BAMS Technology Overview

Micron View Limited

Sept 2020

Content

MICRONVIEW

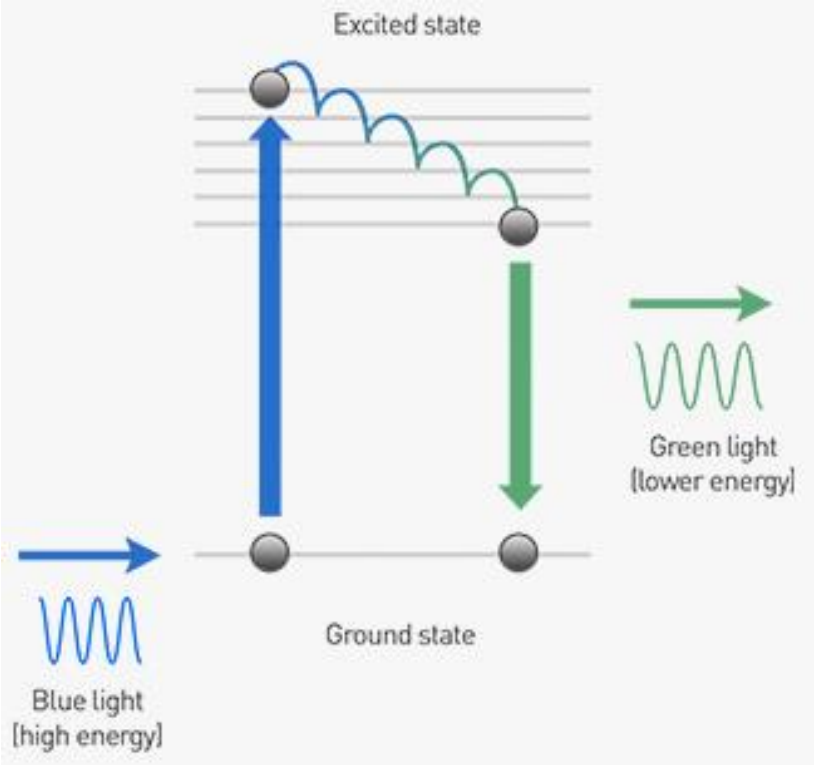
Laser-Induced Fluorescence, LIF

The Heart of BAMS

A fluorescence diagnostic technique with high sensitivity

Principle:

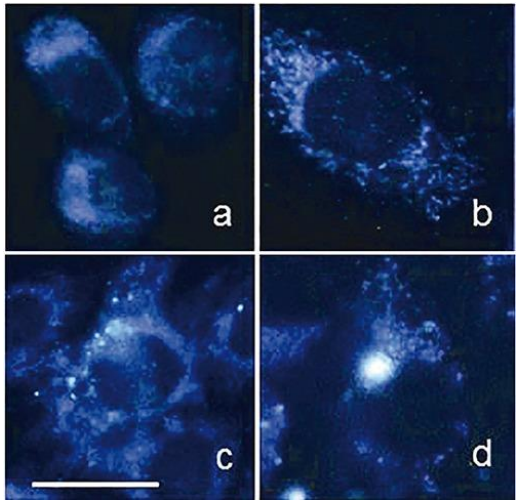
LIF is a method that excites specific kinds of atoms or molecules using a laser of appropriate wavelength. During this process, the molecules emit energy through spontaneous radiation, which makes them fluoresce. The intensity and distribution of laser induced fluorescence is monitored and ground state distribution of the atoms or molecules is observed by the detector, and the laser induced fluorescence spectrum is obtained.



Bio Fluorescing Particles (BFP):

What is Auto-fluorescence?

All cells contain many molecules that naturally fluoresce!

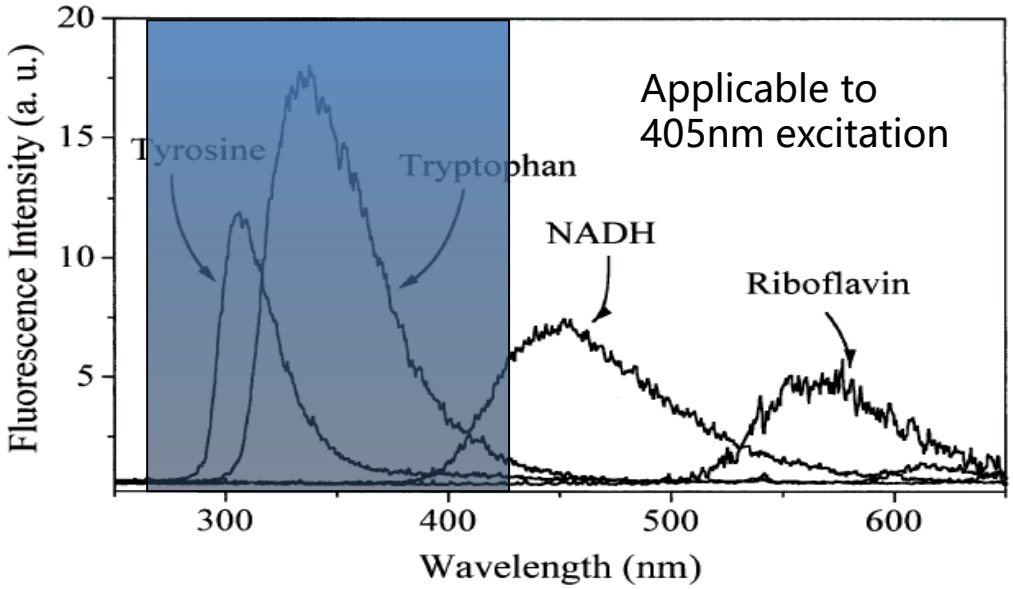


Molecule	Approximate Peak Fluorescence (nm)
NAD(P)H	450
Retinol	500
Riboflavin	550
Folic acid	450
Pyridoxine	400
Tyrosine	305
Tryptophan	325
Flavin	540

Bio Fluorescent Particle Counters (BFPC)

BAMS uses the metabolites found in all cells to differentiate inert particles from biologic

Riboflavin (VitaminB_2) and **nicotinamide adenine dinucleotides (NADH)** are indicators of metabolism in organisms. They can be used as markers of microbial activity and have a specific fluorescence emission wavelength range.



(Hill et al, Field Ana. Chem. & Tech, 3(4-5), 221,1999)

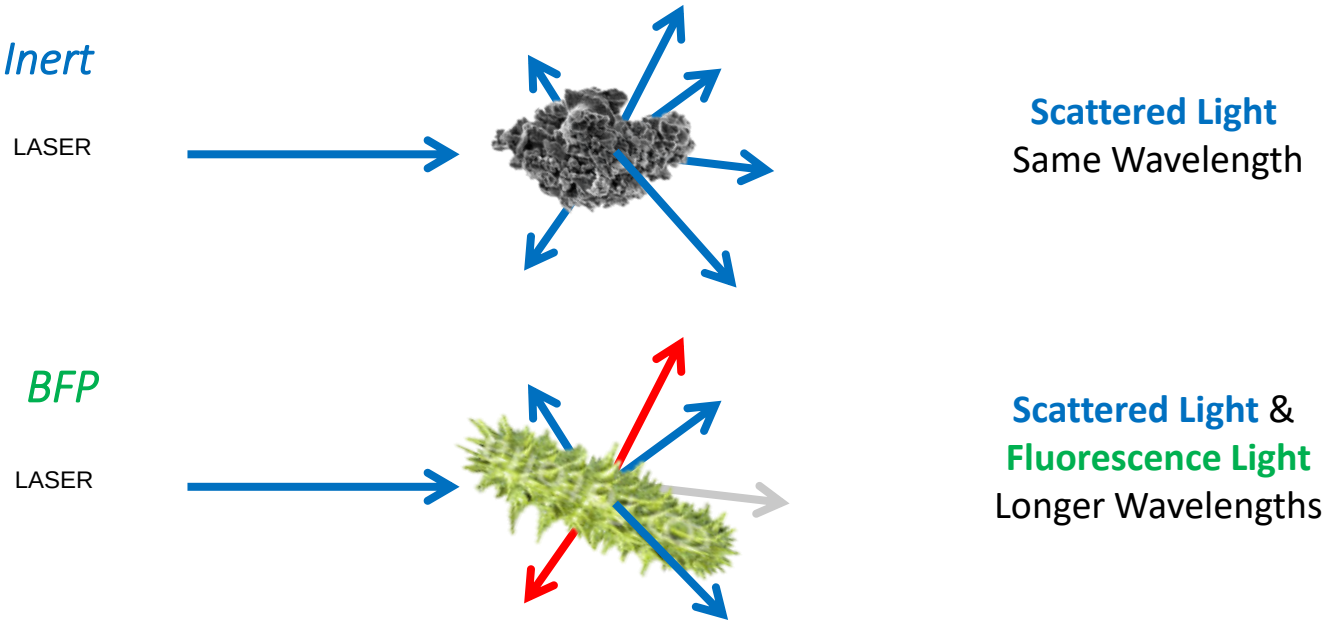
Microbes, including bacteria, fungi and spores have metabolites such as NADH, riboflavin and other protein that can be excited.

Bio Fluorescent Particle Counters (BFPC)

Laser Induced Fluorescence:

Each particle is analyzed:

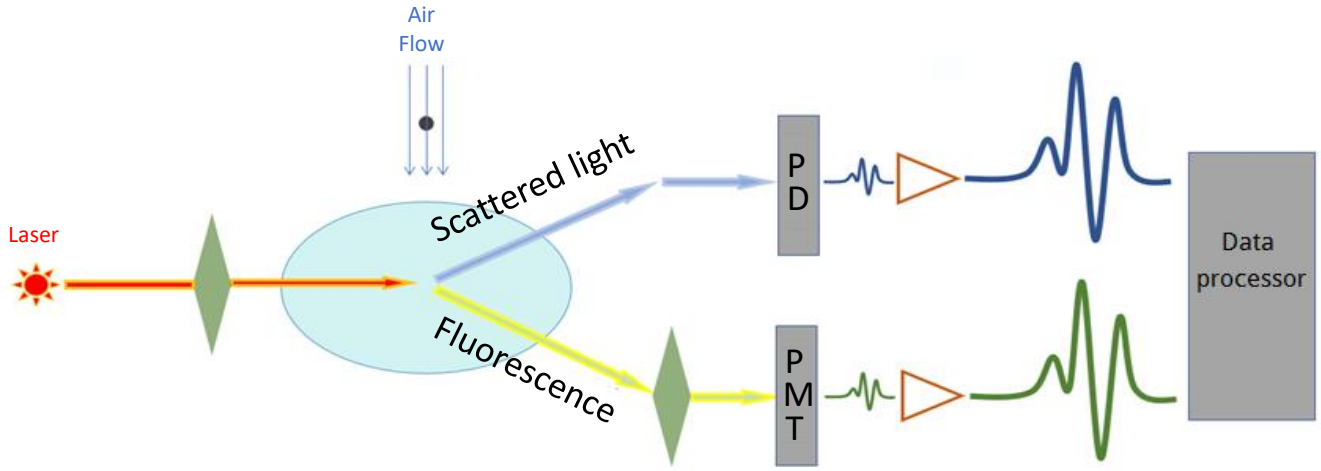
- Scattered light intensity (size)
- Fluorescent light intensity (composition)



Technical Principle of BAM®S

① Sample air is irradiated by a 405nm laser
② All particles, inert and biologic, are assessed for size and fluorescence
③ NADH and riboflavin in the viable particles emit fluorescence
④ BAM®S detects scattered light and fluorescence simultaneously in real time

- Biologic particles scatter light and emit fluorescence, and can be cultured
- VBNC (Viable But Not Culturable) biologic particles excite scattered light and fluorescence, and are non-culturable

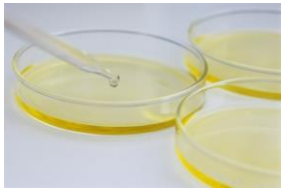


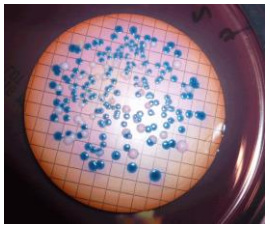
Conventional Environmental Microbial Testing is a 19th Century Technology

- Louis Pasteur – Germ Theory **1861**
- Julius Petri – Petri Dish **1877**
- Sample -> Culture -> Wait many days for result -> Inspect

Advances in collection and inspection technology have been made, but microbial testing today is not much different

Take sample --> plate sample --> culture --> inspect





Case 1 – Monitoring of a controlled area

Sandle T, Leavy C, Jindal H, Rhodes R. Application of rapid microbiological methods for the risk assessment of controlled biopharmaceutical environments. J Appl Microbiol. 2014 Jun;116(6):1495-505

Case 2 – Pfizer Case Study: Rapid Microbial Methods For Investigation and Manufacturing Recovery After Hurricane

Montenegro-Alvarado JM, Salvas J, Weber J, Mejías S, Arroyo R. Pfizer case study: rapid microbial methods for manufacturing recovery after Hurricane María. Pharm Online [Internet]. 2018 July [cited 2019 Sept 02]. Available from: https://www.pharmaceuticalonline.com/doc/pfizercase-study-rapid-microbial-methods-formanufacturing-recovery-after-hurricanemar-a-0001

Montenegro-Alvarado JM. Leveraging rapid microbiological methodology in forensic evaluation to identify elusive root cause. Amer Pharm Rev [Internet]. 2018 Sep [cited 2019 Sept 02]. Available from: https://www.americanpharmaceuticalreview.com/Featured-Articles/353500-Leveraging-Rapid-Microbiological-Methodology-in-Forensic-Evaluation-to-Identify-Elusive-Root-Cause/

Case 3 - Cleanroom operations simulation

BAMS Bio Counts are Higher Than Compendial Methods

It is widely known that less than 1% of captured microbes can be grown on media

The majority of microbes in the environment are Viable but not culturable, VBNC

BAMS LIF technology counts all biologic particles, including VBNC

D50

The minimum size cut off, or D50, is the smallest particle size that the instrument can capture. The D50 of many microbial sample collectors make them inefficient for collecting smaller sized bacteria

Portable Microbial Impactors

RCS High Flow
100 L/min,
agar strip
D_{50} = 1.2 µm

SAS Super 180
180L/min
40 mL agar
D_{50} = 2.1 µm

Millipore Air Tester
140/180 L/min
agar plate
D_{50} = 2.3 µm

BioStage
28.3 L/min,
50 mL agar
D_{50} = 0.65 µm

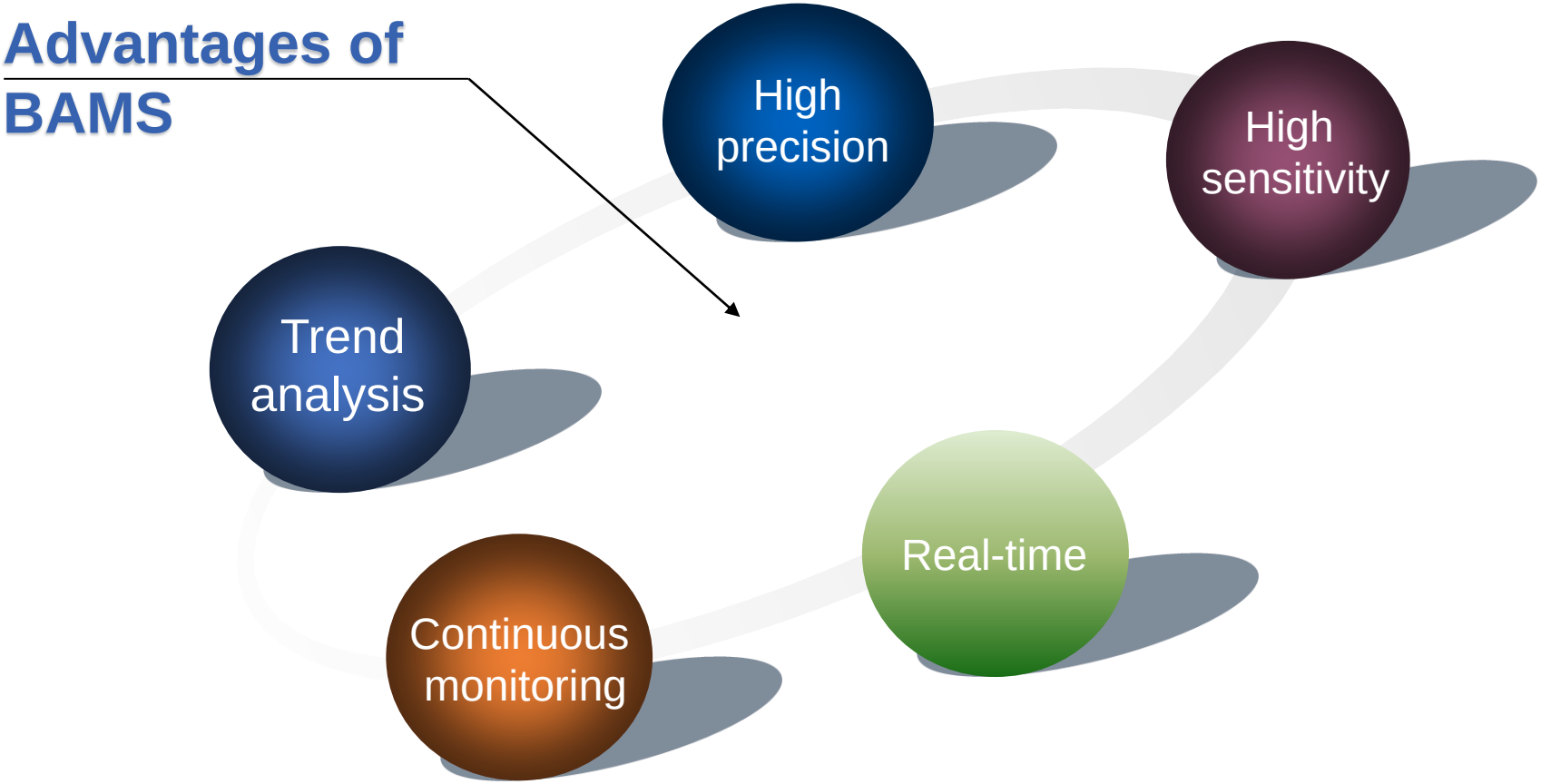
Portable Microbial Impactors

MAS-100
100 L/min,
50 mL agar
D_{50} = 1.7 µm

Bio-Culture
120 L/min,
30 mL agar
D_{50} = 7 µm

Microflow
120 L/min,
25 mL agar
D_{50} = 8.8 µm

SMA MicroPortable
28.3/141.5 L/min,
25 mL agar
D_{50} = 4.8 µm


Advantages of BAMS
High precision
High sensitivity
Trend analysis
Real-time
Continuous monitoring

MICRONVIEW

BAMS
Microbial Monitoring

Market Need

- Timely Data & Results
- Resource Reduction
- Better Control
- Regulatory Demands

- ☑ Real-time results
  - ☑ Microbe presence/count
  - ☑ Microbe sizes in microns
- ☑ No sample consumables
- ☑ Continuous data history
- ☑ Parametric release facilitation
- ☑ Rapid, dynamic solution
  - ☑ Reduced product losses
  - ☑ Root cause certainty

Immediate Results

Greater Control

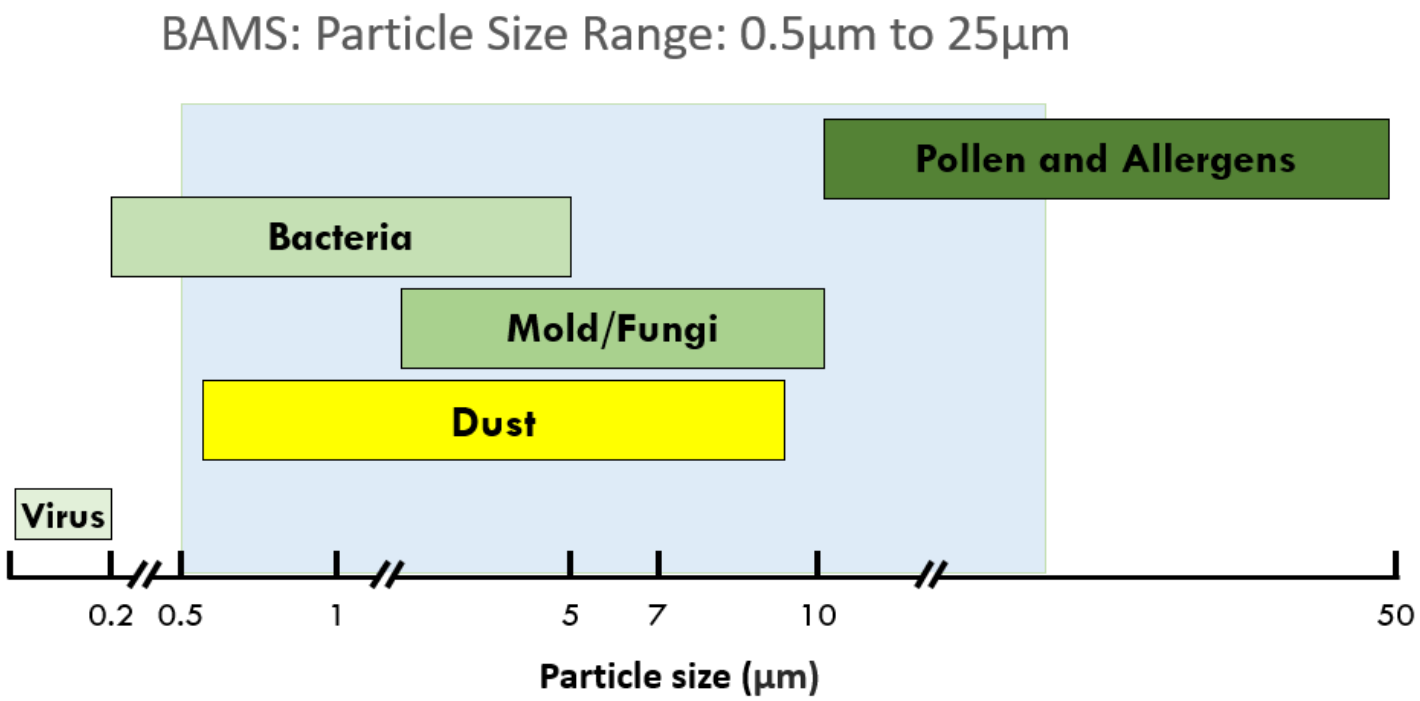
Lower Cost

More Effective

BAMS Difference

- ☑ Truly portable
- ☑ Light
- ☑ Smallest by 2-4 times
- ☑ Quiet
- ☑ Large touch screen
- ☑ Only AC/battery combo
- ☑ Accurate to 0.5µm
- ☑ *Lowest Price*

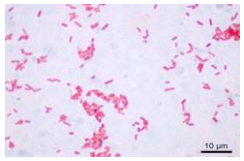
General Size Classifications



Cell size (µm)	0.05-0.2	0.5—5	2—5	3—10	10+
Microbial classification	Virus	Bacteria	Mold spores	Fungi	Dust mites and allergens

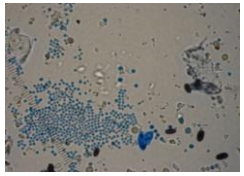
Bacteria

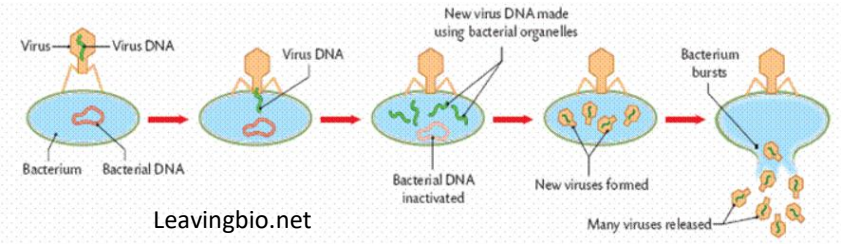
There are thousands of different kinds of bacteria. They live in every conceivable environment all over the world. Many bacteria live on and in the bodies of people and animals without causing any harm.
Only a few kinds of bacteria, called pathogens, cause disease.



Virus

Viruses are very tiny organisms. The main goal of viruses is to gain entry to a host body to infect it causing them to become sick. A virus forces itself into a host cell to make new virus cells. The infected cell will burst, releasing the virus into the person's system. These newly created viruses will go on to infect more and more cells.





Relationship between bacteria and viruses

Most viruses cannot live long without a host. All viruses depend on cells for reproduction. Some viruses use bacteria in the environment to reproduce. The bacteria act as a host allowing the virus to multiply.

BAMS performance and portability make it the best choice for environmental monitoring and cleanliness verification.

Thank you!

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