Single-use bioprocessing

DynaSpin Single-Use Centrifuge
Automation and operation

Keywords
DynaSpin Single-Use Centrifuge, automation

Introduction
Driven by the need to support the production of high-intensity cell cultures of higher volumetric scales, the demand for performance efficiency at each step of bioproduction has grown in tandem. When a manufacturer decides on what technology to use, multiple methods can be applied to facilitate the harvest step of bioprocessing. The Thermo Scientific™ DynaSpin™ Single-Use Centrifuge is designed to be the first step in downstream processing, replacing primary depth filters. This application note details the automation and operation features of the DynaSpin system. Here we present data from a start-up procedure, outlining each key step of the automation, as well as a full 1,700 L harvest process.

Key automation features

The DynaSpin system is designed as a "push button and walk away" harvest solution utilizing features such as:

- System auto-prime
- In-line sensors for outlet monitoring
- Closed-loop clarity control
- Automated rotor start-up
- Automated process flow valving
- Easy pause and resume batch operations
- Live data viewing
- Safety alarms and warnings
- Downstream pressure monitoring
- Automated shutdown and drain

Automation enablement by design

Hardware, safety, and interlock sensors

The DynaSpin system hardware and rotor consumables incorporate a variety of sensors to enable automation. These sensors monitor important process steps to determine when to proceed from one stage to the next. This allows the system to operate efficiently and support safety for the user and downstream operations. Sensors are listed in Table 1 and additional details can be found in the data sheet [1].

Table 1. DynaSpin system sensors.

Sensor	Description
Pressure sensors (inlet, concentrate, centrate, centrate downstream)	Monitor inlet, outlet, and downstream pressure for user safety and downstream operations
Absorbance sensor (centrate)	Monitors centrate clarity during start-up and steady-state operations
Reflectance sensor (concentrate)	Monitors concentrate outlet during start-up and steady-state operations
Flow meter (centrate)	Measures and monitors the volumetric flow rate of centrate. The system uses the data to adjust the speed (RPM) of the centrate outlet pump.

Process and automation workflow

Process flow

The DynaSpin system has been designed to require minimal process oversight. After the user selects an appropriate recipe and enters the batch parameters, automation will control the system prime, rotor start-up, steady-state operations, and shutdown. Figure 1 shows the process flow details from process setup to shutdown.

Recipe setup

The DynaSpin system utilizes a simple touchscreen interface for operation and customization of recipes for batch processes. The user inputs values specific to their process to enable automation of the entire harvest process.

When configuring a recipe, the user will specify a target rotor speed, harvest volume, and two process control parameters. Typically, the two selected parameters are inlet flow rate and packed cell volume (PCV) as shown in Figure 2. Advanced parameters can be adjusted to further customize batch needs in the advanced parameters section. These parameters are addressed in the user guide [2].

Step	Details
Load batch	Set batch process parameters and setpoints.
Press start	Perform manual checks, resolve alarms, and start process.
Prime	The centrate flow meter is tared, and in-line sensors ensure liquid is present and bubbles are removed in each line.
Rotor start-up	Pumps change to process speeds, rotor begins spinning, allowing automation to monitor absorbance and reflectance values to meet specified tolerances.
Steady state	Normal operation. Time required is dependent on batch volume and flow rates.
Shutdown	If enabled, the system will reverse selected outlet pumps and pump the remaining material in the rotor and lines back into the reactor.

Figure 1. Process steps in a typical harvest. The highlighted steps leading up to pressing "Start" are performed by the user, and subsequent steps are performed automatically by the DynaSpin system.

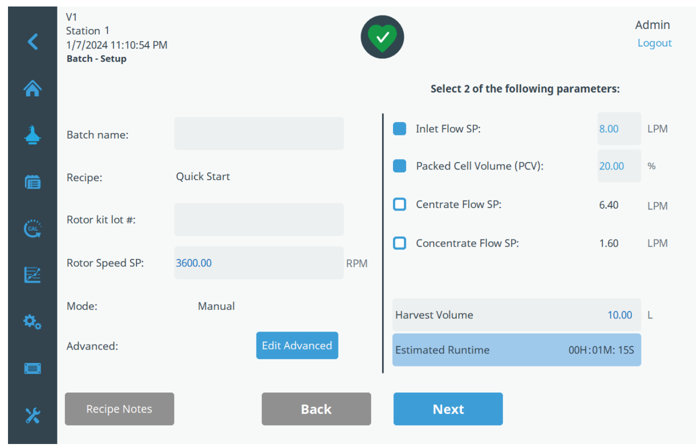

Figure 2. New batch setup screen.

Automation

Press start

After all desired process setpoints are entered, a “verify device readiness” screen reports any errors or alarms present. Alarms due to incorrect loading of the rotor or sensors must be resolved before start-up can occur. The “verify device readiness” screen requires users to manually acknowledge that all clamps, flow paths, and linesets are unclamped, correct, and ready for harvest before the final “Start” button is enabled. Following all final checks of the system, the user may press “Start” to begin automation and harvesting.

Prime

Pressing “Start” in a batch process begins harvest using the DynaSpin system. During the priming and startup procedure, both the centrate and concentrate are recycled back to the reactor to minimize product loss. Upon start, inlet and outlet pumps automatically prime the system by circulating cell culture through the system. Sensors measure the in-line absorbance and reflectance to determine removal of all gas and bubbles from the linesets, indicating the system is completely primed.

Start-up

After the linesets are primed, the rotor ramps up in speed to begin separation. Before the rotor reaches the steady-state speed, a temporary pause in rotor acceleration occurs to allow a final degas of the system. After the rotor has reached the process speed, the system monitors the absorbance and reflectance values to determine when the centrate and concentrate are at the steady-state parameters specified by the recipe.

Steady state

When the centrate and concentrate streams have achieved desired absorbance and reflectance levels, the process valves switch from recycling to steady-state harvest for further downstream processing. The system remains at steady state throughout the process except for errors and normal shutdown procedures.

Pause and restart, and error detection

The DynaSpin system includes a simple pause and restart feature during batch processes. Pausing the batch defaults all valves to the “closed” state, and stops the rotor and pumps. Restarting the batch allows the system to run through the start-up process again, including priming and rotor start-up.

Bowl flush

Depending on process conditions, cell material may build up in the rotor. A bowl flush button is integrated into the batch process screen to enable easy removal of built-up cell material using recipe flush parameters. When pressed, the concentrate pump RPM increases at a set ramp rate until a maximum RPM is reached, and then maintains this RPM for a set duration. After the cell material has been flushed out of the rotor, the concentrate pump RPM returns back to the process setpoint.

Shutdown

Before reaching the preset process volume percentage, any process alarms that occur during the batch will trigger a batch pause rather than a batch shutdown. When the process volume percent parameter has been reached, any process alarm (such as an alarm for low pressure when the reactor is nearly empty) will initiate the shutdown procedure. If enabled, this shutdown procedure will reverse the selected outlet pumps to empty the rotor bowl and lineset. Cell material in the linesets is pumped back to the reactor through the inlet line.

Example data

Start-up data

To demonstrate the process steps listed above, the DynaSpin system was set up to harvest a fed-batch culture of CHO K1 cells grown in Gibco™ ExpiCHO™ Stable Production Medium. Values for the culture and DynaSpin recipe parameters are shown in Table 2. Sensor data from the DynaSpin system were collected for priming, start-up, and steady-state phases and are shown in Figure 3.

The priming step started by increasing the system pressure (Figure 3A, 1) as the rotor filled with culture causing the centrate absorbance to increase and the concentrate reflectance to decrease (Figure 3B, 2). Once absorbance was at a sufficient value showing that air was removed from the lines, the centrate pump stopped (Figure 3C, 3), allowing the flow meter to be tared. The whole priming process totaled only 1.5 minutes to complete. Rotor start-up began and drove the system to steady state. During this phase, the motor speed ramped sharply to initiate separation of material with a brief pause in rotor acceleration to allow final degassing (Figure 3C, 5). The rotor speed then caused the centrate absorbance to drop as material was separated in the rotor (Figure 3B, 4). As a cell pellet was formed in the rotor the concentrate reflectance increased (Figure 3B, 6) and the flow path was switched from recycle to pellet collection. The rotor start-up phase continued until absorbance and reflectance values were maintained as specified by the recipe. This batch took 1.4 minutes for the rotor to start and achieve steady-state parameters. Going from process initiation to steady-state conditions required a total of 2.9 minutes.

Table 2. Culture batch parameters and process parameters on the DynaSpin system.

Parameter name	Value
Peak cell density	51.9 x 10^6 cells/mL
Pre-harvest viability	74%
Pre-harvest density	39.5 x 10^6 cells/mL
Pre-harvest turbidity	1,830 NTU
Packed cell volume	5.6%
Process flow rate	6 LPM
Set packed cell volume	6.1%
Rotor speed	3,600 RPM

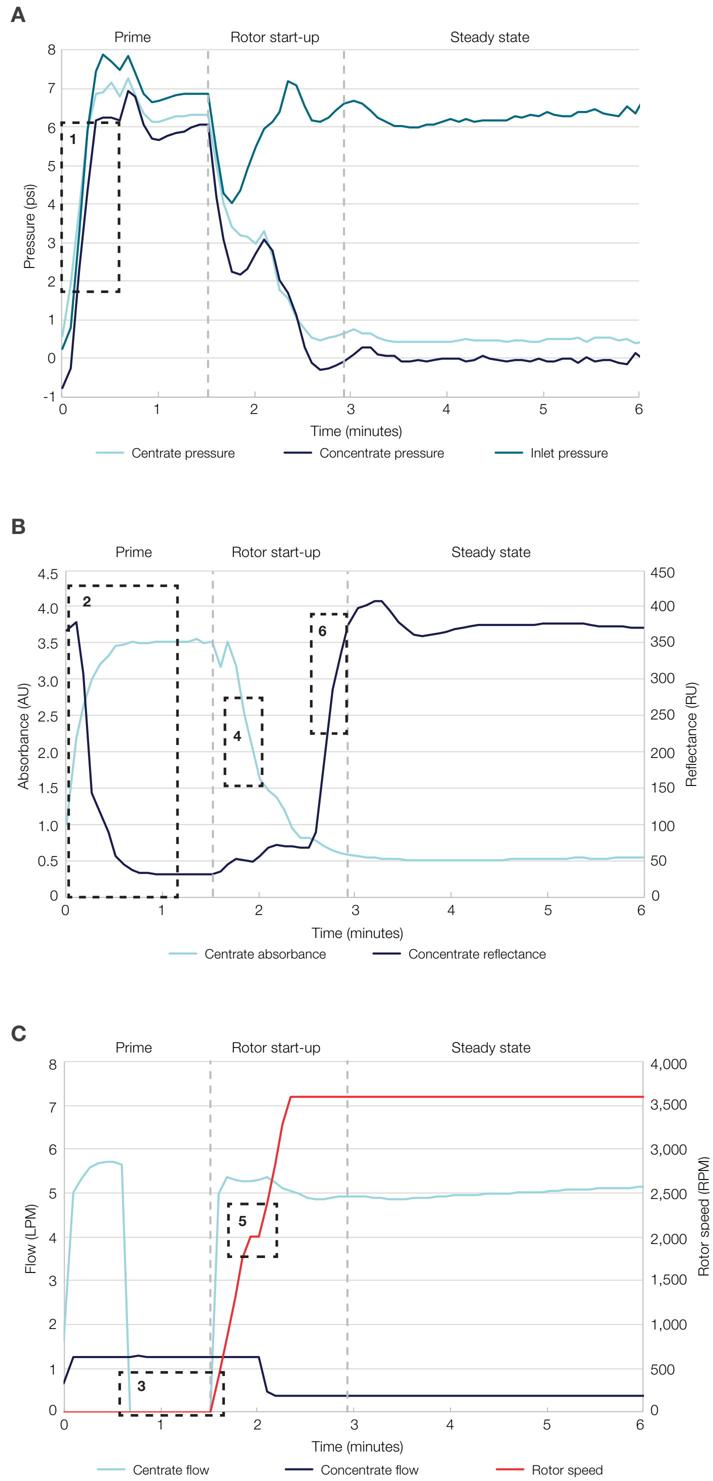

Figure 3. Online parameter values for the various sensors during the start-up procedure. (A) Plot of centrate, concentrate and inlet pressures during prime, rotor start-up, and steady state. **(B)** Plot of centrate absorbance and concentrate reflectance during prime, rotor start-up, and steady state. **(C)** Plot of centrate flow, concentrate flow, and rotor speed during prime, rotor start-up, and steady state.

Steady-state data

The DynaSpin system was used to process a separate CHO K1 batch with a PCV of 7.3%. This process lasted 8 hours at a flow rate of 3.5 LPM. Centrate absorbance was measured online by the DynaSpin system. Additionally, centrate samples were collected and turbidity was analyzed off-line using a Hach™ TL2360 turbidimeter. As seen in Figure 4, there is a correlation between absorbance and turbidity where both showed minimal increase in either parameter indicating no loss in separation performance throughout the 8-hour process.

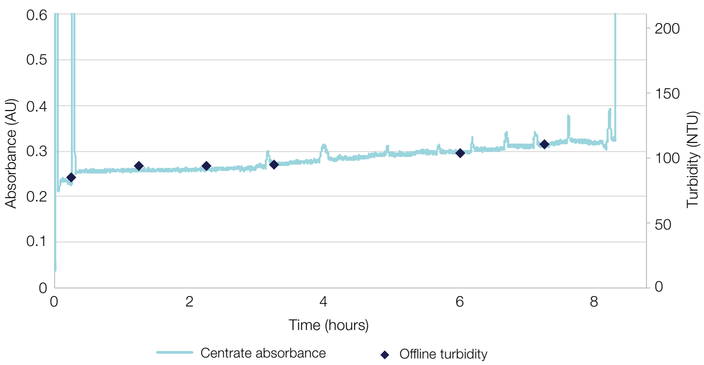

Figure 4. Centrate absorbance data over an 8-hour process with overlay of offline turbidity. Large spikes in absorbance were from starting and stopping the rotor, and short spikes in absorbance were from rotor bowl flushes.

Conclusion

The incorporated sensors and software of the DynaSpin system help enable user-friendly operation with minimal hands-on operation. We have shown that minimal oversight is needed for the DynaSpin system and a quick start-up takes only 2.9 minutes to reach steady state. We also showed that the DynaSpin system was able to maintain steady state for an 8-hour process with minimal operator input and oversight.

Author

Jason Peterson, Engineer II, Systems Design, Thermo Fisher Scientific, Logan, UT

References

1. DynaSpin Single-Use Centrifuge Data Sheet. Thermo Fisher Scientific, May 2023.
2. DynaSpin Single-Use Centrifuge User's Guide. Thermo Fisher Scientific, August 2023
3. Spin it first: Finding an optimal harvest solution by considering both cost and sustainability. White paper. Thermo Fisher Scientific, March 2023.

Ordering information

Product	Cat. No.
DynaSpin Single-Use Centrifuge	DSPIN.9000
DynaSpin Single-Use Rotor	SUT00056

Learn more at thermofisher.com/dynaspin

For Research Use or Further Manufacturing. Not for diagnostic use or direct administration into humans or animals.