BLOG
Automated Cell Counting

What's Better

: Manual or Automated Cell Counting?

logos biosystems
by ALIGNED GENETICS

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Cell counting is a critical and routine part of many cell culture laboratory workflows. The practice usually involves directly counting individual cells in a small volume in order to get an estimate of how many cells are in a larger volume. This can be useful for culture maintenance, setting up assays, assessing the health or viability of cells in a culture, and clinical or diagnostic applications. But when should you take your cell counting to the next level by getting a machine to do it for you?

Manual cell counting

The conventional method of cell counting is done manually at a benchtop microscope using a special type of slide with a grid known as a hemocytometer. The researcher follows a standardized procedure to count individual cells and can use this to calculate how many cells per microliter their culture has.

"***Additionally, the number of live and dead cells can be determined by adding a membrane exclusion dye such as trypan blue. Intact cells do not take up trypan blue, while unhealthy cells with compromised cell membranes will uptake the dye and can be identified under the microscope***," says Mahesh Dodla, Global Product Manager for Monitoring Tools, the life science business of Merck KGaA, Darmstadt, Germany. This can be useful in getting more accurate counts and assessing the health of a culture and is also a technique employed in automated cell counting systems.

Automated cell counting

Automated systems generally rely on either an imaging-based approach or an impedance-based approach. Imaging-based systems use a microscope and camera that will capture an image and then use an algorithm to count the cells. Meanwhile, impedance-based systems measure electrical resistance to determine the number of cells.

Cell counters that use the image-based approach can further be divided into either fluorescent or brightfield imaging. "***The label-based approach is the most common just because it's the most reliable,***" says Joe Clayton, Global Scientific Program Manager at Agilent Technologies

Systems vary in how samples are inserted; some use special disposable slides while others can take many samples at once in tubes or microplates. But in every case having a machine taking the counts removes "***subjective and time-consuming judgement from human eyes and replaces them with much more objective, fast, and accurate technologies***," shares Neon Jung the CEO of Logos Biosystems.

Automated cell counting works across most cell types but usually requires that cells are suspended. "***One big challenge can be extremes on the ends of size, particularly smaller cells. So, if you get into non-mammalian type cells, like bacteria or yeast cell counting, there can be challenges***," according to Clayton.

Other cells that will cause challenges for automated counters include cells that don't retain stains very well such as immune cells. And perhaps most difficult of all, cells that clump together. Clumped cells cause challenges for both image-based and impedance-based systems. "***In this case, a software algorithm that performs accurate cell counting of clumped cells is very important for accuracy***," says Jung.

It is also worth noting that some cell counters offer more than just counting; they may also provide information about cell viability, diameter, live/dead counts, images of cultures, and fluorescence intensity. "***Some instruments such as the LUNA-FL™ of Logos Bio provide transfection efficiency information using fluorescence information***," according to Jung.

Manual vs. automated cell counting

The main considerations between manual and automated cell counting are cost, labor, and accuracy.

Cost-wise, manual cell counting only requires a one-time purchase of a few items. Conversely, automated counters will run on the order of a few thousand to a few tens of thousands of dollars for the system alone and will also require consumable purchases and maintenance costs.

Automated counters are faster than all but the quickest and most adept scientists doing manual counting. But even for those that are speedy at counting cells by hand "***you do have that increased walkaway time. So especially if you have a lot of samples, the ability to hit go, walk away, and have your readout displayed has a lot of utility for folks,"*** notes Clayton.

The primary advantage in accuracy for automated systems is that it removes the variability from user to user or lab to lab. This reproducibility can be very important for assays or protocols that rely on having a certain number of cells as input.

A secondary accuracy advantage is that automated systems usually use a larger field of view than a hemocytometer. "***If you get into lower numbers of cells or lower concentrations of cells, that larger field of view is certainly going to have a benefit to a conventional manual method,"*** says Clayton.

When is an automated cell counter worth it?

The main considerations between manual and automated cell counting are cost, labor, and accuracy.

Clayton recommends thinking about how the system will be used, "***Is this something that is going to be done routinely in the lab by a number of individuals for most projects? And if the answer is yes, I think it makes sense to be considering an automated system. If the lab dabbles in cell culture, and someone goes in there and does counts, you know, a couple times a week, probably not justifiable to get a cell counting system, or at least one that's more sophisticated."***

It is also worth considering how important accuracy and repeatability is in the workflow for which you are counting cells. As well as if you can get a system that will help with other parts of your workflow.

What to consider when considering an automated cell counter

"***The first thing to consider when choosing a cell counter is the sample type and application. A fluorescence cell counter is not necessary in laboratories that mainly use immortalized cell lines. But it is essential in a lab that cultures primary cells***," suggests Jung.

Next, labs should consider the number of samples they need counted at one time and see which systems will meet their needs in terms of throughput.

Then they should also consider each system's accuracy and counting approach as well as any additional features the system might offer. "***I think another really important consideration is: is it possible to get an integrated system that has multi functionality. So, it's not just a dedicated cell counting system, but has cell counting as one of its functions among many others,"*** says Clayton.

Ultimately, the decision to get an automated cell counter and which one to choose depends heavily on the lab. It may be useful to take a hard look at not only what your lab is currently doing but also where the needs of the lab are headed long term.