

Application Note

Technical Application Publication

A SciLog® MabTec® method for automated continuous fed-batch versus manual bolus fed-batch



Summary

The SciLog® MabTec® combines accuracy with convenience to provide an ideal solution for cell culture feeding strategies. Based on the results, MabTec® demonstrated the ability to increase protein production while eliminating several hours of manual daily operation.

Introduction

MabTec® is an add-on bioreactor maintenance system that can gravimetrically manage, automate and document your bioreactor feeding or perfusion strategy (Figure 1). The MabTec® upgrades many manual processes to walk-away automation with minimal investment in terms of capital or time.

The SciLog MabTec® system was designed to monitor and automate perfusion, feeding and recirculation processes to save time, reduce inadvertent errors and enable walk-away bioreactor maintenance.

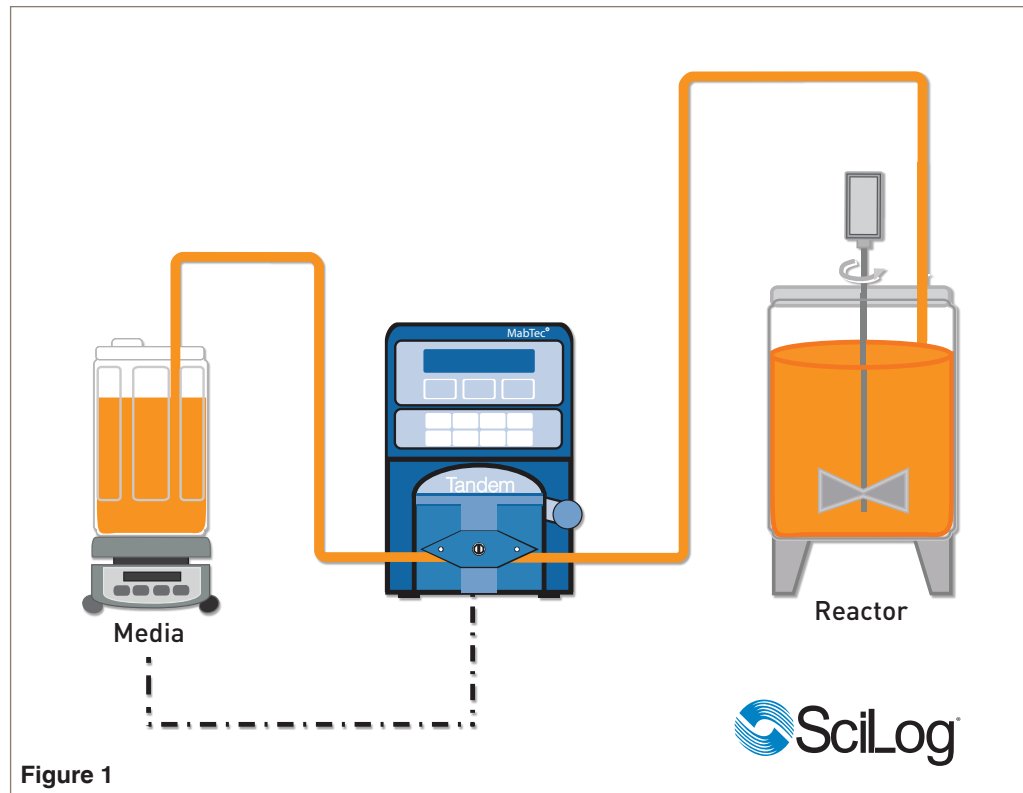


Figure 1

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System Requirements:

- **Safe walk-away operations**
The SciLog MabTec® is a fully automated gravimetric bioreactor maintenance system, which reduces hands-on time and the risk of operator errors. The MabTec® can automate additions at inconvenient hours or perform a complete perfusion strategy. Real-time data collection and optimization tools are included.
- **Ready to plug into your process**
Will fit seamlessly with any bioreactor from 50mL to 2000L and enhance its performance.
- **Maximize bioreactor performance**
Conduct unattended bioreactor inoculations, bolus feed and/or pump flow reversals (to prevent filter fouling) all on one unit. Automate feed, harvest or recirculation in fully disposable or hybrid bioreactor flow paths to achieve high density cell cultures. Run times from hours to months are easily programmed.

ENGINEERING YOUR SUCCESS.

The application flexibility of MabTec® delivers superior growth efficiency within a bioreactor through the replacement of repetitive manual operator steps with an automated solution. The replacement allows for more constructive use of operator time and eliminates the human errors associated with manual production. The objective of the experiment is to:

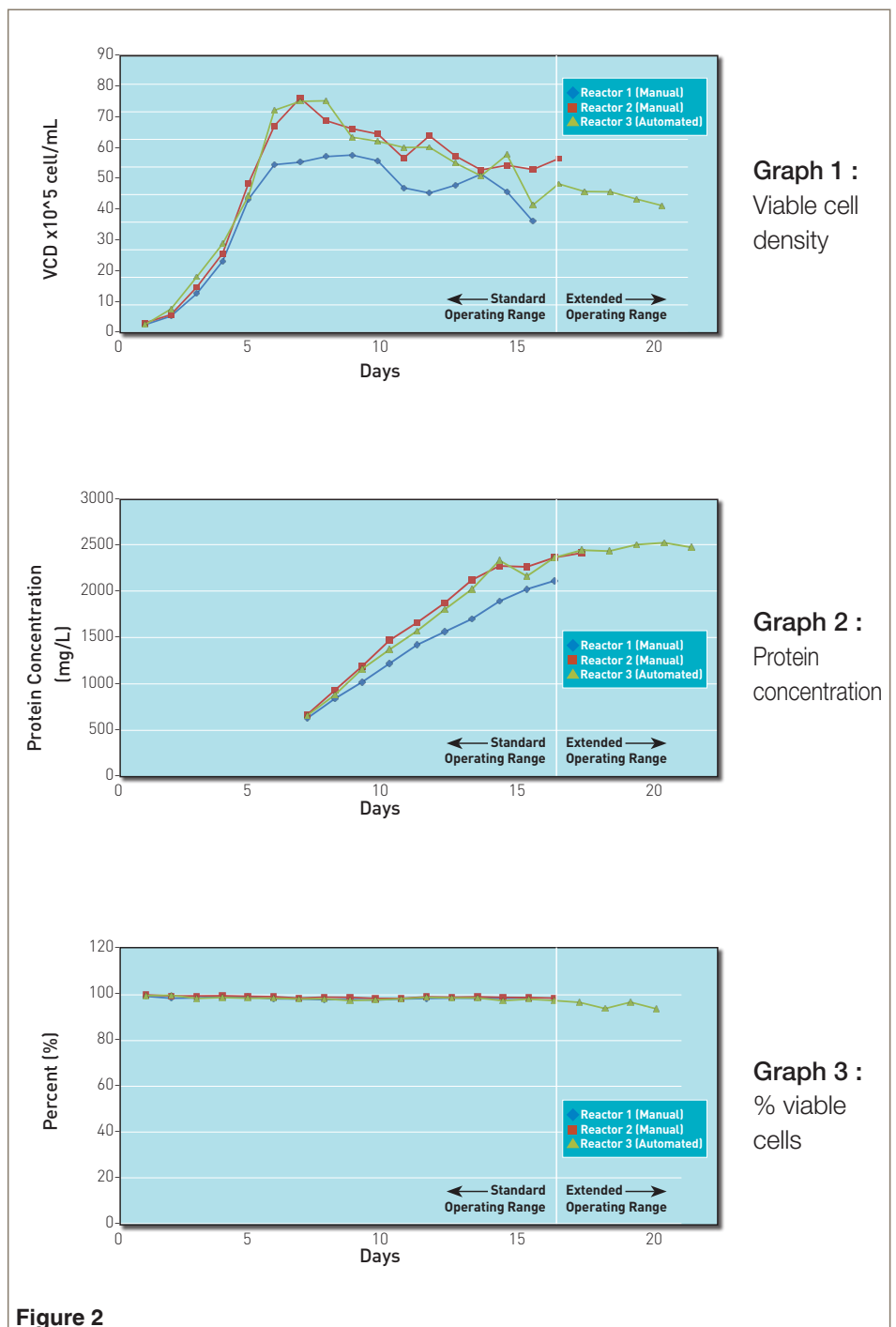
- Demonstrate the feasibility of replacing a manual fed batch process with an automated process.
- Verify automated performance results against manual operations. Automated results must meet or exceed manual operations.
- Determine the number of manual operations.



Test scenario

Three 10L glass bioreactors were filled with 4L of media to be used in a mammalian cell culture. Agitation was started and maintained at the same rate for the duration of the run. After 5 days the culture reached a density point where a feeding strategy is required.

The manual feeding method required an operator to perform 10% bolus reactor fluid additions daily. Each day's bolus media quantity required the operator to autoclave the media feed container and prep the media daily. The automated feeding method was set up to add media to the reactor in a continuous method that totaled a 10% daily reactor weight addition. (Recommendations for MabTec® motor size, pump head, and tubing sizes versus reactor size and number of media exchanges per day can be found in Table 1.) All the media for the automated process was prepared at one time and placed on a cart next to the MabTec®. The run was scheduled for a total of 18 days. The automated method was allowed to continue for an additional 3 days as this method of processing had not been tested previously. The reactor was sampled and tested daily for viable cell density, percentage cell viability, protein concentration, glucose, lactate, glutamine and ammonium.



Results

As shown in Figure 2, initial conditions were extremely similar for all three reactors. % Viabilities for all three reactors on day five was 98% or better when the switch to automated fed batch began.

The three runs were not significantly different which was the intended outcome for the test. The automated MabTec® method was able to reproduce the manual method exactly and added consistency to the method that was not possible before.

MabTec® motor size, pump head and tubing recommendations vs reactor size and reactor exchanges per day

		Reactor Volume Size																					
		0.05	0.25	0.5	1	1.5	2	2	2.2	3	3	4	4	5	5	10	20	50	100	250	500	1000	2000
#Exchange per day	1	0.03	0.17	0.35	0.69	1.04	1		2	2	3	3	4	3		7	14	35	69	174	347	694	1389
	2	0.07	0.35	0.69	1	2	3		3	4		6	6	7		14	28	69	139	347	694	1389	
	3	0.10	0.52	1	2	3	4	4	5	6		8	8	10	10	21	42	104	208	521	1042	2083	
	4	0.14	0.69	1	3	4	6	6	6	8	8	11	11	14	14	28	56	139	278	694	1389		
	5	0.17	0.87	2	3	5	7	7	8	10	10	14	14	17	17	35	69	174	347	868	1736		
	10	0.35	2	3	7	10	14	14	15	21	21	28	28	21	35	69	139	347	694	1736			
	15	0.52	3	5	10	16	21	21	23	31	31		42		52	104	208	521	1042				
20	0.69	3	7	14	21		28	31		63		56		69	139	278	694	1389					
	#13	#15	#24	#16	#14	#15	#14	#16	#24	#15	#24	#15	#24	#15	#24	#35							
	8 RPM			160 RPM						8		160 RPM		600 RPM									
	1081		1082		1081		1082		1081		1082												

- 8 RPM with 1081 and #13 tubing
- 8 RPM with 1082 and #15 tubing
- 8 RPM with 1082 and #24 tubing
- 160 RPM with 1081 and #14 tubing
- 160 RPM with 1081 and #16 tubing
- 160 RPM with 1082 and #15 tubing
- 160 RPM with 1082 and #24 tubing
- 600 RPM with 1082 and #15 tubing
- 600 RPM with 1082 and #24 tubing
- 600 RPM with 1082 and #35 tubing

*Flow rates in grams per minute

Table 1

Conclusion

The viable cell densities produced in the bioreactor fed by the MabTec® was on par with the two manual methods. The MabTec® also allowed slightly higher protein production than the other two vessels. The switch to an automated process eliminated thirty manual operations, 15 autoclave cycles and 15 buffer preparations, which equated to several hours of operator time freed up. The MabTec® has demonstrated its feasibility to replace a manual fed-batch operation.

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