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CELL SCIENCE AT A GLANCE

SPECIAL ISSUE
IMAGING CELL ARCHITECTURE AND DYNAMICS

Single-cell size and growth measurements at a glance

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ABSTRACT

The cell, the basic unit of life, can range over 13 orders of magnitude in volume between species. The size of a cell sets its maximum biosynthetic capacity, molecular content and physical properties. Cell size measurements can inform research into cell growth, the cell cycle and physiology, and are used to describe disease states and guide physical and ecological models. However, measuring size – and its dynamic increase, growth – is technically challenging, and data interpretation depends on the technology used. This Cell Science at a Glance article and the accompanying poster summarize the key methods for measuring single-cell volume or dry mass. The performance, potential biases and convenience of each method are discussed to guide experimental setup and interpretation. In addition, technological limitations and the need for future collaborative efforts are highlighted.

KEY WORDS: Cell size, Volume, Mass, Growth, Composition, Measurement, Method, Detection, Metrology

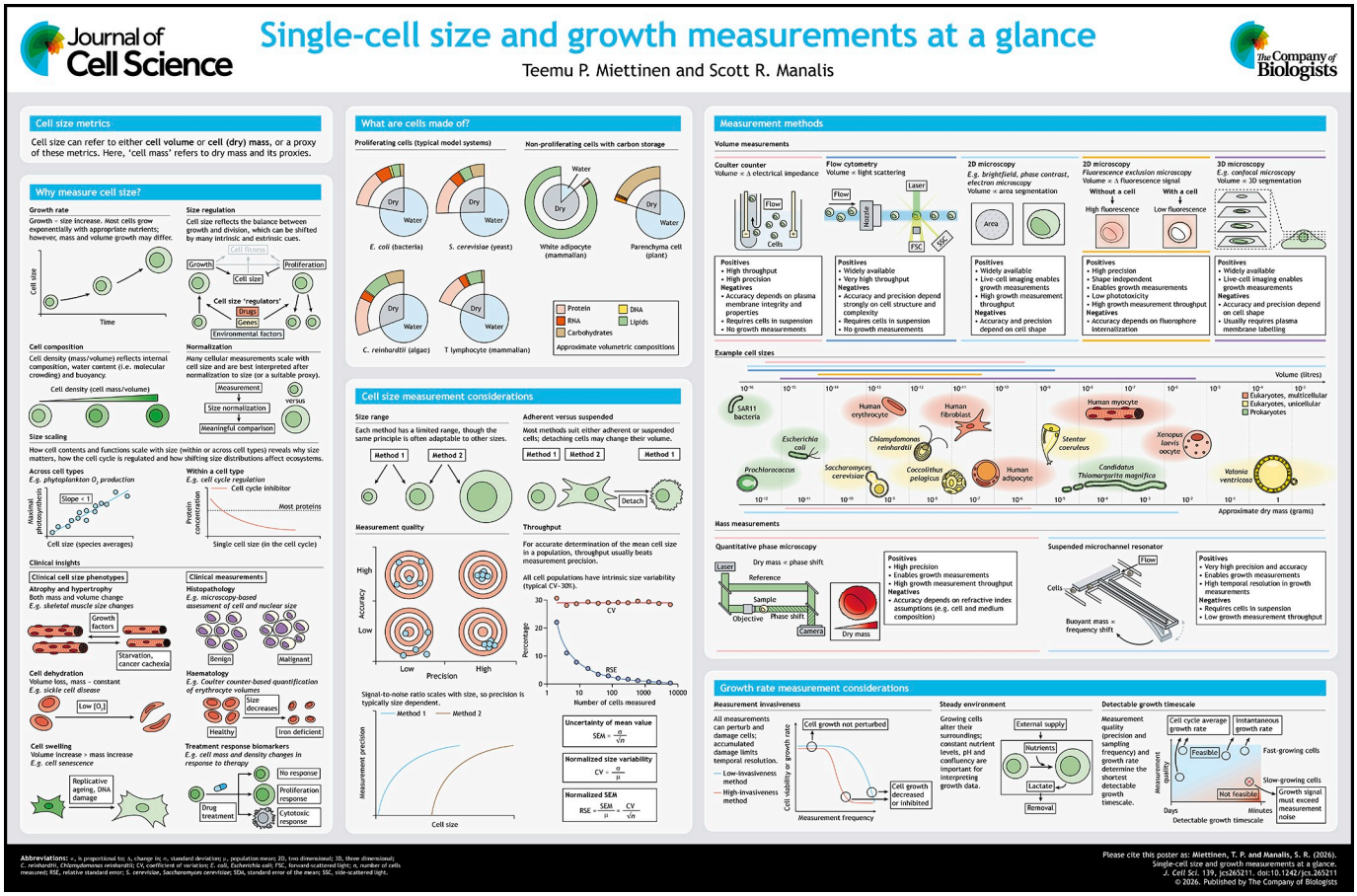
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Introduction

The size of a single cell can range over 13 orders of magnitude. Some of the smallest bacteria, such as SAR11 or the synthetic 'minimal cell' JCVI-syn3B, can be less than 0.1 fl, whereas the largest multinucleated phytoplankton, such as *Valonia ventricosa* or *Caulerpa taxifolia*, achieve more than 1 ml in volume (Moger-Reischer et al., 2023; Schulz and Jørgensen, 2001; Shihira-Ishikawa, 1987; Zhao et al., 2017). Even in humans, cells range



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Box 1. Why measure cell size?

Size regulation and scaling

Cell size changes are associated with altered cell contents and functions, and these size relationships often enable first-principle research approaches. For example, such size scaling within a given cell type is fundamental for cell cycle regulation, as cell cycle progression typically requires cell growth and the dilution of cell cycle inhibitor proteins (Bjorklund, 2019; Chadha et al., 2024; Xie et al., 2022). More broadly, the expression of many genes and proteins is linked to cell size (Chen et al., 2020; Cheng et al., 2021 preprint; Lanz et al., 2022). Similarly, size scaling across different cell types or species can inform physical and ecological models of large-scale trends (Andersen and Visser, 2023; Hillebrand et al., 2022; Malerba et al., 2017; Wickman et al., 2024).

Growth rate

Cell growth is the increase of size. Most cells grow approximately exponentially. Determining this on a single-cell level requires repeatable and high-precision measurements of cell size. Notably, our understanding of growth regulation on a single-cell level is still limited (Kellogg, 2025).

Cell composition

Measurements of single-cell density (mass/volume) are informative of intracellular crowding, which influences diffusion and reaction rates (Huang and Ferrell, 2026; Neurohr and Amon, 2020). Cell density also sets cell buoyancy (Fahimi et al., 2026; Wu et al., 2025c).

Normalization

Cell size is an important normalization parameter. Differences in biochemical content, gene expression, or functionality between individual cells or groups (e.g. treatments) can often reflect differences in cell size.

Clinical biomarkers

Abnormal cell sizes are hallmarks of disease. For example, cellular and nuclear size are routinely used for diagnosis and grading in cancer pathology, cancer cachexia decreases skeletal muscle cell size, and cell senescence is associated with cell hypertrophy and swelling. Measurements of erythrocyte volumes are among the most widely used single-cell clinical assays, informing the diagnosis of anaemias and erythrocyte hydration defects, for example (Aslinia et al., 2006; Gallagher, 2017). More recently, high-precision measurements of single-cell mass and density have also emerged as biomarkers predictive of cancer drug sensitivity and immunotherapy responses (Stevens et al., 2024; Wu et al., 2025a).

around seven orders of magnitude in volume from ∼20 fl spermatozoa and ∼70 fl red blood cells to ∼1 µl large muscle fibres (Hatton et al., 2023). Yet, a given cell type typically exists within a characteristic size range. The size regulation that maintains cells within this range is considered important for cellular fitness, although the mechanistic basis for this remains unclear. Studying cell size and growth (i.e. the increase in size) can inform many fields of research, from cell biology to medicine and ecology (see poster and Box 1). However, choosing the right cell size measurement technology can be challenging and context dependent.

This Cell Science at a Glance article and the accompanying poster summarize the best-established methods for quantifying single-cell size and growth to guide experimental design and data interpretation. Emphasis is placed on the distinction between size metrics, data quality and quantity requirements, cell type limitations, and measurement-induced artifacts. Finally, future needs for interdisciplinary collaboration and technology development are highlighted.

Key considerations when choosing a method

There are many single-cell size measurement methods, but no single method can measure all cell types or all cell size metrics, and only a few methods are well suited for monitoring cell growth (for a side-by-side comparison of method details, see poster). The following details should be considered, as they determine the most appropriate methods for any given study:

Separation of different size metrics

'Cell size' typically refers to either cell volume or cell mass, or some proxy of these two fundamental metrics. In this article, the term 'cell mass' will be used to refer to dry mass and its proxies, unless otherwise specified. This should not be confused with total cell mass, which includes the mass of intracellular water. The most common cell volume proxies are cell diameter and area, and the most common mass proxies are buoyant mass (the effective mass of the cell submerged in a fluid, which is proportional to dry mass under typical measurement conditions) and protein content. Because these quantities reflect different physical properties of cells, they are not always interchangeable. Consequently, selecting a measurement method is fundamentally a decision about which aspect of cell size is most relevant to the biological question being asked.

When choosing which metric to measure, it is useful to consider what a cell is made of (see poster). Most cells are predominantly water (Neurohr and Amon, 2020), whereas dry biomass typically accounts for ∼10–35% of total volume. The fractional water content (v/v) is often even higher in plant cells and single-celled species with large vacuoles (Schulz and Jørgensen, 2001; Volland et al., 2022), and markedly lower in cells dominated by stored carbon, such as lipid-filled white adipocytes (Stenkula and Erlanson-Albertsson, 2018). In cells that are predominantly water, volume measurements are sensitive to water content changes. In growth studies, cell volume growth can be uncoupled from cell mass growth, especially on short timescales, owing to fluctuations in cellular water content (Son et al., 2015; Srivastava et al., 2025 preprint; Zlotek-Zlotkiewicz et al., 2015).

The dry portion (i.e. the dry volume) of cells is almost exclusively macromolecules – especially proteins (typically ∼50% of all dry mass), and to a lesser but highly variable degree lipids, carbohydrates and nucleic acids (Feijó Delgado et al., 2013). In cells that accumulate large carbon stores, the fraction of dry mass that is lipids or carbohydrates can be substantially higher, depending on environmental conditions (Wu et al., 2025c). Mass measurements reflect the summed mass of these biomolecules. Proxies of dry mass – such as total cellular protein content and, to a lesser degree, buoyant mass – can be biased by changes in the dry composition of the cell. However, within a given growth condition, cellular protein content, and buoyant mass in particular, correspond closely to dry mass (Liu et al., 2022; Miettinen et al., 2022).

In practice, it is important to consider how changes in cell composition can bias size measurements, especially when studying cells under changing conditions. For example, under steady conditions, proliferating cells – from bacteria to human lymphocytes – will increase most cellular components in proportion. Thus, cell size and growth can be studied using proxy measurements of cell mass or volume, such as protein content. In contrast, the growth of non-proliferating white adipocytes cannot be accurately studied with measurements of protein content, because cellular components do not grow in proportion when cell size increase is driven by lipid accumulation. Yet, direct measurements of cell mass or volume can still capture size increases driven by lipid accumulation.

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Cell type limitations

Most cell size and growth measurements are not suitable for all cell types, with the measurement size range, cell shape, cell adhesion state and multicellular context being the main factors to consider. For example, most microscopy methods require cells to be adherent or immobilized, whereas cytometry measurements require cells to be in suspension (see poster). Although most adherent cells can be dissociated into suspension, it is important to note that this may increase cell volume, because cellular water content depends on the osmolarity of the medium and the strength of cell adhesion (Guo et al., 2017; Srivastava et al., 2025 preprint). For the study of single cells in a multicellular context, only imaging-based approaches are suitable.

In addition, a cell wall or other extracellular structures, such as coccolithophore coccoliths or diatom frustules, can impose a disproportionate influence on the results of both mass and volume measurements. Some of these structures can either prevent rapid volume increases, such as cell swelling, or exaggerate volume measurements that detect the cell wall as the boundary of the cell, such as those made using two-dimensional (2D) microscopy. These structures can also be highly dense, thus having a disproportionate impact on cell mass measurements.

Data quality versus quantity

For all experiments, it is important to consider measurement precision (repeatability), accuracy (closeness to a 'true' value) and throughput requirements (see poster). When the conclusions concern a single cell, high precision is essential. Notably, the precision of all measurements is typically size dependent, because the signal-to-noise ratio increases with cell size. Measurement precision is often inversely correlated with measurement throughput, and repeated measurements can be averaged to increase precision. Prioritizing throughput over precision is typically beneficial when final conclusions focus on population averages, as the standard error of the mean (SEM) decreases with the square root of the number of cells measured, and because all cell populations have intrinsic size variability with a typical coefficient of variation (CV) at ∼30% (Hatton et al., 2023). Assuming measurement precision is substantially better than the population size variability, and that the population approximates a normal distribution, sample size requirements can be approximated as $n = \left(\frac{\mathrm{CV}}{\mathrm{RSE}}\right)^2$, where n is the number of cells measured and RSE is the desired relative standard error (SEM/mean).

All measurements can have technical biases that can skew accuracy, and measurement calibration and validation with standardized particles and solutions is always desirable. If these biases are systematic and well defined, they can be normalized out of final data. For example, 2D microscopy-based volume estimates can systematically overestimate cell diameter by a constant length, producing a volume bias, especially for small cells. Such a measurement bias can be identified and corrected through measurements of standard particles and measurements with parallel methods. Overlooking measurement accuracy makes comparisons between different studies challenging. It is also worth considering measurement stability (i.e. the time-dependency of precision and accuracy) as not all measurements are quantitatively reproducible over weeks or months. Finally, measurements that report physical rather than arbitrary units are preferrable, as this eases method comparison, standardization and downstream physical modelling.

Additional growth measurement requirements

Cell size can be studied using end-point measurements, but studying single-cell growth rate (i.e. the rate of cell size increase) requires repeated size measurements. In this article, growth can refer to either volume or mass increase, as both are used to study single-cell growth regulation, despite fundamental differences in how data should be interpreted, as discussed above. Most studies focus on the average growth rate of a cell (across the whole cell cycle), but growth can also be studied on shorter timescales. Instantaneous growth rates can reveal, for example, cell-cycle-dependent growth regulation (Cadart et al., 2022; Miettinen et al., 2019) or provide estimates of average growth rates that are challenging to monitor across the whole cell cycle (Wu et al., 2025b preprint). The exact timescale of instantaneous growth rate depends on measurement quality.

The temporal resolution of most single-cell growth studies is limited by measurement invasiveness. All measurements can perturb cells, whether through phototoxicity, shear stress or other mechanisms. This can decrease growth rate and cause cell death and other changes in cell physiology (see poster). This should be considered, especially when carrying out cell growth studies or downstream measurements from the same cells. Notably, on short timescales (e.g. minutes), cell (water) volume is more prone to perturbations than dry mass (Cadart et al., 2019). Another key consideration is the maintenance of steady-state environmental conditions (e.g. through constant exchange of culture medium). Cell growth consumes nutrients, changes media pH and alters cell confluency, all of which can alter cell growth rates. Thus, growth measurements often require specialized equipment.

Measuring instantaneous growth rates requires frequent, high-precision size measurements. Although measurement frequency sets the fundamental limit on temporal resolution, measurement precision is often the more practical constraint, requiring multiple consecutive size measurements to estimate meaningful growth rates. In addition, the analysis of instantaneous growth rates can also be skewed by the analysis approach and noise in the data (Holtzman et al., 2026 preprint; Kar et al., 2021). In contrast, measurement of average growth rates in a cell cycle can be achieved with modest precision and temporal resolution (e.g. by taking measurements only at the start and end of a cell cycle). Measurements of adherent cell growth are typically limited to monitoring growth over two to six cell cycles due to culture confluency (Cadart et al., 2022; Liu et al., 2024a; Zhang et al., 2024), whereas some microfluidic devices, which continuously discard some of the daughter cells, can monitor single-cell growth over tens of cell cycles (Levien et al., 2026; Wang et al., 2010).

Cell volume measurements

Electrical sensing of cell volume

Coulter counting is a classical approach for cell volume measurements (see poster) that relies on the electrical properties of the cell, as measured using a standalone benchtop instrument (Gregg and Steidley, 1965). The electrical impedance of culture medium is low, whereas the impedance of a cell is high when the plasma membrane is intact (Dadkhah Tehrani et al., 2025). The Coulter counter and other impedance-based cytometers detect impedance changes as cells flow through a sensing region within the instrument. These impedance changes are proportional to cell volume and can achieve precision as good as ∼1% (measurement CV); however, deviations from a spherical shape decrease precision (Hurley, 1970). Measurement accuracy is high for standardized particles but is difficult to validate in biological samples because

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the electrical properties of cells may vary between cell types and conditions. Coulter counter measurement throughput is typically thousands of cells measured in a minute, and the measurements can handle a large size range from small bacteria to large plankton and mammalian cells (Miettinen et al., 2024). However, Coulter counters require the samples to be in suspension. Although technically feasible (Wang et al., 2025), impedance-based volume measurements have not been adapted to high-quality single-cell growth studies (Dadkhah Tehrani et al., 2025).

Flow cytometry

Perhaps the most widely used cell size measurement method is the detection of forward- and side-scattered light in standard flow cytometry (see poster). Flow cytometers are extremely high throughput, measuring thousands of cells in a minute. However, the light-scattering properties of a cell are influenced by its shape and structural complexity, which can vary between cells and conditions. Consequently, measurement accuracy and precision are non-generalizable and difficult to calibrate (Davies et al., 2025; Tzur et al., 2011), as uniform standard particles scatter light differently to complex cells (Miettinen and Björklund, 2016). However, over large size scales (an order of magnitude), light scattering does correlate with cell volume, providing a convenient, qualitative proxy for cell volume. Notably, many of these measurement limitations are overcome by imaging flow cytometers (Rees et al., 2022). Most flow cytometers are suitable for measuring all but the largest (>100 µm diameter) cells. Cell size measurements with flow cytometers can also rely on fluorescent cell labelling (e.g. total protein staining) as a proxy for dry mass. Additionally, flow cytometry requires samples to be in suspension and does not enable single-cell growth measurements.

Optical detection of cell volume

2D microscopy

One of the most common measurements of cell size is through 2D microscopy (see poster), typically relying on brightfield or phase contrast imaging. Such approaches assume that cell length or area correlates with volume, which is justifiable for specific, symmetrical model systems. For example, in *Escherichia coli*, cell length is an accurate predictor of cell volume (Kar and Amir, 2025), but this conclusion does not extend to all bacteria (Reyes-Matte et al., 2026). Consequently, the precision and accuracy of 2D microscopy-based volume estimates are highly dependent on the predictability of cell shapes. In animal cells with complex morphology, cell area is a low-accuracy proxy of cell volume, although it remains commonly used, for example, in histology. Additionally, 2D microscopy-based volume measurements require accurate cell segmentation, which can be achieved using various analysis approaches (Liu et al., 2024b; Padovani et al., 2022). The precision of light microscopy is also much lower for small cells that approach the limit of detection (e.g. cells of 1 µm diameter). Measurement throughput is usually high, with hundreds of cells measured in a minute.

The use of 2D microscopy is suitable for growth studies of cells with highly predictable shapes that enable accurate image segmentation and volume determination (Pietsch et al., 2023). In bacteria, ‘mother machines’ have enabled long-term single-cell growth monitoring by physically constraining bacteria to a microfluidic channel (Thiermann et al., 2024; Wang et al., 2010). Such approaches achieve the highest-throughput single-cell growth measurements available, although the precision of the growth measurements is modest. The long-term monitoring of cells in such microfluidic devices can also be sensitive to cell size, shape and adhesion to the device.

An alternative proxy for cell volume is nuclear area: nuclei have a more regular shape than most cells, and nuclear volume correlates with cell volume (Jorgensen et al., 2007; Neumann and Nurse, 2007; Wu et al., 2022). Such volume estimates are useful for irregularly shaped cells, but the correlations between nuclear area and cell volume are noisy, making such cell volume estimates inherently low in precision.

A key advantage of 2D microscopy-based cell size measurements is their suitability for vastly different-sized cells. Only the smallest cells (<0.5 µm diameter) cannot be accurately measured with light-microscopy-based approaches.

Fluorescence exclusion

The fluorescence exclusion principle (see poster) (Gray et al., 1983) is an important extension of 2D microscopy-based cell volume measurements, typically using a standard widefield epifluorescence microscope and an imaging chamber of known height. The culture medium is supplemented with cell-impermeable fluorescent dye, and the cell will exclude the fluorescence signal proportionally to cell volume and independently of cell shape. The resulting decrease in fluorescence can be converted to an accurate estimate of cell volume when considering the imaging chamber volume. This approach can achieve high precision (∼1–2% measurement CV) and has been used with yeast and mammalian cells (Cadart et al., 2017; García-Ruano et al., 2022; Wu et al., 2025a). Measurement throughput varies based on imaging chamber and sample type, reaching up to hundreds of cells measured in a minute (Wu et al., 2025a). Importantly, the imaging depth of field must capture the height of the imaging chamber to ensure accurate volume measurement – this limits the use of most fluorescence exclusion setups to cells with a height of 20 µm or less.

The high precision and low phototoxicity of fluorescence exclusion microscopy make it well suited for single-cell volume growth measurements with high temporal resolution (Cadart et al., 2018, 2022; Zlotek-Zlotkiewicz et al., 2015). However, fluorophore internalization and binding to the cell (or calibration particle) can become a biasing factor. Use of a high-molecular-weight fluorophore (e.g. 2000 kDa FITC–dextran) can limit fluorophore internalization, as smaller fluorophores (e.g. 70 kDa FITC–dextran) can be actively internalized via macropinocytosis (Charpentier et al., 2020). Fluorophore internalization and binding is likely to be dependent on cell type and conditions.

3D microscopy

Three-dimensional (3D) microscopy of cell volume (see poster) is typically carried out using various forms of confocal microscopy, although deconvolution microscopy can also be used. It relies on fluorescent labelling of the plasma membrane to enable cell segmentation and volume determination. Such approaches have been used in numerous model systems, ranging from yeast to plant and animal cells (Willis et al., 2016; Wirshing et al., 2025; Wolny et al., 2020; Xie and Skotheim, 2020).

The accuracy and precision of 3D volume measurements are highly variable, depending on imaging and segmentation quality. Image segmentation is especially challenging in cells with complex shapes, such as most mammalian cells where the various folds and protrusions of the plasma membrane are never perfectly revealed by light microscopy, resulting in measurement bias. Similarly, 3D cell segmentation is generally better for single cells than for confluent layers or tissues, where cell boundaries are harder to separate.

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Notably, there are numerous traditional and deep-learning-based cell segmentation approaches, and the suitability of each approach is dependent on data quality and sample type (Wen et al., 2022; Zhou et al., 2025).

Cell volume measurements made using 3D microscopy can also suffer from the effects of photobleaching and phototoxicity, especially for single-cell growth measurements when high temporal resolution is required. Alternative imaging approaches, such as light sheet fluorescence microscopy, can partly mitigate these limitations. Additionally, measurement throughput is lower than that of most other volume measurement approaches, typically 5–20 cells measured in a minute. Furthermore, 3D microscopy cannot accurately measure cells smaller than 0.5 µm in diameter. Similarly, the largest cells (with diameters in the hundreds of micrometres) are challenging to measure due to limited light penetration of thick samples and the working distances of most objective lenses.

Other measurements of cell volume

Electron microscopy approaches are common for volume determination in the very smallest cells (see Oikonomou and Jensen, 2021 for a visual summary), although the results can be biased by sample dehydration, and the measurement throughput is low. Cell volumes can also be determined using inertial sensing methods (see below). Many other cell volume measurements exist (Model, 2018), but they have been omitted here due to low or poorly established measurement quality, or the lack of information at the single-cell level.

Cell mass measurements

Quantitative phase imaging of cell dry mass

Cell dry mass can be measured using quantitative phase imaging (QPI, also known as quantitative phase microscopy; see poster) (Barer, 1952). Cellular biomass, such as proteins and nucleic acids, has a different refractive index to water, resulting in a phase shift in light passing through the cell. Whereas normal light microscopy detects only the intensity of light, in QPI, this phase shift is detected with a specialized phase-retrieval module. Consequently, the measured phase shift can be used to estimate dry mass. Notably, there are many QPI techniques for detecting the phase shift (e.g. interferometry, holography and wavefront sensing; reviewed in Nguyen et al., 2022).

QPI can achieve high throughput for cell dry mass determination, with approximately a hundred cells measured per minute (Liu et al., 2020) when imaging in 2D. It can also achieve high precision (∼1–2% measurement CV) when cell segmentation is not precision limiting (Liu et al., 2020; Nguyen et al., 2022). Because different molecules have different refractive indexes, a change in the molecular composition of the cell may bias the QPI-based dry mass measurement. Under steady-state growth where cell dry mass is predominantly protein and lipid, such biases should be largely negligible, resulting in good measurement accuracy. Notably, QPI does not record cell volume, unless combined with an orthogonal volume measurement. More recent versions of QPI have expanded to 3D imaging, where tomography methods, such as optical diffraction tomography (ODT), use different illumination angles to reconstruct the dry mass of the cell in 3D (Biswas et al., 2025; Huang and Cao, 2024; Kim et al., 2025). These approaches suffer from the same image segmentation-driven precision and accuracy limitations as other forms of 3D imaging.

QPI methods can image a wide range of different-sized cells, ranging from small bacteria to mammalian cells (Cotte et al., 2013; Liu et al., 2024a; Polanco et al., 2022). However, thick samples (with a depth of more than tens of micrometres) are not suitable for QPI (Huang and Cao, 2024; Nguyen et al., 2022; Zhao et al., 2022). Importantly, QPI can track the growth of single cells, with many dozens of cells tracked at a time (Liu et al., 2024a; Srivastava et al., 2025 preprint). Although phototoxicity typically limits QPI experiments, a temporal resolution of less than 5 min can be achieved without preventing growth (Zhang et al., 2024). These qualities make QPI well suited for adherent cell growth rate studies, especially when high throughput is more important than short timescale growth dynamics.

Inertial sensing of cell buoyant mass

Micro-electromechanical systems can detect cell mass based on inertial sensing. The most developed of such methods is the suspended microchannel resonator (SMR; see poster) (Burg et al., 2007), a microfabricated resonator device. Here, cells flow through a microchannel embedded inside a resonating cantilever. The transit of a cell changes the resonant frequency of the cantilever proportionally to the buoyant mass of the cell.

The SMR measurement principle works across size scales, from the smallest microbes to large mammalian cells and beyond (Katsikis et al., 2026; Khachikyan et al., 2019; Miettinen et al., 2024; Mu et al., 2020). Buoyant mass can be measured with precision as good as 0.1% (measurement CV) and a throughput of up to hundreds of cells measured in a minute (Miettinen et al., 2019; Wu et al., 2025a). It is also possible to determine additional cell size metrics, including total cell volume, dry volume and dry mass, by measuring the buoyant mass of a cell in different fluids (Feijó Delgado et al., 2013; Katsikis et al., 2026; Oskui et al., 2017), although this substantially lowers measurement throughput.

SMR measurements have only limited sensitivity to cell shapes, but extremely elongated shapes cannot transit through the microfluidic system. Additionally, the SMR requires samples to be in suspension, although alternative resonator platforms that measure the total mass of adherent cells have been developed (Martinez-Martin et al., 2017; Park et al., 2010). However, the location and mass distribution of an adherent cell on the resonator can bias the mass measurement accuracy, and these methods do not achieve the same precision as the SMR.

The SMR can track single-cell growth over long time periods with high precision and a temporal resolution of 1 min or less (Levien et al., 2026; Wu et al., 2025b preprint). However, only a single cell can be tracked at a time, making the SMR mainly suitable for growth studies that require high precision, such as the study of extremely slow growth rates or fast-timescale growth dynamics. As with other microfluidic devices, these growth measurements are sensitive to sample adhesion to the device.

Other measurements of cell mass

Cell dry mass can be investigated indirectly using broadly accessible proxy measurements, such as fluorescent labelling of cellular protein content (Kafri et al., 2013). However, such measurements lack absolute units, making standardization and comparisons to other methods challenging. An alternative and more standardizable approach to single-cell protein content determination is Raman imaging (Oh et al., 2022). Brillouin microscopy can also, in principle, probe the dry mass of a cell (Fiore et al., 2019).

Perspectives

Technology development

Single-cell size and growth research has advanced significantly in the past decade, as modern methods can measure the mass and

volume of most existing cell types *in vitro* and *ex vivo*. However, major technological limitations still exist. First, high-precision single-cell growth measurements lack throughput for large-scale perturbation studies, leaving most current growth studies largely descriptive. Second, systematic and quantitative comparisons between different methods are lacking, which hinders meta-analyses of existing literature and leads to potential inconsistencies in published results. The development of shared, NIST (National Institute of Standards and Technology)-traceable standards that are suitable for different measurement principles could alleviate this problem by connecting measurements to a shared reference, but there is also a need for theoretical frameworks that relate different measurements across changing cellular compositions. Third, integrating single-cell size and growth measurements with downstream molecular profiling remains rare. As automated cell handling and imaging-based molecular profiling improve, future studies can better link single-cell phenotypes with molecular mechanisms. Fourth, most current methods are not suitable for single-cell growth studies *in vivo* in multicellular organisms. Some studies have achieved this in plants (D'Ario et al., 2021; Willis et al., 2016; Wolny et al., 2020), where the predictable cell shapes make volume measurements manageable, and a few notable exceptions have achieved animal cell volume tracking *in vivo* by focusing on easily accessible tissues, such as mouse skin (Xie and Skotheim, 2020; Xie et al., 2025). In principle, QPI approaches can be extended to small multicellular samples, but accurate cell segmentation and tracking remain key challenges for achieving high data quality with all imaging methods. With *in vivo* evidence lagging significantly behind *in vitro* studies, we still know little about cell growth regulation in complex organisms.

Collective efforts

Cell size is studied in different fields, ranging from ecology to medicine (Box 1), but these fields rarely communicate. Moreover, many single-cell size and growth measurement techniques are not widely available and require a high amount of technical expertise. Improving communication across fields and sharing expertise would help establish more unified datasets and measurement standards, while also allowing subfields to learn from each other. There is a lack of high-quality cell size and growth datasets that could be integrated into other consortium-led datasets, such as the Human Cell Atlas (Regev et al., 2017), the various immune cell atlases (Ota et al., 2021; Yin et al., 2026), microbial atlases (Delgado-Baquerizo et al., 2018; Matias Rodrigues et al., 2026) or the Biodiversity Cell Atlas (Sebé-Pedrós et al., 2025). The generation of large single-cell size and growth datasets could eventually help establish more unified theories of size and growth regulation that are not limited to a specific model system.

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Competing interests

T.P.M., S.R.M. and Massachusetts Institute of Technology hold and have filed patents on related measurement technologies and their applications. S.R.M. is a cofounder of and affiliated with the companies Travera and Affinity Biosensors, which develop techniques relevant to the research presented.

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High-resolution poster

A high-resolution version of the poster is available for downloading at https://journals.biologists.com/jcs/article-lookup/doi/10.1242/jcs.265211#supplementary-data.

Special Issue

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