

Week 1 Lesson 3

Developments in microscopy

Aim: To understand how developments in microscopy have allowed scientists to view materials on an increasingly smaller scale.

Keywords: microscope, magnification, lenses, scanning electron microscope

People have been copying from nature for a long time but recently the concept of 'biomimicry' has really taken off. Many research scientists are now investigating how plants and animals solve certain problems.

This has been made possible, in part, by developments in nanoscience and nanotechnology. Improvements in microscopes and the techniques of microscopy have also played a crucial role.

Starter activities

1. Microscope images

Show students images taken using light and electron microscopes. The following website has some good examples of images produced by different types of microscopes. Click on the images to enlarge them.

<http://web.uri.edu/gsc/image-gallery/>

Ask students to say what each image is showing. What units would they use to measure objects in the images? Which images do they think are the most recent? Why?

2. Simple microscopes

Students could make a simple magnifying glass with a loop of wire (approx 5mm diameter) and a drop of water and use it to magnify writing, desk surface etc.

Main activities

1. Using microscopes

Remind students how to use a light microscope by viewing a range of prepared slides at different powers. Ask them to discuss the limitations of light microscopes.

2. Important developments in microscopy

Students identify key developments in microscopy by sequencing statements, using the resource 'Important developments in microscopy'.

Differentiation

Depending on ability give students a smaller selection of developments to put into order.

Extension

Students could create a timeline of the developments.

3. Different types of modern microscope

This is a challenging extension activity using the resource 'Different types of microscope'.

Differentiation

Students could be given details of just one or two types of microscopes depending on ability.

Plenary activity

1. Most important developments

Give students a choice of 3-5 significant developments in microscopy. They should choose the one they think is the most important and think of a reason why. Pick two students who have chosen different developments. They should each give their reason why their choice is most important. The rest of the class should vote with a show of hands for the most convincing reason. The winner goes up against someone who has chosen a different development.

Main 2

Important developments in microscopy –

Teaching notes and answers

Before the lesson the table should be photocopied and cut up, making sure that the dates and descriptions are separated. Give students the dates and descriptions and using the information in the descriptions, they should try to put them in order and match them up with a date.

Differentiation

Students who need more support could be given a smaller number of dates and descriptions. The number given can be increased according to ability.

Extension

Create a timeline of the developments. What do students notice about the position of significant developments?

Further questions

1. The design of microscopes has improved over the years. What other developments were made which enabled better images to be produced?
2. Why does the description for 2014 say that 'this will enable scientists to...'?

Answers

1. Improvements in glass and grinding of lenses, tissue preservation, oil immersion technique, fixing and staining specimens, computer and laser technology, fluorescent markers.
2. The technology is very new and is not yet available for general use in science labs. New technologies such as this have to be adjusted and improved so they are relatively easy for lab technicians to use and are not too expensive to produce or run.

Important developments in microscopy

1590	A Dutchman Zacharias Jansen, combined lenses within a tube to produce one of the first light microscopes. The invention revealed a previously invisible and unexpected world teeming with microscopic life and structures.
Mid 17th century	Another Dutchman made the next significant development: Anthony Van Leeuwenhoek, invented a microscope with a magnification of x266.
1768	Using a microscope developed from Leeuwenhoek's design, Italian naturalist Lazzaro Spallanzani, demonstrated that one organism comes from another organism and does not simply emerge from non-living material.
1830s	Major improvements in glass and in the grinding process led to the manufacture of improved lenses. Scientists could now magnify objects to x400 or more. Techniques of tissue preservation also advanced.
1831	Robert Brown, a Scottish botanist, reported his discovery of the nucleus and its occurrence in all plant cells.
1850s	Three scientists, Remak, Virchow and Kölliker, demonstrated that cells are formed through cell division.
1870s	The oil immersion lens and new fixing and staining techniques became available. Structures inside the nucleus could be made visible.
1879	Walter Fleming discovered thread-like structures within the nucleus.
1897-8	Organelles (smaller than chromosomes in the nucleus) in cell cytoplasm, such as mitochondria, were described.
1930-46	Development of the electron microscope revealed the structures inside mitochondria and chloroplasts
1981	Scanning tunnelling microscopes (STM) provided images of atoms. The process damages the structure of molecules. Improvements in computer technology and lasers enabled images to be constructed.
1985	Atomic force microscopes revealed the structure of molecules. This is after images of atoms first appeared using STM.
2014	Eric Betzig, Stefan Hell and William Moerner received a Nobel prize for their work on super-resolved fluorescence microscopy. This will enable scientists to see the movement of individual molecules within a living cell.

Main 3

Different types of modern microscope – Teaching notes

The background information sheets could be used in a variety of ways.

Suggested activities

1. Provide students with access to scientific dictionaries and textbooks. Ask students to define these keywords: artefact, depth of field, diffraction, photon, refraction, resolution.
2. Ask students to summarise the advantages and disadvantages of each technique in a table.
3. Students convert the information into a simple chart which indicates how each method works and the advantages and disadvantages of each.
4. Ask students to underline how the microscope works in blue; advantages in orange and disadvantages in green.

Differentiation:

Depending on ability give each student the background information on just one or more of the types of microscopes.

Background information - different types of modern microscope

Light microscopes

Light microscopes are the simplest, least expensive and most widely-used type in microscopy. In their most basic form they consist of a light source, a lens and the human eye. **Compound microscopes** use two or more lenses to obtain high magnification. Specimens viewed under a light microscope can be living or dead.

Light microscopy typically has a maximum resolution of about 200 nm which enables the viewer to see cells and some structures but not to see details of organelles. An **oil immersion lens** reduces refraction and subsequent loss of light and is used when a high resolution is required.

The resolving power of a light microscope is limited by the wavelength of light. As blue light has the shortest wavelength of visible light some microscopes are fitted with **blue filters**.

However, despite these adaptations, light microscopes were thought to have a fundamental physical limit: that resolution could be no better than half a wavelength of light (the Abbe diffraction limit).

Electron microscopes

An electron microscope operates on the same principles as a light microscope. The light source is replaced by a beam of electrons which are focussed with electromagnets and detected by using photographic film or a phosphor screen. Electrons are easily deflected so the specimen must be viewed in a vacuum. The specimen is completely dehydrated, fixed in plastic and stained with an electron-dense chemical such as osmium, lead or gold. Initially, **artefacts** were a problem but improved techniques have eliminated most of these.

The wavelength of the beam of electrons used is 0.005 nm and so, a **transmission electron microscope (TEM)** can resolve details 1 nm apart. This is the most common form of electron microscope and is used to view ultra-thin sections of cells. The **scanning electron microscope (SEM)** scans an electron beam onto the surface of a specimen and collects electrons reflected from the surface. Of the two, the SEM has the poorer resolution but a good depth of field, producing outstanding 3-dimensional images.

Super-resolved fluorescence microscopes

Fluorescence is used to track and analyse biological molecules. If a light is shone on some molecules e.g. fluorescein, light of a different colour will be emitted by the molecule for a very short period of time afterwards. This is fluorescence. Molecules with this property absorb high energy light (e.g. blue). This increases the energy of the molecule. Some of the absorbed energy will be lost within the molecule before the molecule emits a lower energy photon (e.g. green light) which can be seen through the microscope.

Fluorescent markers can be attached to specific biological structures or molecules. Only those parts will be seen in the microscope. Different markers respond to different energy levels of light. By changing the excitation light it is possible to see how different parts of the sample interact.

Three scientists, Eric Betzig, Stefan Hell and William Moerner were awarded the 2014 Nobel Prize in Chemistry. Their work overcame the problem of using light for high resolution microscopy - the Abbe diffraction limit. They used fluorescence to image molecules and to precisely determine their location. **Super-resolved fluorescence microscopy** enables scientists to see the behaviour of **molecules in real time** inside **living cells**.

This technology is still under development. The cost of the technique and the expertise required to utilise it mean it will be some time before this type of microscopy is widely available.

Scanning tunnelling microscopes

These were developed in 1981. The sample is held in a chamber which is kept very cold to reduce the natural vibration of the atoms. Air is removed to prevent the molecules and atoms in air from colliding with the atoms in the sample. The chamber is also designed to block any stray magnetic fields from entering.

A needle (known as a stylus) with a tip one atom wide is moved across the surface of the sample and a small electric current is passed between the needle and the sample. This current increases as the needle gets closer to the atoms in the sample. Computers are used to convert this data into an image.

The bonds which hold molecules together can be disrupted by this method so it is not suitable to visualise molecules. Also, the STM can only be used on substances which conduct electricity such as metals.

Atomic force microscopes

Again, a tiny needle is passed across the surface of the sample. The needle is moved by the minute atomic forces found in atoms and molecules and this movement is measured. The measurements are translated into an image by computers. AFMs can be used on a wide variety of molecules and atoms can even be manipulated and positioned by this technique.