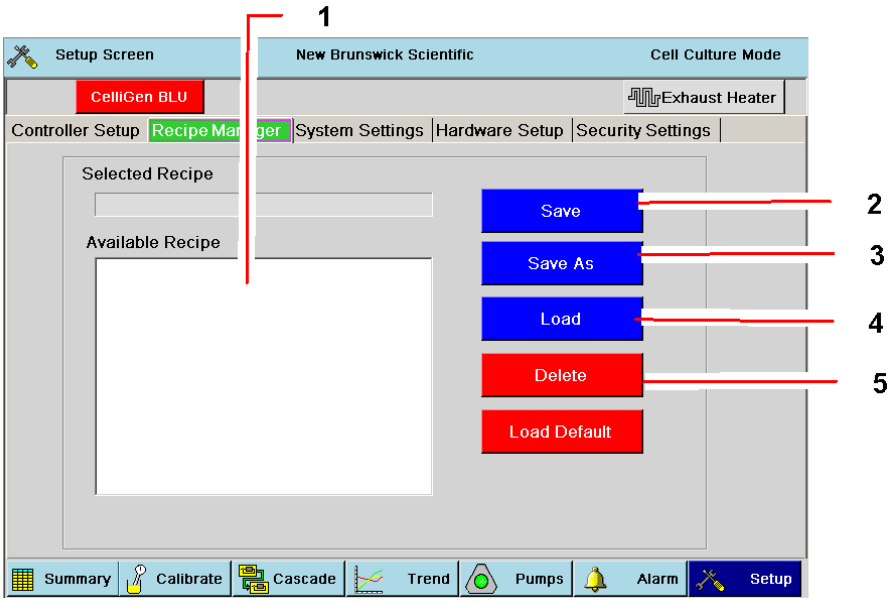

Fig. 71: Recipe Manager Screen

1 Available Recipe pane (list of stored recipes)	**2 Save button**
3 Save As button	**4 Load button**
5 Delete button	

1. Press the recipe file of choice in the list shown in the Available Recipes pane. The file name appears in the Selected Recipe box.
2. Press the Save button to save the recipe as is, or press the Save As button if you wish to rename the file; use the pop-up touchpad to designate a new name.
3. Press the Load button to load the Selected Recipe file.
4. To delete a recipe from the system, select it (see Step 1), then press the Delete button.

The controller is capable of storing up to 10 recipes. You can retrieve any of these recipes by opening the Recipe Manager screen, where all saved recipes are listed in the Available Recipes pane. Select the desired recipe by following Step 1, then load it as shown in Step 3.

13.4 System settings

Press the third tab in the SETUP screen to open the System Settings screen. Use this feature to select the onscreen language you prefer, to reset the date and/or time, to update the software, and to calibrate the CelliGen BLU touchscreen.

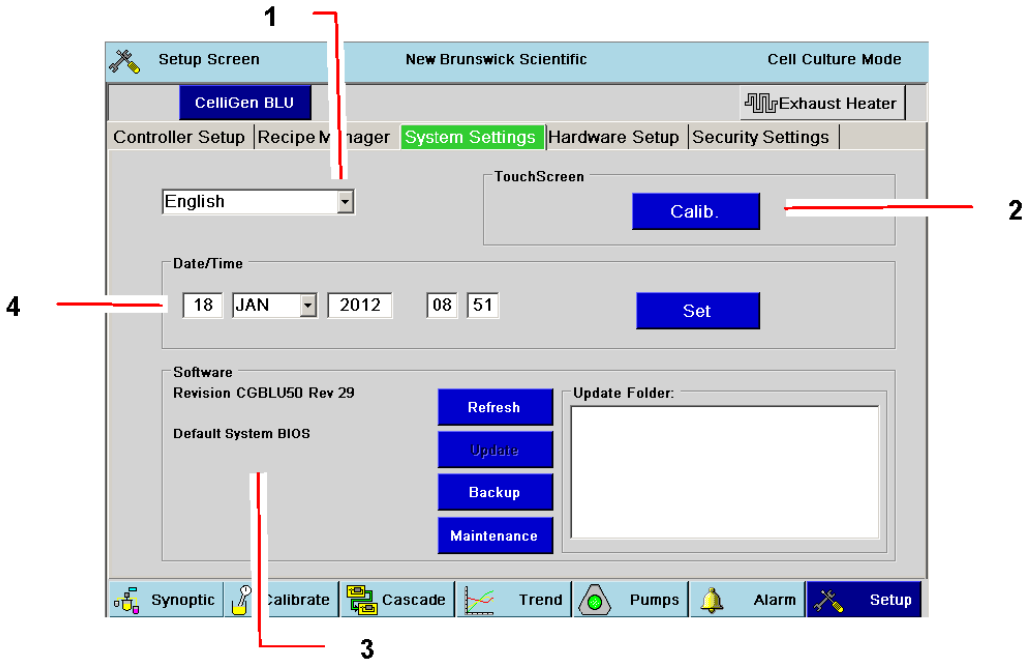

Fig. 72: System Settings Screen

1 Other languages are not available at this time	**2 To recalibrate the system's touchscreen, press the Calib. Button, then touch the onscreen target each time it appears. You will be guided through the process.**
3 Listed here are the current User Interface and Control Program versions. To update the software, see Section below.	**4 To change the Date and/or Time, see Section below.**

13.4.1 Resetting Date/Time

To reset the onscreen date and/or time (displayed in the lower righthand corner of every screen):

1. In the System Settings screen press the edit box for the numeric parameter you wish to change.
2. Use the pop-up touchpad to input the new number and press the OK button.
3. To change the month, press the down arrow and press the month you wish to select from its associated drop-down menu.
4. Press the Set button to save the new information. You can do this after each change, or after all changes have been made.

13.4.2 Updating software

To update the system software, obtain a new version of the software in a USB drive and plug the drive into the USB port on the control cabinet:

1. In the System Settings screen, press the Refresh button to update the current software status and to search for a new USB drive.
2. The name of the new drive folder appears in the Update File box.
3. Press the Update button to install the file.

   The file will reboot twice; this may take a little time. The Software pane will reflect the changes.

Updating software will not affect any previous user settings.

13.5 Hardware setup

The CelliGen BLU system you purchased is preset in the factory as “Unit1” with all the accompanying hardware. In the Unit1 hardware list shown in the sample Hardware Setup screen (see Fig. 73 on p. 88), the system has the Base Power module, the Main pH/DO module, the Main Analog module and the Opto pH module.

This system is also set to Modbus communication mode (see the SCADA pane (see Fig. 73 on p. 88)), and has the Unit ID number of 6. This is the system’s multidrop identification number.

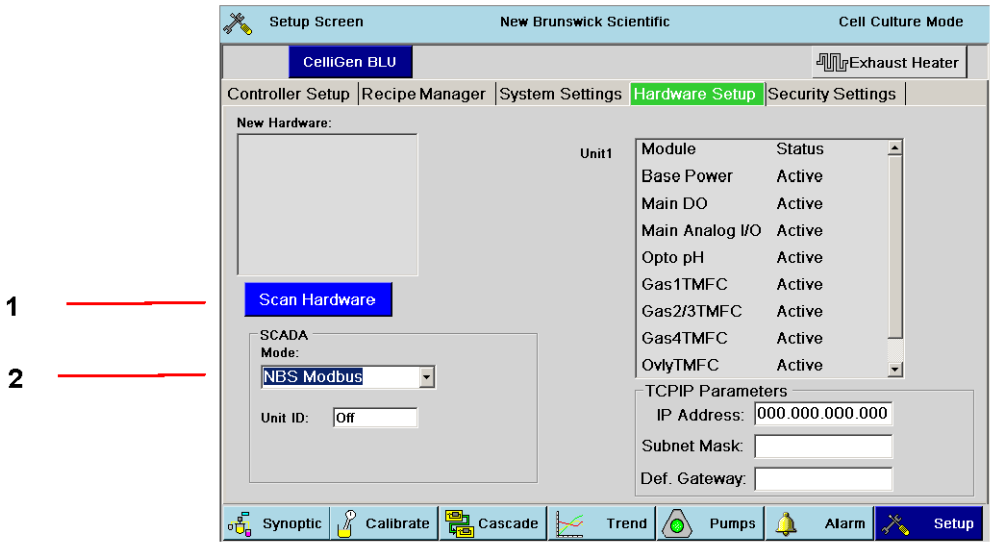

Fig. 73: Hardware Setup Screen

1 The Scan Hardware function is reserved for use only by authorized Service Technicians.	**2 SCADA address**

13.6 Security settings

The security feature on the BLU provides three user access levels:

- Operators have access to routine operations but they cannot load or change recipes. They do not have access to any Setup screen.
- Supervisors can do everything Operators can; in addition, they can load or change recipes. They do not have access to System, Hardware or Security settings.
- Administrators have access to all operations including defining new users (operators, supervisors and administrators) and setting security parameters.

If you are an Administrator, press the fifth tab in the SETUP screen to open the Security Settings screen:

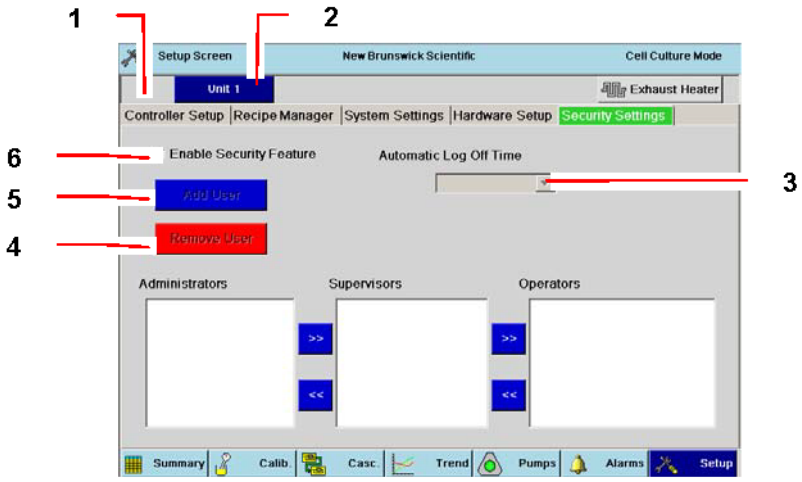

Fig. 74: Security Settings Screen

1 When security is enabled, the User button appears in this corner of all main screens.	**2 This block will show the name of your system.**
3 Use the dropdown menu here to define the time before the system automatically logs off, leaving only the SUMMARY, SYNOPTIC and TREND screens available.	**4 Remove User button (see text below)**
5 Add User button (see text below)	**6 Only a user in the Administrator group has access to this feature: checking "Enable Security Feature" turns security on; deselecting it turns security off.**

In this screen, a user with Administrator status can move users from one group to another group by highlighting the user name in the appropriate pane (Administrators, Supervisors or Operators), then pressing the >> or << button to move that user from one pane to another.

An Administrator can also add users to or remove users from the system using the Add User and Remove User buttons. To remove a user, press the user name to select it in the pane where it appears, then press the Remove User button. To add a user, press the Add User button, use the keypad screen that opens (see the following page) to type in the user name (and assign a Password if desired; if you add a Password, you will be prompted with "Confirm PW" to type it again to confirm it), then press the OK button.

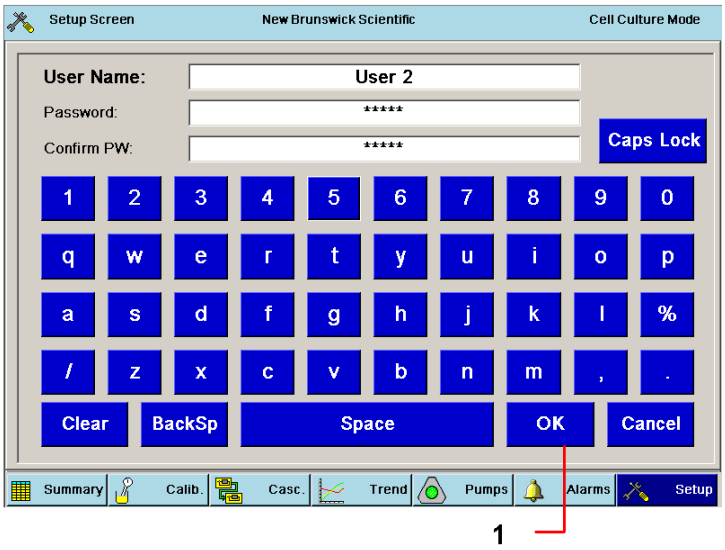

Fig. 75: Security Keypad

1	**When the User Name and Password are entered as desired, press the OK button.**

As indicated in the Security Settings Screen on the previous page and as shown in the sample screen below, when security is enabled, the User button appears in the top left corner of all major screens.

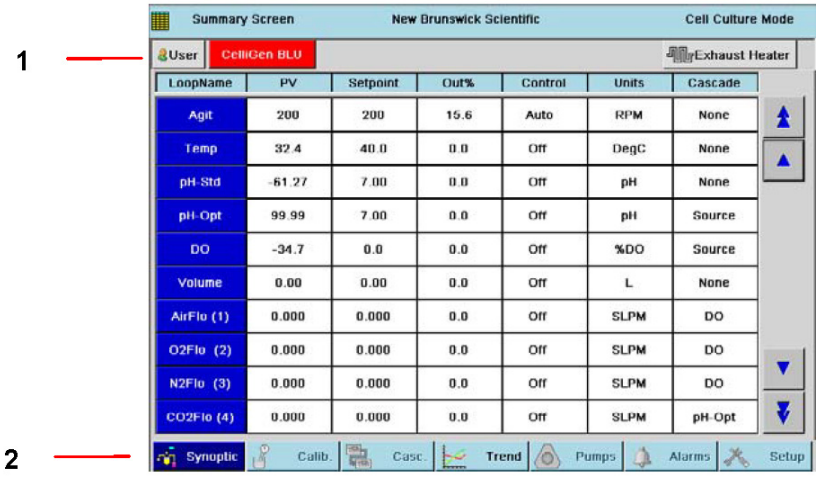

Fig. 76: User Button

1 **When a user presses the User button, that user can use the popup buttons to Log Off or to Log On by pressing the appropriate button. If the user has Administrator status, the Change Password button will also be available. Pressing it will open the security keypad to change his/her password. ADMIN is the default password.**	2 **When Security is enabled, only the Synoptic/ Summary and Trend navigation buttons remain active; the other navigation buttons will be greyed out and inaccessible.**

14 Performing a cell culture run

14.1 Preparing for start-up

NOTICE!

Risk of equipment damage!

- Agitation can only be increased 25 rpm at a time; any greater increase will cause the magnetic drive to uncouple.
- Vessels are designed for static operation: do not handle or move the vessel after the initial media fill.

1. Add sterile filtered media: Aseptically connect the addition port tubing to the addition vessel (which contains the media). This can be done using a tube welder or by making the connection under a hood. Open the addition tubing clamps. Using gravity or a peristaltic pump, move the media into the vessel. Close the addition tubing clamps.
2. Set temperature control to the desired working temperature.
3. Set mode to AUTO.
4. Check that agitation is in OFF mode.
5. Connect the motor.
6. With attention to the Notice above, set agitation to the desired speed.
7. Set mode to AUTO.
8. Draw a sample from the vessel (see *Sampling the vessel on p. 95)*.
9. With an external pH meter, measure the pH of the liquid, noting its pH and temperature.
10. Adjust the display reading of the pH function to read the value displayed on the external pH meter. Make a correction for the pH value if the temperature of the vessel is different from that of the sample. During prolonged cell growth it is advisable to take a sample from the culture and measure its pH with an external pH meter. If the readings are different, the pH sensor's zero has drifted. Readjust the zero on the Vessel pH function to match the reading of the external pH meter.
11. When the vessel reaches the desired working temperature, calibrate the DO probe (see *DO probe calibration: setting zero on p. 47)* and (see *DO probe calibration: setting span on p. 48)*.

14.2 Recommended setpoints

For optimum results, we recommend the use of setpoints as indicated below (see Tab. on p. 92):

Tab. 11: Recommended Setpoints

Vessel Aeration	Loop	Mode	Setpoint
5 L Microsparge M1363-0125	Temp	AUTO	37°C
	Agit	AUTO	70 – 100 rpm
	pH	AUTO	7.0 ± 0.1
	DO	AUTO	35 – 50%
	GasFlo (Cascade Min Limit)	3-Gas/AUTO	0.002 SLPM
	GasFlo (Cascade Max Limit)		0.1 SLPM
	Overlay gas flow	AUTO	0.20 SLPM
	Overlay mix	MANUAL	100% Air
5 L Macrosparge M1363-0121	Temp	AUTO	37°C
	Agit	AUTO	70 – 100 rpm
	pH	AUTO	7.0 ± 0.1
	DO	AUTO	35 – 50%
	GasFlo (Cascade Min Limit)	3-Gas/AUTO	0.0 SLPM
	GasFlo (Cascade Max Limit)		1.0 SLPM
	Overlay gas flow	AUTO	0.20 SLPM
	Overlay mix	MANUAL	100% Air
14 L Microsparge M1363-0126	Temp	AUTO	37°C
	Agit	AUTO	70 – 100 rpm
	pH	AUTO	7.0 ± 0.1
	DO	AUTO	35 – 50%
	GasFlo (Cascade Min Limit)	3-Gas/AUTO	0.002 SLPM
	GasFlo (Cascade Max Limit)		0.1 SLPM
	Overlay gas flow	AUTO	0.40 SLPM
	Overlay mix	MANUAL	100% Air
14 L Macrosparge M1363-0122	Temp	AUTO	37°C
	Agit	AUTO	70 – 100 rpm
	pH	AUTO	7.0 ± 0.1
	DO	AUTO	35 – 50%
	GasFlo (Cascade Min Limit)	3-Gas/AUTO	0.0 SLPM
	GasFlo (Cascade Max Limit)		1.0 SLPM
	Overlay gas flow	AUTO	0.40 SLPM
	Overlay mix	MANUAL	100% Air

50 L Microsparge M1363-0131	Temp	AUTO	37°C
	Agit	AUTO	50 – 100 rpm
	pH	AUTO	7.0 ± 0.1
	DO	AUTO	35 – 50%
	GasFlo (Cascade Min Limit)	3-Gas/AUTO	0.002 SLPM
	GasFlo (Cascade Max Limit)		1.0 SLPM
	Overlay gas flow	AUTO	1.0 SLPM
	Overlay mix	MANUAL	100% Air
50 L Macrosparge M1363-0129	Temp	AUTO	37°C
	Agit	AUTO	50 – 100 rpm
	pH	AUTO	7.0 ± 0.1
	DO	AUTO	35 – 50%
	GasFlo (Cascade Min Limit)	3-Gas/AUTO	0.0 SLPM
	GasFlo (Cascade Max Limit)		7.5 SLPM
	Overlay gas flow	AUTO	1.0 SLPM
	Overlay mix	MANUAL	100% Air
5 L Macrosparge With Basket Impeller M1363-0119	Temp	AUTO	37°C
	Agit	AUTO	50 – 100 rpm
	pH	AUTO	7.0 ± 0.1
	DO	AUTO	35 – 50%
	GasFlo (Cascade Min Limit)	3-Gas/AUTO	0.002 SLPM
	GasFlo (Cascade Max Limit)		0.10 SLPM
	Overlay gas flow	AUTO	0.20 SLPM
	Overlay mix	MANUAL	100% Air
5 L Macrosparge With Basket Impeller M1363-0133	Temp	AUTO	37°C
	Agit	AUTO	50 – 100 rpm
	pH	AUTO	7.0 ± 0.1
	DO	AUTO	35 – 50%
	GasFlo (Cascade Min Limit)	3-Gas/AUTO	0.0 SLPM
	GasFlo (Cascade Max Limit)		0.50 SLPM
	Overlay gas flow	AUTO	0.20 SLPM
	Overlay mix	MANUAL	100% Air

14.3 Inoculation

NOTICE!

Risk of equipment damage!

- Agitation can only be increased 25 rpm at a time; any greater increase will cause the magnetic drive to uncouple.

NOTICE!

Risk of filter blockage!

- For all macrosparge vessels and 50 L microsparge vessels: to avoid exhaust filter blockage, if excess condensate is observed within the exhaust line or the exhaust filter housing, use the hose-cock located on the filter housing to drain it off.

1. All addition and harvesting vessels should be sterile. The addition vessel should also be siliconized for microcarrier culture.
2. Aseptically connect the addition port tubing to the addition vessel.
3. Aseptically place the sterile media and cells (and the sterile microcarriers, if you are using them; see important Hint below) in the addition vessel.
4. Open the addition tubing clamps.
5. Dispense the contents of the inoculation vessel into the vessel by gravity or by using a peristaltic pump if appropriate to the working volume.

If microcarriers are being used, they should be placed in the addition vessel with cells and part of the media.

After dispensing this into the vessel, the rest of the media should be placed in the addition vessel and dispensed into the vessel. This rinses microcarriers from the addition vessel and tubing.

6. Close the addition tubing clamps.
7. Aseptically disconnect the addition port tubing from the addition vessel.
8. Set Agitation to the desired rpm and the mode to AUTO.

For microcarrier culture, the agitation should initially be set at 30-50 rpm. After the cells have attached to the microcarriers, the agitation can be increased above 50 rpm, depending upon the microcarrier and cell being used. For suspension culture, the speed should be 30-50 rpm.

9. Set the DO and pH to the desired control value.
10. Set the DO and pH mode to AUTO.
11. Connect the Gas Inlet tubing to the filtered Gas Delivery System being used.
12. Turn on the gases to 5 PSIG pressure.
13. Display gas screen and set mode to 3-GAS or 4-GAS.

If, at the very beginning of operation, the pH value of the media is higher than the setpoint by 0.3 or more, it is recommended to set the control mode to “Manual” and add sufficient percentage of CO_2 gas into the vessel to bring down the pH value. Then change mode to “3-GAS” or “4-GAS”.

14. Adjust the airflow to the desired flow rate. It is best to start at the lowest airflow rate at which the system can control pH and DO and increase the flow rate only when the system can no longer control pH and DO at that flow rate. We recommend that you maintain pH and DO using an overlay, then using overlay and sparge.
15. Check to see that the flow is stable. Check to see that all the gases are connected properly.

14.4 Sampling the vessel

A sample port with clear, flexible tubing, a needle-free connector and Luer-style needle-free syringes are supplied as the sampling method for every vessel. Follow this procedure to draw a sample from your vessel:

1. Aseptically remove the cap from the needle-free connector and swab the exposed area with sterile IPA.
2. Open a sterile needle-free syringe package and swab the Luer-style connector with IPA.
3. Attach the needle-free syringe to the needle-free connector.
4. Open the tubing clamp is one is attached to the sample tubing.
5. Slowly draw the sample by pulling back the syringe plunger until the desired volume has been removed. You may need to use one syringe to purge the line of old media, then a fresh syringe to draw the sample.
6. Aseptically disconnect the syringe.
7. Swab the needle-free connector again with IPA and reinstall the cap.
8. When you draw additional samples, we recommend that you flush the sample line by pulling a small sample first with one syringe to remove any old media and cells from the line (the standard sample tube holds approximately 5 ml of liquid), then draw a second sample with a fresh syringe to be your actual sample.

14.5 Shutdown

1. Turn off all gases.
2. Set the control mode of all loops to OFF and disconnect the agitation motor.
3. Turn the mains/power OFF.
4. Disconnect the mains/power plugs.
5. Disconnect the probe cables.
6. Remove the DO and temperature probes and store them properly (see their respective manuals).
7. Aseptically harvest the contents of the vessel.
8. Clamp off all tubing connections.
9. Properly dispose of the entire vessel assembly, including the pH probe, respecting all appropriate precautions regarding biohazards.

15 Maintenance

15.1 Cleaning

To clean the device, proceed as follows:

1. At least once a month, clean all the metal parts of your control cabinet, using a soft, damp cloth moistened with water or mild detergent. If a detergent is used, remove all residue by rinsing them with clean water.
2. When you clean the heat blanket, wipe it with a clean cloth moistened with isopropyl alcohol.
3. Use soft facial tissue to clean the DO and temperature probes.

15.2 Service

If any problems occur with your CelliGen BLU system, do not attempt to perform any service on it. Unauthorized servicing may void the warranty.

- Please contact your local New Brunswick Service Department or your local New Brunswick distributor.
- In any correspondence with New Brunswick Scientific, please refer to the Model Number (CelliGen BLU), and the Manufacturing Part Number and Serial Number of the system.

16 Troubleshooting

16.1 General troubleshooting

CAUTION!

Risk of electrical shock!

- Always turn your CelliGen BLU off and disconnect the mains/power cord before performing maintenance.

As with any equipment, difficulties sometimes arise. You may be able to resolve the situation easily and quickly yourself.

- If you experience a problem with the operation of your CelliGen BLU, consult the following list of symptoms (see Tab. on p. 98).

If the problem is not listed below, or if the suggested solutions do not work:

- Please call your New Brunswick representative to request a service technician.
- Other than the solutions proposed below, do not attempt to fix the equipment yourself.

Tab. 12: Troubleshooting Table

Problem	Possible Solution
TEMPERATURE:	
Readout is a negative value (typically –225° C).	• Make sure the temperature probe is connected to the cabinet jack.
The system will not heat up	• Make sure the temperature probe is plugged into the vessel thermowell.
AGITATION:	
Agitator does not turn, or turns only slowly.	• The motor drive may not be seated securely on the coupling; check the orientation of the notches. • Make sure the motor is plugged into the cabinet receptacle; TURN OFF MAINS/POWER BEFORE CONNECTING THE PLUG.
DO and pH PROBES:	
DO probe readings are erratic.	• Recalibrate the probe, carefully following instructions in this manual. • Recharge the probe, carefully following instructions in this manual. • Probe may need a new membrane and a refill of electrolyte. • Check for a secure connection. • Replace probe cable or DO probe.
pH probe readings are erratic.	• Recalibrate the probe, carefully following instructions in this manual. • Check for a secure connection.
GASFLOW:	
There is insufficient gas flow.	• Check that the air pressure is within the specified range. • Make sure the control mode for DO and for pH is set to AUTO (not OFF). • Make sure that the GasFlow loop is ON. • Make sure that the Air loop is in O_2 Enrichment mode. • Make sure that the DO cascades are Enabled. • Make sure that the exhaust filter is not blocked.
GENERAL:	
Touchscreen is not responding.	• Calibrate touchscreen.

17 Technical data

17.1 Specifications

CelliGen BLU System					
Single-Use Cell Culture Vessels	Total Volume	5.0 L	14.0 L	50.0 L	5.0 L Packed-Bed Vessel
	Max. Working Vol.	3.75 L	10.5 L	40.0 L	3.75 L
	Min. Working Vol.	1.25 L	3.5 L	16.0 L	3.75 L
	Vessel ratio Height : Diameter	1.5:1	2:1	1.7:1	N/A
	Impeller Diameter	100 mm	100 mm	160 mm	N/A
Controller	Control Station	Controls up to 32 control loops; stores 10 recipes and 8 process variables for trend graphing. Includes three built-in peristaltic pumps and connectors for all utilities and communications signals.			
	Touchscreen Interface/Display	15-inch industrial color monitor with adjustable angle and swivel.			
Weight and Dimensions	Control Station Weight	40 kg (88 lb) with touchscreen			
	Control Station Dimensions	63 cm wide x 61 cm deep x 86 cm high (25 in wide x 24 in deep x 34 in high)			
	Vessel Weights (1) (without motor)	5.0 L	14.0 L	50.0 L	5.0 L Packed-Bed Vessel
		1.3 kg (2.9 lb)	1.8 kg (3.9 lb)	4.5 kg (9.9 lb)	1.5 kg (3.3 lb)
	Motor Weight	4.8 kg	4.8 kg	4.8 kg	4.8 kg
Temperature	Range	From 5 °C above ambient temperature to 40 °C			
	Control	PI for heating and cooling: heating via Silicone Heat Blanket and cooling via ambient temperature			
	Control Accuracy	± 0.1 °C			
	Sensor Type	Pt 100 platinum RTD probe			
Agitation	Range	25 - 200 rpm for 5.0 L and 14.0 L 25 - 150 rpm for 50.0 L			
	Control	PI-controlled			
	Control Accuracy	± 3 rpm			
	Sensor Type	Optical photo-plastic disc 500 lines/rev with quadrature output			
	Impellers	Pitched blade			
	Power Number (nP)	1.3 for pitched blade vessels			
	Drive	Magnetic motor			

pH	Range	pH 6 - 8 with optical probe or pH 2 - 12 with gel-filled probe
	Control	PI-Control
	Control Accuracy	± 0.1
	Sensor Type	Non-invasive optical pH probe. Single-use fluorescence sensor included with each vessel. Gel-filled probe optional
DO	Range	0 - 200%
	Control	PI control
	Control Accuracy	± 2%
	Sensor Type	Non-invasive polarographic probe
Aeration	Gas Mix	Up to 4 gases delivered to sparge and overlay (Air, O_2, CO_2, and N_2,)
	Sparge Flow Control	3 TMFC only (N_2 and O_2 share a TMFC) High Flow option (0.04 - 7.5 SLPM) Low Flow option (0.002 - 1.0 SLPM)
	Sparge Elements	Porous Microsparge (7 - 12 µm) Drilled Macrosparge (0.7 mm)
	Overlay Flow Control	1 TMFC (0.05 - 5.00 SLPM) Automatic Option 1 Rotameter (0.2 - 5.0 SLPM) Manual Option
	Inlet Filters	0.2 µm Absolute filter
Exhaust	Exhaust Filter	0.2 µm Absolute filter (heat-blanketed tube to reduce clogging)
Pumps (2)	Pump 1	Assignable 14 rpm peristaltic pump Fixed speed or variable duty cycle Available control modes: Off, On, Prime.
	Pumps 2 and 3	Assignable 109 rpm peristaltic pumps Fixed speed or variable duty cycle Available control modes: Off, On, Prime, Acid, Harvest, Add.
Utilities	Electrical	100 - 120 VAC 50/60 Hertz, Single phase, 15 AMPS
		200 - 240 VAC 50/60 Hertz, Single phase, 15 AMPS
	Gas	Clean dry gases regulated to 6 PSIG (0.41 Bar) maximum
External Connections	Analog Input/ Outputs	7 inputs and 7 outputs to connect auxiliary equipment. 3 inputs/outputs interchangeable 4 - 20 mA or 0 - 5 V 4 inputs/outputs 0 - 5 V
	2 USB Ports	Import software updates, export trend data, connect to scale interface box
	RS-485 Communication Port	For optional BioCommand/SCADA software
Ambient Operating Conditions		15 - 30 °C, up to 80% relative humidity, non-condensing
Regulatory Compliance		ETL, CE UL 61010A-1 and 61010A-2-010 CAN/CSA-C22.2 No. 1010.1 and 1010.2.010

(1) Vessel weight does not include probes, exhaust condenser or other options.

(2) For pump flow rates according to tubing size, (see Tab. on p. 72).

17.2 Validation documentation/shelf life

On overview of our validation documentation is available online at www.nbsc.com/BLU. Double click on the PDF icon for the CelliGen BLU Validation Guide in the lefthand column. You can also enter your vessel's lot number in the field at the bottom of the lefthand column to view validation certificates specific to your vessel.

17.3 Certifications

As indicated in the Specifications, the CelliGen BLU has been tested to ETL standards, to comply with these safety standards:

- UL 61010A-1
- UL 61010A-2-010
- CAN/CSA-C22.2 No. 1010.1
- CAN/CSA-C22.2 No. 1010.2.010

In addition, as attested in the CE Declaration of Conformity reproduced on the following page, they also conform to the appropriate CE standards.

New Brunswick
an eppendorf company

CE CE

DECLARATION OF CONFORMITY

New Brunswick Scientific hereby declares that the product(s) listed below conform to the European Union directive and standards identified in this declaration.

Product(s)

CelliGen BLU Single-Use Bioreactor System

EU Directive(s)

Low Voltage (2006/95/EC)
Electromagnetic Compatibility (2004/108/EC)
CE Marking Directive (93/68/EEC)

Standard(s)

EN61010-1
EN61010-2-10
EN55011 (CLASS B)
EN61000-3-2
EN61000-3-3
EN61000-4-2
EN61000-4-3
EN61000-4-4
EN61000-4-5
EN61000-4-6
EN61000-4-11

The conformity assessment procedures were performed at the following:

- **Intertek Testing Services, 41 Plymouth Street, Fairfield, NJ 07004; Advanced Compliance Laboratory, 6 Randolph Way, Hillsborough, NJ, 08844; New Brunswick Scientific, 44 Talmadge RD, Edison, NJ 08818.**

The technical documentation relevant to the above equipment will be held at:
New Brunswick Scientific
175 Freshwater Blvd
Enfield, CT 06082 U.S.A
Tel. (860) 253-3400
Fax. (860) 741-0859

H. Couture
Henry Couture
Director of QA RA

21-OCT-11
Date

18 Transport, storage and disposal

18.1 Transport, storage and disposal

When transporting or storing the device, always use the original packaging.

When they are not in use in a vessel, the DO and temperature probes should be stored. At no time should either probe be allowed to rest on its tip.

NOTICE!

Risk of equipment damage!

- Never let a probe rest on its tip.

For details on biological waste disposal, contact your local regulatory body.

18.2 Disposal

In case the product is to be disposed of, the relevant legal regulations are to be observed.

Information on the disposal of electrical and electronic devices in the European Community:

Within the European Community, the disposal of electrical devices is regulated by national regulations based on EU Directive 2002/96/EC pertaining to waste electrical and electronic equipment (WEEE).

According to these regulations, any devices supplied after August 13, 2005, in the business-to-business sphere, to which this product is assigned, may no longer be disposed of in municipal or domestic waste. To document this, they have been marked with the following identification:

Because disposal regulations may differ from one country to another within the EU, please contact your supplier if necessary.

In Germany, this is mandatory from March 23, 2006. From this date, the manufacturer has to offer a suitable method of return for all devices supplied after August 13, 2005. For all devices supplied before August 13, 2005, the last user is responsible for the correct disposal.

18.3 Return procedure

Should you need to return your CelliGen BLU to New Brunswick for any reason, first contact Customer Service to obtain a Returned Material Authorization (RMA) number. This number must appear on the outside of the shipping container, otherwise New Brunswick Receiving will refuse to accept the shipment.

In addition, you must also certify that the instrument being returned has been thoroughly cleaned and decontaminated. A form for this purpose is provided on the following page; you can photocopy it and fill it out by hand. It can also be downloaded from our website (www.nbsc.com), if you prefer to fill it out electronically.

A copy of the completed Return Authorization and Decontamination Certificate must be attached to the outside of the container, with a second copy packed inside with the instrument. A sample form for you to copy and fill out is provided on the following page.

New Brunswick
an eppendorf company

Equipment Return Material Authorization (RMA) and Decontamination Certificate

Contact New Brunswick Scientific for an RMA number prior to returning any equipment, then complete this form and attach it to the outside container of the equipment being returned to our facility. In addition, attach a duplicate copy of the completed form to the item being returned.

Returned Material Authorization (RMA) Number _____

Equipment being returned: Model Number _____ Serial Number _____

Reason for its return:

_____

_____

This equipment (check all that apply):

New Product
☐ Never used

Biohazards
☐ Not used
☐ Used, but decontaminated with _____

Hazardous Chemicals
☐ Not used
☐ Used, but decontaminated with _____

Radioactive Materials
☐ Not used
☐ Used, but decontaminated with _____

I certify that the equipment described above has been thoroughly cleaned and decontaminated of all chemical, biological and radioactive contaminants and also certify that the returned equipment is safe for unprotected human contact.

By: _____ _____
Signature Print name

Title: _____ Date: _____

Company: _____

Address: _____

_____

_____

Phone: _____ Fax: _____ Email: _____

Form 2847a

19 Appendix A: Stackable pumps

19.1 General

A novel optional feature of the CelliGen BLU pumps is that you can add another identical pump onto the front of one of the pumps in the array. The pump that serves as the base, however, must be specially ordered to have no lower front cover and an exposed screw face on which to mount the second pump.

The stacked pump will be twinned to—in other words, controlled in exactly the same way, at the same time, as—its base pump.

To stack a pump (see Fig. 77 on p. 106) and (see Fig. 78 on p. 107):

1. Remove the standard pump that you wish to stack by pressing the pump release lever, turning the pump to the left until it clicks, then pulling it away from its baseplate mating surface. See baseplate (see Fig. 77 on p. 106).
2. Carefully align the center hole on the back of the special base pump with the “nose” of the baseplate screw face, also aligning the curved slots (like parentheses on either side of the hole) with their male counterparts on the baseplate screw face—you will need to tilt the pump a little to the left to catch all three mating surfaces (see Fig. 77 on p. 106).

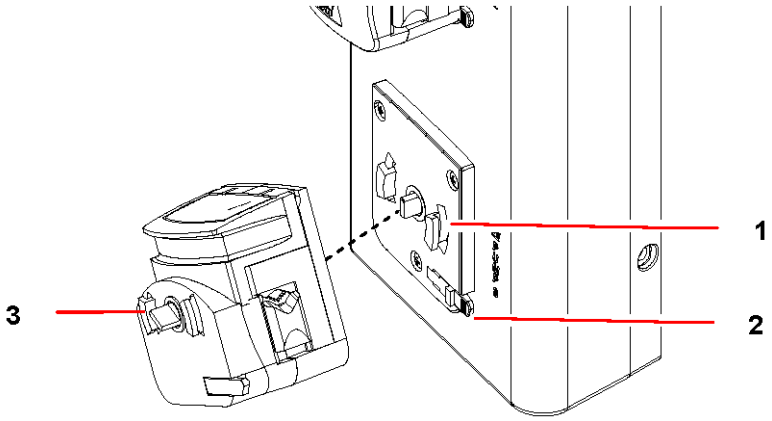

Fig. 77: Mounting Base Pump for Stacking

1 Baseplate screw face	**2 Exposed screw face of base pump**
3 Pump release lever	

3. Once all three mating surfaces are aligned, push the pump back against the baseplate, turning it until it is straight upright and snaps into place.
4. Now add the standard pump in the same way to the screwface of the base pump.

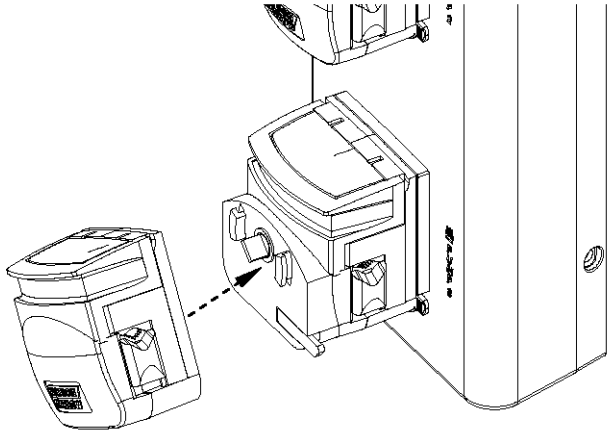

Fig. 78: Stacking the Pumps

5. When you have stacked pumps, load the tubing one pump at a time, starting with the base pump. If you open both at the same time, the back pump channel will be blocked by the front pump's cover.

The drawing below shows two pumps stacked:

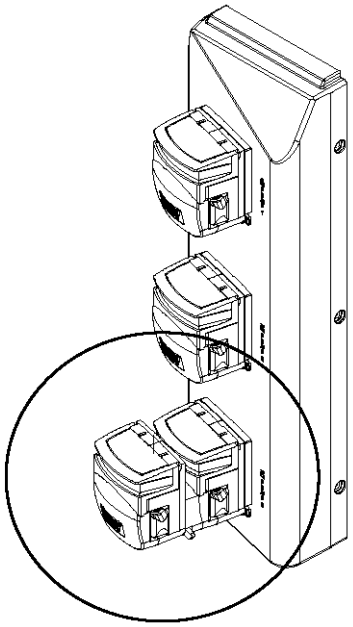

Fig. 79: Stacked Pumps

20 Appendix B: Some general concepts

20.1 What is a controller?

The local process controller is a multi-loop controller, which means it can control several process parameters simultaneously. It compares process values with setpoints and creates independent control signals for each controlled parameter. The control signals are used to drive appropriate actuators that maintain the various parameters at their setpoints.

Using temperature as an example, the controller compares the output of a temperature sensor to the user-entered temperature setpoint, and generates a signal to activate either a heater or a cooler to maintain vessel temperature at the temperature setpoint. The controller provides the logic that generates appropriate drive signals to various actuators so that process parameters remain at their setpoints.

20.2 What is a control loop?

A control loop is the basic element of automatic process control. Three components comprise one control loop: a sensor, a controller, and an actuator. Based on information from a sensor, the controller generates an actuator control signal that maintains a parameter at its setpoint. Control will fail if any element in the control loop fails.

20.3 What is probe calibration?

In bioprocess control, calibration generally refers to establishing a correspondence between a probe's output and the actual value of whatever that probe senses. For example, pH probes are often calibrated with pH 7.0 and pH 4.0 buffers to establish a "zero" (pH 7.0) and a "span" (pH 4.0). Other buffers can be used, but the principle is always the same. For any probe calibration, two values—a zero and a span—are required for the controller to correctly translate inputs from that probe. DO and pH probes are routinely calibrated before each use. Most other probes need be calibrated only infrequently.

20.4 What are P-I-D constants?

The mathematics of P-I-D control is familiar to most control and process engineers.

In P-I-D mode, the controller creates a control signal that is based upon setpoint and input from a sensor. The magnitude of the control signal is determined by a mathematical formula that can include proportional ("P"), integral ("I") and derivative ("D") terms. The P, I and D constants are three numbers that determine the relative sizes of the proportional, integral and derivative terms, respectively. To use a temporal analogy, the P or proportional part of the control signal reflects present deviations between setpoint and process value. The I or integral component reflects past deviations, and the D or derivative term anticipates future values of the error.

Generally, with noisy or slow-responding sensors, such as dissolved oxygen and pH probes, the D constant should be set to zero. If the constants for a loop are too large, that loop will oscillate, displaying extreme swings in actuator output. If, for example, agitation changes suddenly and frequently between minimum and maximum rpm, one should suspect incorrect P, I and D values for the agitation control loop. This condition can easily be mistaken for a defective component when it actually results from incorrect settings.

If the constants are too small, control response will be slow, and setpoints may never be reached. Again, this can be mistaken for defective components. P-I-D constants are usually established by methodical trial and error.

20.5 What is P-I-D tuning?

Tuning consists of establishing controller settings (the proportional, integral, and derivative constants) such that the controller provides proper control. If the P-I-D constants are incorrect, the control signal may be too weak for the parameter to ever reach setpoint or, at the other extreme, the controller may respond excessively to small errors, causing the actuator to oscillate between high and low values. Usable P-I-D constants must be determined for each P-I-D loop. The process is largely one of calculated trial and error.

All loops that are configured with the P-I-D control mode must be tuned. When delivered as part of a New Brunswick system, P-I-D loops will have been tuned at the factory to work correctly with the New-Brunswick-controlled instruments. For other applications, the user is responsible for P-I-D tuning.

Tuning can be a complex task for those unfamiliar with the process, which is why a trained engineer or technician normally performs this task. A number of textbooks that explain the theory and describe the process could be useful for the mathematically-inclined novice. The Ziegler-Nichols method, described in the footnoted reference, is used at our production facilities.

The following suggestions are intended for novices. Be sure to refer to a textbook, and consider utilizing the services of a technician.

- Allow sufficient time for the task. Tuning is an iterative process. It consists of configuring a loop with trial P, I and D values, evaluating loop response, then readjusting the constants. The process is repeated until the loop responds fully and without oscillation.
- One usually begins with a trial P, setting I and D to zero. After P is established, a similar iterative process establishes I.
- Most bioreactor probes respond too slowly or are too noisy to utilize the D term to advantage. In most cases, D should remain at zero. Agitation is sometimes an exception.
- The magnitude of the control signal depends on the P, I and D constants. It also depends inversely on a Normalizing Constant.

20.6 What do the constants mean?

The control signal, S_N, for a loop that has been N seconds in AUTO mode is expressed mathematically as:

$S_N = P(e_N/k) + \Sigma(I/60)(e_n/k) + D[(e_N-e_N\text{-}1)/k]$

Where:

P, I, and D are, respectively, the proportional, integral and derivative constants

e is the loop setpoint minus the process value, or error

k is a normalizing constant for the loop

The controller reevaluates S_N every second. I is divided by 60, so any value entered by the user should be in reciprocal minutes.

The normalizing constant k can be set to any non-zero value, but is usually set to the full-scale reading of the loop. For example, if the range of expected temperatures is 0 to 125, setting k to 125 results in a P term value of P when the error is at a maximum, i.e.:

$P(e_N/k) = P(125/125) = P$

Similarly, with a full-scale error, the I term (after 1 minute) and the D term will be I and D respectively.

21 Appendix C: Corrosion resistance

21.1 General corrosion resistance

Websites such as www.outokumpu.com provide up-to-date information about the 316 type stainless steel used in your CelliGen BLU vessels.

Index

Evaluate your operating manual

www.eppendorf.com/manualfeedback

eppendorf

In touch with life

Your local distributor for New Brunswick products: www.nbsc.com/ContactUs
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New Brunswick Scientific Europe B.V. · Nijmegen · The Netherlands · Tel: +31 (0) 24 3717 600 · Email: europe@nbsbv.nl
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