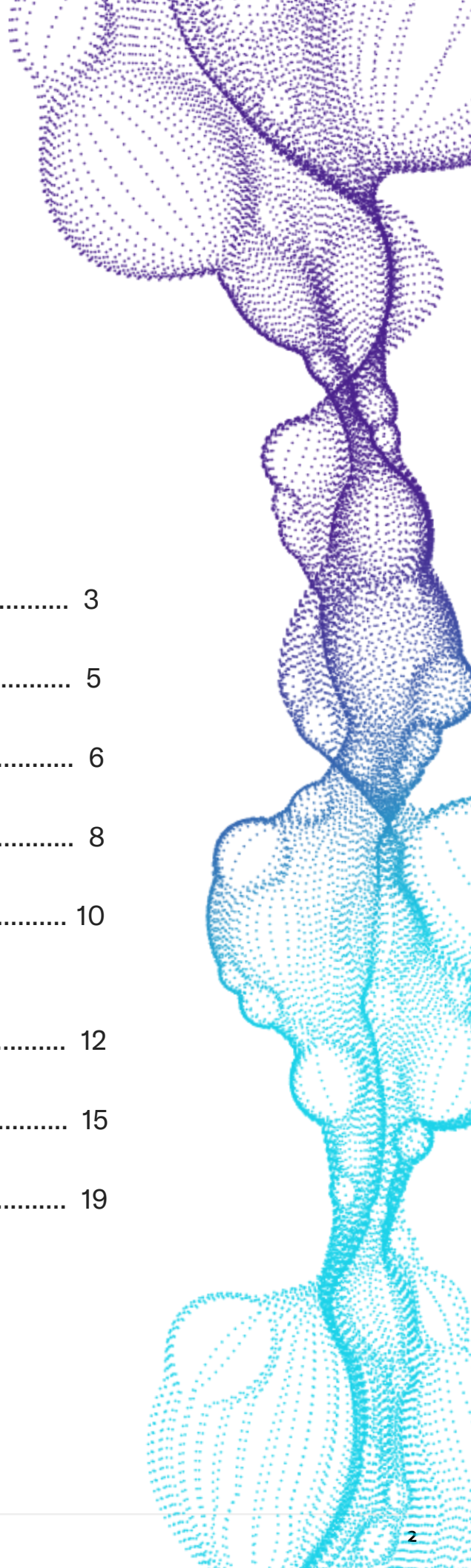
SCIENTIFIC BIOPROCESSING

Biomass Monitoring

Find the Best Fit for Your Bioprocess With This 360° View on Available Technologies.

Contents



The Importance of Biomass Monitoring

Biomass is one of the most important critical process parameters (CPPs) in microbial upstream bioprocessing, using living organisms to convert one or several substrate/s into a desired product. The method is used nearly everywhere today, from the environmentally-friendly production of chemical building blocks to the creation of cutting-edge pharmaceuticals like monoclonal antibodies, to animal nutrition, flavors and fragrances.

A broad range of products can be produced by cultivating microorganisms such as bacteria, fungi (including yeast and filamentous organisms), archaea, plants, or algae. But monitoring the biomass — tracking the development of the cell concentration over time and characterizing the growth of the cultivated microorganism — is critical. Scientists need to be able to screen and time manual workflows, ensure quality control, keep projects running smoothly, adhere to budgets, and deliver the expected results. And while there are numerous options as to the technology used, the monitoring approach needs to fit the bioprocess: the challenge is matching the most effective, appropriate technology to the bioprocess being monitored.

Common Pain Points

We're seeing scientists under a great deal of pressure to solve technological problems without being technologists. They don't possess the technical background to assess the key factors involved in choosing the best biomass monitoring strategy — yet the quality of their work depends on it.

The Need for Guidance

What we hear frequently from scientists and researchers is that they need more guidance to decide the best route to a successful outcome when it comes to biomass monitoring. One of the most common pain points they report in terms of bioprocessing are black-box bioprocesses that are "under-sampled" — naturally, shorter sampling intervals will lead to a better data-density, which will provide deeper insights into the bioprocess.

Making Critical Decisions

As more and more industries adopt biomass monitoring as part of their approach to bioprocessing, that's also putting more pressure on scientists to act as technology decision-makers. At the same time, it's also changing how we treat bioprocesses and raising the standards for data and outcomes. As biomass monitoring increases across a whole range of industries, it's becoming a must-do — and a must-know. Putting scientists in the driver's seat on making critical decisions means providing them with the right criteria to make the best choice for the desired outcome.

Industries Using Biomass Monitoring

New innovations are prompting a surge in bioprocessing across a range of industries. With that comes a need for effective biomass monitoring.

Food & Beverage

- Fermented beverages
- Animal-free food
- Artificial meat
- Animal feed

Chemicals (White Biotech)

- Flavors and fragrances
- Cosmetics
- Fuels
- Chemical building blocks
- Enzymes

Biopharma (Red Biotech)

- Biopharmaceuticals
- Diagnostics

Agriculture (Green Biotech)

- Optimized seeds
- Biopesticides

Biomass Monitoring: A Vital Lab Partner

Measuring the biomass in a culture and plotting it over time creates an organism- and process-specific growth curve — which enables researchers to not only understand, optimize, and control the bioprocess, but also the production of the desired product.

Screen for the Best Strain and/or Conditions

Biomass monitoring enables scientists and researchers to accurately compare the growth curves of various strains and then of the same strain under various bioprocess conditions — such as temperature, media composition, pH, and batch vs. fed-batch.

Time Experimental Workflows

Monitoring facilitates accurate timing of manual workflow steps — such as inoculation, induction, feeding, sampling, cell or product harvesting, and cooling. Monitoring the growth phase of an organism at a given point greatly increases experimental efficiency and scientific outcome.

Detect Events in Real Time

Biomass monitoring gives scientists a detection system for the key events that may occur during microbial fermentation — such as diauxic shifts, oxygen-, substrate-, product- or metabolite-inhibitions, and morphological changes. Detecting these events enables better characterization and optimization of both the microorganism and the bioprocess.

Control Quality

Monitoring the growth curve can help determine if an experiment is reproducible or not, and if this cultivation can be used for further experiments or production steps. It can also help scientists detect a problem — and avoid costly problems further downstream.

“So many of our customers are biologists facing technical challenges. Their objective is to modify the biology so their bioprocesses achieve the best results and organisms produce the target product.

Without question, their success depends on having the best tools and the best methods. But they don’t have the time, energy, or bandwidth to conduct screening, comparing, and assessing to determine the right sensors and software.

We wanted to provide them with an informative shortcut to making the best decision. Using this guide can greatly reduce time spent comparing technologies, so scientists can spend more time doing what they need to do: their research science.”

Daniel Grünes, President & CEO, SBI

Selecting the Right Technology

Selecting the right technology for monitoring a bioprocess starts with knowing the key factors to consider. In essence, no matter what you're working on, there are three essential elements at play: application, bioprocess, and cultivation vessel.

The Application May Include:

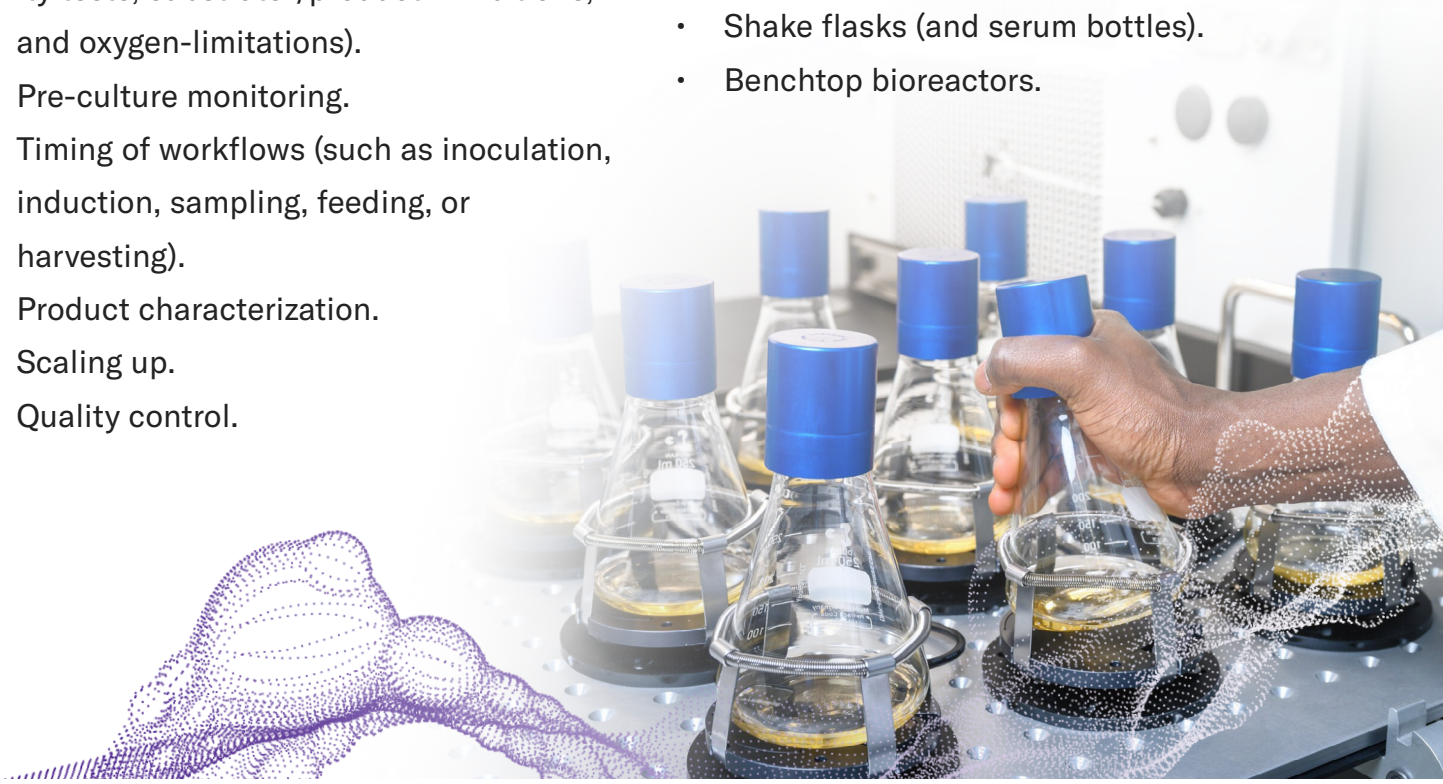
- Strain development, screening and characterization.
- Bioprocess optimization.
- Media optimization.
- Growth characterization (including toxicity tests, substrate-/product-inhibitions, and oxygen-limitations).
- Pre-culture monitoring.
- Timing of workflows (such as inoculation, induction, sampling, feeding, or harvesting).
- Product characterization.
- Scaling up.
- Quality control.

The Bioprocess Includes:

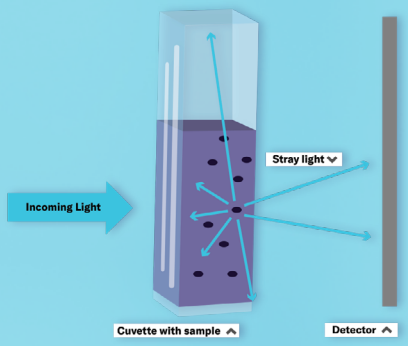
- The kind of organism being used.
- The number of parallel strains to be monitored.
- The amount of culture volume needed for product characterization.
- The available time for hands-on manual workflows.
- The level of data resolution needed.

The Cultivation Vessel May Include:

- Titer- or Microtiter plates (MTPs).
- Shake flasks (and serum bottles).
- Benchtop bioreactors.

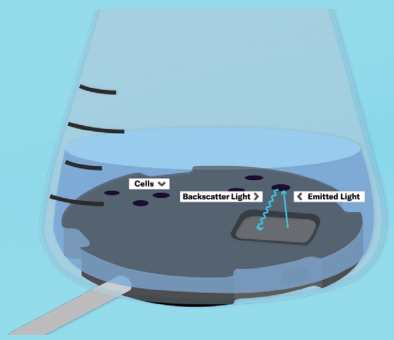


Principles of Measurement



Absorbance

Light with a specific wavelength is emitted into the fermentation broth. A sensor on the other side of the broth detects the intensity of the light as it passes through. The more cells in the culture, the less light. Using the Lambert Beer law, this signal can be used to calculate the optical density, or OD.

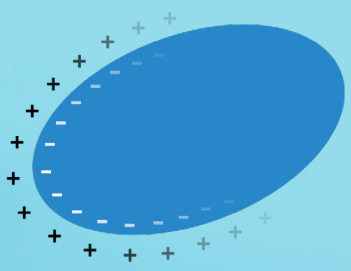


Backscatter

Light with a specific wavelength is emitted into the fermentation broth. A sensor close to the light source detects the amount of the light scattered back by the cells and other particles in the broth. The more cells in the culture, the more light is scattered back.

Cell Dry Weight

Scientists take a defined volume of cells from the cultivation broth and transfer it in a pre-weighed tube. The cells are then dried overnight, so that any water is removed and weighed precisely. Substracting the weight of the empty tube equals the weight of the dried cells per defined volume.



Capacitance

Microorganisms have a cell membrane, that, if intact, can act as a capacitor when an electric field is applied. The resulting capacitance can be monitored and used to derive information about the cell concentration and the amount of cells with intact membranes — in other words, viable cells.

The Biomass Monitoring Comparison Guide

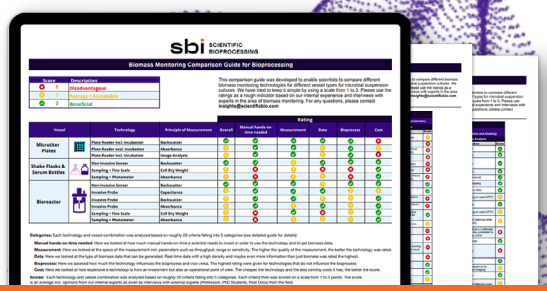
To simplify the decision-making, we created a comparison guide that lays out all the factors in combination, showing the advantages and disadvantages depending on the specific need. It's our solution to a common problem faced by scientists working with microbial suspension cultures: they haven't had the means to compare different biomass technologies for different cultivation vessels.

Creating the Guide

This comparison chart is the first guide of its kind, created by scientists for scientists. To create it, SBI looked at data from 8 years of experiments conducted by our customers, and reviewed a dozen biomass monitoring technologies in detail. Over the course of months, we compiled and compared the information, discussing the results with a hand-picked group of experts, including fermentation scientists, university academics specialized in bioprocessing, and experienced lab experts. The resulting guide was designed to encompass a broad range of problems faced by scientists when it comes to monitoring bioprocesses.

"We're already seeing how this Comparison Guide helps our customers select the right approach and technologies for monitoring a given bioprocess. The Guide does the heavy lifting for researchers, connecting all the dots in one place, removing the guesswork, and freeing up valuable time to focus on the science. We wanted it to be a gamechanger for scientists."

— Jens Bayer, VP of Marketing, SBI



Access the Full Biomass Comparison Guide!

How to Use the Comparison Guide

While all three factors form that all-important triad, knowing how to best determine the technology can seem like a juggling act. For instance, the bioprocess used will determine the application used; from there, you can determine the best cultivation vessel. But we also know that scientists and researchers face countless variations and combinations.

Consider, for instance, a process whose principle of measurement is cell dry weight, versus backscatter: if a scientist is looking to measure biomass in a non-invasive way — without any time delays — and has a high biomass concentration, backscatter with optical sensors measuring biomass in shake flasks is a far more advantageous approach than cell dry weight – which is an inherently invasive approach that involves offline sampling, multiple measurements, and time delays. Knowing your goals, conditions, and your choices will make all the difference in the outcome.

Using the Biomass Monitoring Comparison Guide: A Case Study

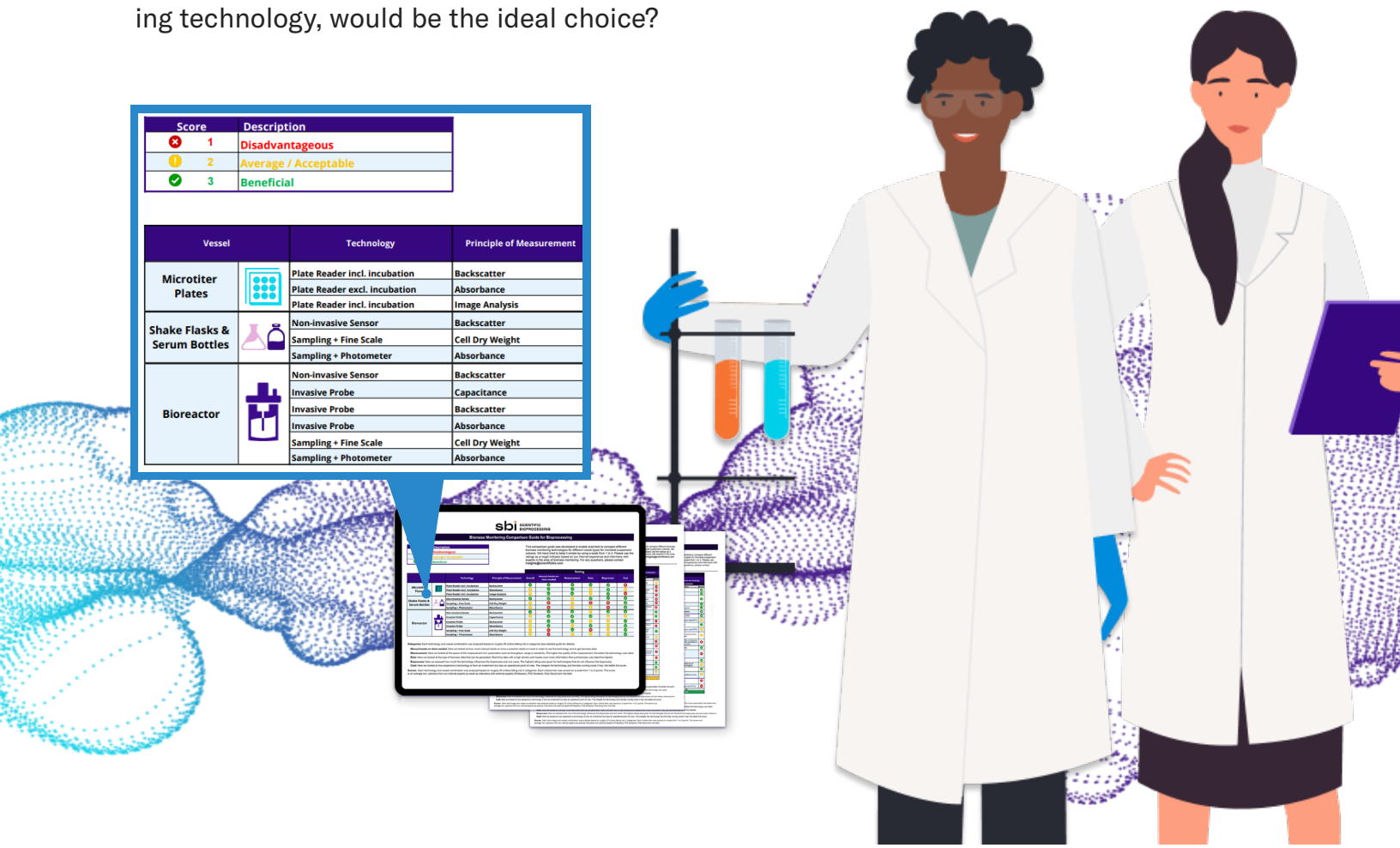
Frank and Emma are fermentation scientists working in the nutrition industry who have been working to characterize a strain from the metabolic engineering department. Based on early screening in microtiter plates, the biomass development they've seen correlates with their desired product. Now they want to scale up and test the lead strain on a larger scale while allowing for biomass monitoring. The question they face is: which vessel type, in combination with which biomass monitoring technology, would be the ideal choice?

To Determine the Answer, They Must First Factor In Several Requirements.

- The technology to monitor biomass production needs to be both inexpensive and efficient.
- It needs to produce real-time, high-density data — so they can see when something happens during the bioprocess.
- They also need to be able to test with greater volumes to increase their product yields, and allow for improved characterization.

Score		Description
1		Disadvantageous
2		Average / Acceptable
3		Beneficial

Vessel		Technology	Principle of Measurement
Microtiter Plates		Plate Reader incl. incubation	Backscatter
		Plate Reader excl. incubation	Absorbance
		Plate Reader incl. incubation	Image Analysis
Shake Flasks & Serum Bottles		Non-invasive Sensor	Backscatter
		Sampling + Fine Scale	Cell Dry Weight
		Sampling + Photometer	Absorbance
Bioreactor		Non-invasive Sensor	Backscatter
		Invasive Probe	Capacitance
		Invasive Probe	Backscatter
		Invasive Probe	Absorbance
		Sampling + Fine Scale	Cell Dry Weight
		Sampling + Photometer	Absorbance



Assessing the Conditions

Using the Biomass Monitoring Comparison Guide, Frank and Emma start working out the conditions they face to determine the best vessel and technology for the next phase.

Knowing they want to work with increased volumes, they skip straight to the shake flask or bioreactor sections listed on the guide. They know that shake flasks are inexpensive, easy to use, and enable work to happen in multiples, meaning they could conduct many parallel tests easily. The problem is that they need control tools, which they would have if they worked with a bioreactor. But bioreactors can get expensive, which won't help them stick to their budget. Considering costs, they decide on shake flasks.

Pros & Cons

Their next step is to consider the pros and cons of the different technologies available with this vessel type. They need a non-invasive sensor that can be automated, so they don't have to run a lot of time-consuming manual steps. With this in mind, they land on backscatter as a principle of measurement. According to the guide, they would:

- Have no running costs.
- Obtain more data than what they get from their current process of offline monitoring.
- Have a reduced risk of contamination.

They report all of their findings to their manager with a clear recommendation: use shake flasks and non-invasive sensors. This approach provides the greatest ease of use along with lower costs. And it gives Frank and Emma the ability to run more screenings in parallel, yet keep the principle of measurement constant as they scale up.
The manager gives them the thumbs up.

Had Frank and Emma not had the guide to refer to, they would have been mired in a long process of researching individual biomass monitoring technologies, comparing product sheets, and talking to vendors. Instead, the guide offers all the information they need in one place:

- Price
- Performance
- Compatibility with their bioprocess
- The advantages / disadvantages of each technology

Having Accomplished Their Goal and Settled on the Right Technology, They Can Now Get Back to What They Love to Do Best: The Science.

Keep Reading for the Full Biomass Comparison Guide

Biomass Monitoring Comparison Guide for Bioprocessing

Score		Description
✖	1	Disadvantageous
!	2	Average/Acceptable
✔	3	Beneficial

This comparison guide was developed to enable scientists to compare different biomass monitoring technologies for different vessel types for microbial suspension cultures. We have tried to keep it simple by using a scale from 1 to 3. Please use the ratings as a rough indicator based on our internal experience and interviews with experts in the area of biomass monitoring. For any questions, please contact **insights@scientificbio.com**

Vessel		Technology	Principle of Measurement	Rating: Overall	Manual hands-on-time needed	Measurement	Data	Bioprocess	Cost
Microtiter Plates		Microbioreactor System	Backscatter	✔	✔	✔	✔	✔	✖
		Microbioreactor System	Absorbance	!	✔	✔	!	✔	!
		Microbioreactor System	Image Analysis	!	✔	✔	!	✔	✖
Shake Flasks & Serum Bottles		Non-invasive Sensor	Backscatter	✔	✔	!	✔	✔	✔
		Sampling + Fine Scale	Cell Dry Weight	!	✖	!	✖	✖	✔
		Sampling + Photometer	Absorbance	!	✖	!	!	✖	✔
Bioreactor		Non-invasive Sensor	Backscatter	✔	✔	✔	!	✔	✔
		Invasive Probe	Capacitance	!	✔	✔	✔	!	!
		Invasive Probe	Backscatter	!	✔	✔	!	!	✔
		Invasive Probe	Absorbance	!	✔	!	✔	!	✔
		Sampling + Fine Scale	Cell Dry Weight	!	✖	✔	✖	!	✔
		Sampling + Photometer	Absorbance	!	✖	!	!	!	✔

Categories: Each technology and vessel combination was analyzed based on roughly 20 criteria falling into 5 categories (see detailed guide for details):

Manual hands-on-time needed: Here we looked at how much manual hands-on-time a scientist needs to invest in order to use the technology and to get biomass data. The more automated, the better the technology was rated.

Measurement: Here we looked at the specs of the measurement incl. parameters such as throughput, range or sensitivity. The higher the quality of the measurement, the better the technology was rated.

Data: Here we looked at the type of biomass data that can be generated. Real-time data with a high density and maybe even more information than just biomass was rated the highest.

Bioprocess: Here we assessed how much the technology influences the bioprocess and vice versa. The highest ratings were given for technologies that do not influence the bioprocess and are hardly influenced themselves by the bioprocess.

Cost: Here we looked at how expensive a technology is from an investment but also an operational point of view. The cheaper the technology and the less running costs it has, the better the score.

Scores: Each technology and vessel combination was analyzed based on roughly 20 criteria falling into 5 categories. Each criteria was then scored on a scale from 1 to 3 points. The score is an average incl. opinions from our internal experts as well as interviews with external experts (Professors, PhD Students, Post Docs) from the field.

sbi SCIENTIFIC BIOPROCESSING

Biomass Monitoring Comparison Guide for Bioprocessing

Score		Description
✗	1	Disadvantageous
!	2	Average/Acceptable
✓	3	Beneficial

This comparison guide was developed to enable scientists to compare different biomass monitoring technologies for different vessel types for microbial suspension cultures. We have tried to keep it simple by using a scale from 1 to 3. Please use the ratings as a rough indicator based on our internal experience and interviews with experts in the area of biomass monitoring. For any questions, please contact **insights@scientificbio.com**

MICROTITER PLATES

MICROTITER PLATES

Technology		Microbioreactor System (incl. incubation and shaking)		Plate Reader (excl. incubation and shaking)		Plate Reader (incl. incubation and shaking)	
Principle of Measurement		Backscatter		Absorbance		Image Analysis	
		Explanation	Score	Explanation	Score	Explanation	Score
Manual hands-on-time for…	Measurement Preparation	No	✓	Yes (blanking of media)	!	No	✓
	Sampling	No	✓	No	✓	No	✓
	Vessel/Sample Transfer	No	✓	Yes (taking MTP from incubator and bringing it to plate reader and back)	✗	No	✓
	Sample Dilution	No	✓	No (not applicable for MTPs)	✓	No	✓
	Measurement	No (automated)	✓	No (automated)	✓	No (automated)	✓
	Data Transfer/Handling	No (automated)	✓	No (automated)	✓	No (automated)	✓
Measurement	Throughput per Device	High (up to 48)	✓	High (most often 96)	✓	High (up to 960)	✓
	Sensitivity	Low	✗	High	✓	Medium (depending on used MTP)	!
	Reproducibility (well to well)	High	✓	High	✓	High	✓
	Range	High	✓	Low (< OD 1)	✗	Medium (depending on used MTP)	!
Data	Density	Medium (limited by read-out-time per well)	!	Low (theoretically higher if one is willed to bring the plate to the reader very often)	✗	Medium (limited by read-out-time per well)	!
	Parameter	Backscatter [a.u.] - established parameter that can be correlated to e.g., OD or CDW	!	Optical Density [a.u] - Gold Standard and no need for conversion	✓	Biomass equivalent [a.u.] unknown parameter that can be correlated to e.g., OD or CDW	✗
	Availability	Real-time	✓	Real-time	✓	Real-time	✓
	Additional parameters available from same device	Yes (e.g., fluorescence, pH, DO)	✓	Yes (e.g. fluorescence, absorbance for some)	!	No	✗
Bioprocess	Loss of culture volume	No	✓	No	✓	No	✓
	Bioprocess interruption	No	✓	Yes, moving plate from shaker to reader and back	✗	Yes, shaking needs to be interrupted for imaging	!
	Risk of contamination	No	✓	No	✓	No	✓
	Compatible with different vessel sizes and types	Only for special MTPs	✗	Standard MTPs	✓	Special MTPs but different sizes	!
Cost	CAPEX (investment costs per device)	High	✗	Medium	!	High	✗
	OPEX (e.g., consumables)	High (special single use MTPs)	✗	Medium (standard MTPs)	!	High (special single use MTPs)	✗
Total Score		50		42		48	
% of maximal Score		83%		78%		80%	

Categories: Each technology and vessel combination was analyzed based on roughly 20 criteria falling into 5 categories (see detailed guide for details):

Manual hands-on-time needed: Here we looked at how much manual hands-on-time a scientist needs to invest in order to use the technology and to get biomass data. The more automated, the better the technology was rated.

Measurement: Here we looked at the specs of the measurement incl. parameters such as throughput, range or sensitivity. The higher the quality of the measurement, the better the technology was rated.

Data: Here we looked at the type of biomass data that can be generated. Real-time data with a high density and maybe even more information than just biomass was rated the highest.

Bioprocess: Here we assessed how much the technology influences the bioprocess and vice versa. The highest ratings were given for technologies that do not influence the bioprocess and are hardly influenced themselves by the bioprocess.

Cost: Here we looked at how expensive a technology is from an investment but also an operational point of view. The cheaper the technology and the less running costs it has, the better the score.

Scores: Each technology and vessel combination was analyzed based on roughly 20 criteria falling into 5 categories. Each criteria was then scored on a scale from 1 to 3 points. The score is an average incl. opinions from our internal experts as well as interviews with external experts (Professors, PhD Students, Post Docs) from the field.

Biomass Monitoring Comparison Guide for Bioprocessing

Score		Description
✗	1	Disadvantageous
!	2	Average/Acceptable
✓	3	Beneficial

This comparison guide was developed to enable scientists to compare different biomass monitoring technologies for different vessel types for microbial suspension cultures. We have tried to keep it simple by using a scale from 1 to 3. Please use the ratings as a rough indicator based on our internal experience and interviews with experts in the area of biomass monitoring. For any questions, please contact **insights@scientificbio.com**

SHAKE FLASKS / SERUM BOTTLES

SHAKE FLASKS / SERUM BOTTLES	Technology		Non-invasive Sensor		Fine Scale		Photometer / Spectrophotometry	
	Principle of Measurement		Backscatter		Cell Dry Weight		Absorbance	
			Explanation	Score	Explanation	Score	Explanation	Score
	Manual hands-on-time for…	Measurement Preparation	No	✓	Yes (weighing empty tubes, drying samples)	✗	Yes (blanking of media)	!
		Sampling	No	✓	Yes	✗	Yes	✗
		Vessel/Sample Transfer	No	✓	Yes (e.g. flask to sterile hood, sample to drying cabinet)	✗	Yes (e.g. flask to sterile hood, sample to photometer)	✗
		Sample Dilution	No	✓	No	✓	Yes (for OD > 1)	✗
		Measurement	No (automated)	✓	Yes (weighing of tubes)	✗	Yes (handling photometer)	✗
		Data Transfer/Handling	No (software)	✓	Yes (manual recording)	✗	Yes (manual recording)	✗
	Measurement	Throughput per Device	Medium (up to 16), with several devices up to 64	!	Low (limited by manual workflows and available volume)	✗	Low (limited by manual workflows and available volume)	✗
		Sensitivity	Low	✗	Low (often too little volume for high sensitivity)	✗	High	✓
		Reproducibility (vessel to vessel)	Medium (depends on flask material/condition)	!	Medium (fault-prone method)	!	High	✓
		Range	High	✓	High	✓	Low (above OD 0.8-1 requires dilution)	✗
	Data	Density	High	✓	Low (limited by available culture volume/personnel)	✗	Low (limited by available culture volume/personnel)	✗
		Parameter	Backscatter [a.u.] - established parameter that can be correlated to e.g., OD or CDW	!	Cell Dry Weight [g/L] - Gold Standard and no need for conversion	✓	Optical Density [a.u] - Gold Standard and no need for conversion	✓
		Availability	Real-time	✓	Delayed by several hours/days	✗	Delayed by a couple of min	!
		Additional parameters available from same device	Yes (e.g., RPM, Temperature, pH/DO for some)	!	No	✗	No	✗
	Bioprocess	Loss of culture volume	No	✓	Yes	✗	Yes	✗
		Bioprocess interruption	No	✓	Yes (e.g., stopping shaker/moving flask from shaker to sterile hood)	✗	Yes (e.g., stopping shaker/moving flask from shaker to sterile hood)	✗
		Risk of contamination	No	✓	Yes (invasive)	✗	Yes (invasive)	✗
		Compatible with different vessel sizes and types	Yes	✓	Yes	✓	Yes	✓
	Cost	CAPEX (investment costs per device)	Medium	!	Low	✓	Low	✓
		OPEX (e.g., consumables)	None	✓	Medium (Tubes)	!	Medium (Cuvettes)	!
	Total Score		50		32		33	
	% of maximal Score		88%		53%		55%	

Categories: Each technology and vessel combination was analyzed based on roughly 20 criteria falling into 5 categories (see detailed guide for details):

Manual hands-on-time needed: Here we looked at how much manual hands-on-time a scientist needs to invest in order to use the technology and to get biomass data. The more automated, the better the technology was rated.

Measurement: Here we looked at the specs of the measurement incl. parameters such as throughput, range or sensitivity. The higher the quality of the measurement, the better the technology was rated.

Data: Here we looked at the type of biomass data that can be generated. Real-time data with a high density and maybe even more information than just biomass was rated the highest.

Bioprocess: Here we assessed how much the technology influences the bioprocess and vice versa. The highest ratings were given for technologies that do not influence the bioprocess and are hardly influenced themselves by the bioprocess.

Cost: Here we looked at how expensive a technology is from an investment but also an operational point of view. The cheaper the technology and the less running costs it has, the better the score.

Scores: Each technology and vessel combination was analyzed based on roughly 20 criteria falling into 5 categories. Each criteria was then scored on a scale from 1 to 3 points. The score is an average incl. opinions from our internal experts as well as interviews with external experts (Professors, PhD Students, Post Docs) from the field.

sbi SCIENTIFIC BIOPROCESSING

Biomass Monitoring Comparison Guide for Bioprocessing

Score		Description
✗	1	Disadvantageous
!	2	Average/Acceptable
✓	3	Beneficial

This comparison guide was developed to enable scientists to compare different biomass monitoring technologies for different vessel types for microbial suspension cultures. We have tried to keep it simple by using a scale from 1 to 3. Please use the ratings as a rough indicator based on our internal experience and interviews with experts in the area of biomass monitoring. For any questions, please contact **insights@scientificbio.com**

BIOREACTORS

BIOREACTORS

Technology		Non-invasive Sensor		Invasive Probe						Fine Scale		Photometer / Spectrophotometry	
Principle of Measurement		Backscatter		Capacitance		Backscatter		Absorbance		Cell Dry Weight		Absorbance	
		Explanation	Score	Explanation	Score			Explanation	Score	Explanation	Score	Explanation	Score
Manual hands-on-time for…	Measurement Preparation	Yes (installation)	!	Yes (installation, autoclaving, cleaning)	✗	Yes (installation, autoclaving, cleaning)	✗	Yes (installation, autoclaving, cleaning)	✗	Yes (weighing empty tubes, drying samples)	✗	Yes (blanking of media)	!
	Sampling	No	✓	No	✓	No	✓	No	✓	Yes	✗	Yes	✗
	Vessel/Sample Transfer	No	✓	No	✓	No	✓	No	✓	Yes (e.g., sample to drying cabinet)	✗	Yes (e.g., sample to photometer)	✗
	Sample Dilution	No	✓	No	✓	No	✓	No	✓	No	✓	Yes (for OD > 1)	✗
	Measurement	No (automated)	✓	No (automated)	✓	No (automated)	✓	No (automated)	✓	Yes (weighing of tubes)	✗	Yes (handling photometer)	✗
	Data Transfer/Handling	No (software/integration)	✓	No (software/integration)	✓	No (software/integration)	✓	No (software/integration)	✓	Yes (manual recording)	✗	Yes (manual recording)	✗
Measurement	Sensitivity	Medium	!	High	✓	Medium	!	Medium	!	High (at the cost of culture volume loss)	✓	High	✓
	Range	High	✓	Medium (limited at high cell densities)	!	High	✓	Different probes needed for different ranges	✗	High	✓	Low (> OD 0.8-1 requires dilution)	✗
Data	Density	High	✓	High	✓	High	✓	High	✓	Low (limited by personnel)	✗	Low (limited by personnel)	✗
	Parameter	Backscatter [a.u.] - established parameter that can be correlated to e.g., OD or CDW	!	capacitance [pF/cm] - unknown parameter can be correlated to e.g., OD or CDW	✗	Backscatter [a.u.] - established parameter that can be correlated to e.g., OD or CDW	!	Optical Density [concentration units] - Gold Standard and no need for conversion	✓	Cell Dry Weight [g/L] - gold Standard and no need for conversion	✓	Optical Density [a.u] - Gold Standard and no need for conversion	✓
	Availability	Real-time	✓	Real-time	✓	Real-time	✓	Real-time	✓	Delayed by several hours/days	✗	Delayed by a couple of min	!
	Additional parameters available from same device	No	✗	Yes (viability information)	✓	No	✗	No	✗	No	✗	No	✗
Bioprocess	Loss of culture volume	No	✓	No	✓	No	✓	No	✓	Yes	✗	Yes	✗
	Influence of Foaming / Aeration / Agitation	High	✗	High	✗	High	✗	Medium	!	Low	✓	Low	✓
	Risk of contamination	No	✓	No	✓	No	✓	No	✓	Yes (invasive)	✗	Yes (invasive)	✗
	Blocking Ports of Bioreactor	No	✓	Yes	✗	Yes	✗	Yes	✗	No	✓	No	✓
	Compatible with different vessel sizes and types	Yes	✓	Different probe lengths for different vessel sizes	!	Different probe lengths for different vessel sizes	!	Different probe lengths for different vessel sizes	!	Yes	✓	Yes	✓
Cost	CAPEX (investment costs per device)	Low	✓	High	✗	Medium	!	Medium	!	Low	✓	Low	✓
	OPEX (e.g., consumables)	None	✓	None	✓	None	✓	None	✓	Medium (Tubes)	!	Medium (Cuvettes)	!
Total Score		50		45		45		45		36		34	
% of maximal Score		88%		79%		79%		79%		63%		60%	

Categories: Each technology and vessel combination was analyzed based on roughly 20 criteria falling into 5 categories (see detailed guide for details):

Manual hands-on-time needed: Here we looked at how much manual hands-on-time a scientist needs to invest in order to use the technology and to get biomass data. The more automated, the better the technology was rated.

Measurement: Here we looked at the specs of the measurement incl. parameters such as throughput, range or sensitivity. The higher the quality of the measurement, the better the technology was rated.

Data: Here we looked at the type of biomass data that can be generated. Real-time data with a high density and maybe even more information than just biomass was rated the highest.

Bioprocess: Here we assessed how much the technology influences the bioprocess and vice versa. The highest ratings were given for technologies that do not influence the bioprocess and are hardly influenced themselves by the bioprocess.

Cost: Here we looked at how expensive a technology is from an investment but also an operational point of view. The cheaper the technology and the less running costs it has, the better the score.

Scores: Each technology and vessel combination was analyzed based on roughly 20 criteria falling into 5 categories. Each criteria was then scored on a scale from 1 to 3 points. The score is an average incl. opinions from our internal experts as well as interviews with external experts (Professors, PhD Students, Post Docs) from the field.

sbi SCIENTIFIC BIOPROCESSING

Have Questions?

Let’s work together to find a solution that works best for you.

SPEAK WITH AN EXPERT