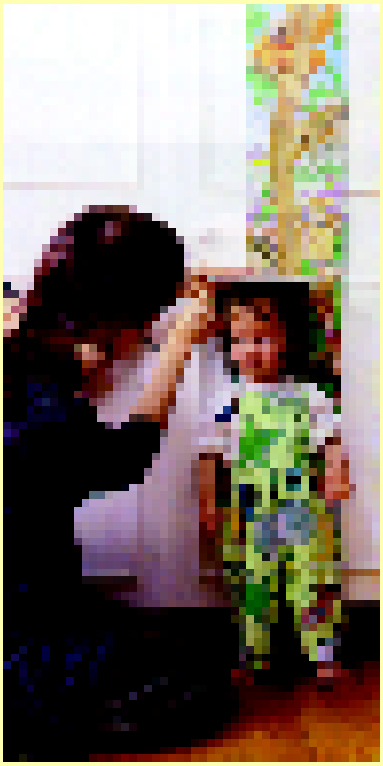
CHAPTER

23

Growth



Living beings grow both in body mass and height.

Growth is an increase in size of an organism, reflecting an increase either in the number of its cells, or in its protoplasmic material or both. Cell number and protoplasmic content do not always increase together; cell division can occur without any increase in protoplasm, giving a larger number of smaller cells (e.g., cleavage). Alternatively, protoplasm can be synthesized with no cell division so that the cells become larger. Any increase in protoplasm requires the synthesis of cell components such as mitochondria, cell membranes, enzymes and other proteins.

Growth, thus, involves increase in size and weight of the organism due to the synthesis of new protoplasm. It also includes increase in amount of **apoplasmatic substances** such as the fibres and matrix of connective tissues of higher animals such as mammals. So the growth of body of a higher organism takes place by the addition of new substances, both protoplasmic and apoplasmatic, when the anabolic process dominates the metabolic activity. Conversely, when decomposition exceeds synthesis, first the internal food reserve (such as fat in the adipose tissues) is consumed to run the body machine, and then the energy is obtained at the expense of proteins of the protoplasm. This causes depletion of the living matter, resulting in **degrowth**.

LEVELS OF GROWTH

Among living organisms, growth can be recognised at the following two levels :

A. Cell growth. At the cellular level, the growth of all multicellular organisms is governed by two main activities. These are **reproduction** and **growth** of individual cells of the body. In Chapter 18 of Cell Division, we have already described that during the interphase stage, new materials such as nucleic acids (DNA, RNAs) and proteins are synthesized in the cells and, thus, the cells grow. The growth of individual cells comprising the body is the vital and the most essential factor of growth in all multicellular organisms. The rhythmicity of cell multiplication and growth can be studied well in tissue culture or in culture of unicellular organisms.

B. Growth of multicellular organisms. The growth of multicellular animals and plants in relation to growth and multiplication of their individual cells falls under the following three categories:

(1) Auxetic growth. (*Auxesis* = growth resulting from increase in cell size). In this type of growth, the volume of the body increases due to the growth of body cells without any increase in the number of cells. Examples of auxetic growth are quite rare and include nematodes, rotifers and tunicates.

(2) Multiplicative growth. This type of growth results due to the rise in the number of cells constituting the body. The increase in the number of cells is brought about by the mitotic divisions. In this case, however, the average size of the cells remains the same or increase insignificantly. This type of growth is called **multiplicative growth** and occurs in embryos during morphogenesis. It is also involved in prenatal growth of higher vertebrates.

(3) Accretionary growth. Generally post-embryonic growth of animals and plants occurs due to mitotic multiplication of some special types of cells occurring in specific locations of the body. The differentiated cells of organs and tissues of the body lose the capacity of division and growth (*e.g.*, muscles, nerve cells, osteocytes of bone, fat cells, xylem, phloem, parenchymal cells, etc.). These cells tend to perform physiological functions for the survival of the animal, whereas the special cells exist in an undifferentiated state as **reserve cells**, *e.g.*, **meristematic cells** in angiosperms, **stem cells** such as erythropoietic tissue of red bone marrow, periosteum cells of bone, ciliary body cells of vertebrate eye, and epidermal cells of stratum germinativum. In case of necessity, these reserve cells reinforce and replace the worn-out differentiated cells. In such an event they differentiate into the type of cells that they reinforce and replace. This type of growth is called **accretionary growth**.

According to **Green** and **Taylor** (1990), starting with an individual cell, growth of a multicellular organism can be divided into following three phases: (i) **cell division** or **hyperplasia**, *i.e.*, an increase in cell number as a result of mitotic division; (ii) **cell expansion** or **hypertrophy**, *i.e.*, an irreversible increase in cell size as a result of the uptake of water or the synthesis of living material: and (iii) **cell differentiation**, *i.e.*, the specialization of cells; in its broad sense, growth also includes this phase of cell development (*viz.*, differentiation).

LIMITED AND UNLIMITED GROWTH

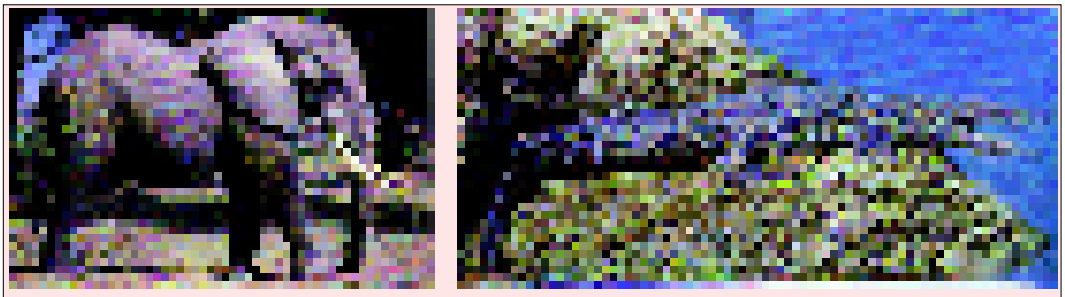
Studies of the duration of growth in plants and animals show that there are two basic patterns, called **limited** (definite or determinate) **growth** and **unlimited** (indefinite or indeterminate) **growth**. Growth in annual plants is limited and after a period of maximum growth, during which the plant matures and reproduces, there is a period of **negative growth** or **senescence** before the death of the plant.

Several plant organs show limited growth but do not undergo a period of negative growth, for example, fruits, organs of vegetative propagation, dicotyledonous leaves and stem internodes. Animals exhibiting limited growth include insects, birds and mammals.

Woody perennial plants on the other hand show unlimited growth. Unlimited growth also occurs in fungi, algae, monocotyledonous leaves, and many animals, particularly nonchordates, fishes and reptiles.

CELL GROWTH

The cell is a dynamic system that exhibits a unique phenomenon of growth. A cell grows at the expense of food materials that it draws from its environment and converts it into its cellular constituents. An increase in active cell mass is the result of synthetic and degenerative processes acting



An elephant's growth is limited while a crocodile shows unlimited growth.

simultaneously. When a cell has reached its maximum limiting size, it divided into two daughter cells. Such a cell is said to be in **growth-duplication cycle**. Single celled organisms such as *E.coli*, yeast, *Amoeba*, etc., and somatic cells in culture are examples of a growth-duplication cycle. A cell, born after a division, proceeds to grow by macromolecular synthesis, reaches species – specific division size and replicates to repeat the cycle. Mitosis (or nuclear division) marks the end of the growth-duplication cycle in eukaryotic cells and is usually preceded by DNA replication.

Kinetics of Cell Growth

There is a great problem to determine the kinetics of cell enlargement of the cells between divisions, since the criteria for measuring growth (for example, dry mass, volume and linear dimensions) do not behave consistently even within the same cell. Studies on fixed cells and on living cells have revealed the following two patterns of growth: linear and exponential. An **exponential growth pattern** means that growth rate is a function of total mass; as mass increases, growth rate increases accordingly. The curve is sigmoidal, behaving as an autocatalytic process with growth rate proportional to the amount of active protoplasm or replicating entities. **Linear growth pattern** means that growth rate is constant throughout the cell cycle and does not increase. Here, growth rate is independent of cell mass but is related to a constant number of elements (synthetic sites), the activities of which remain unchanged throughout the growth cycle.

Examples. 1. A growing cell not only increases in size but increases in weight too. This means that growth is a linear measure and can be studied as a function of time. *E.coli* has been largely used to study growth in laboratory conditions on a well-defined medium. The nutrient medium contains glucose as the carbon source and several inorganic ions dissolved in an aqueous medium. Growth is best studied at 37^0 C and it takes about 60 minutes to double the cell mass. However, growth of *E.coli* can be accelerated (20 minutes) by supplementing the medium with various amino acids, purine, and pyrimidine bases.

Observations on the growth of a single *E.coli* cell have shown that the cell grows and divides into daughter cells after a unit time, which is a constant factor for each generation. This unit time is

called the **generation time**. The number of bacteria increases in an exponential phase, where growth and division are synchronized. Growth takes place as an exponent of 2, *i.e.*, 2^0, 2^1, 2^2, 2^3, 2^4...cells, and the pattern is represented in the form of a growth curve (Fig. 23.1). The linear portion of the curve represents exponential growth, suggesting increase in number of cells as a function of time. Subsequently the growth curve flattens and this part of the curve represents a period of maximum stationary growth. During this period the cells divide slowly and growth no longer remains exponential. The cause of stoppage of exponential growth is attributed to several factors such as depletion of nutrients and lack of oxygen. Since the vitality of the genome is greatly reduced, so cells cannot divide infinitely.

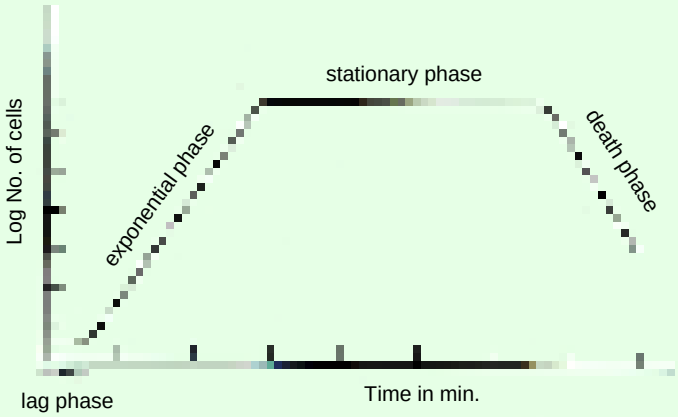


Fig. 23.1. Various patterns of growth in *E.coli*.

2. **Mitchison** (1963) measured the dry mass and volume of a budding yeast cell and demonstrated that mass increases **linearly** after division without a lag and continues at a constant rate until it doubles before the next division; that is, combined growth rate of daughter cells is double the original rate of the mother cell. On the other hand, cell volume follows a roughly **exponential curve** for the first three quarters of cell cycle, reaching a plateau prior to division.

Yeast growth kinetics emphasises various features common to the growth of cells that absorb nutrients through their surface : (1) growth rate is constant between divisions, and doubles immediately after; (2) cell mass doubles between divisions, (3) mass increase is correlated with a nuclear change rather than cytoplasmic; (4) there is no lag period – linear growth begins immediately after division. Exceptions to this pattern are found in *Amoeba*. Though mass in *Amoeba* doubles between divisions, its growth shows a diminishing rate of increase, reaching a plateau several hours before mitosis.

Evidently genetic factors determine growth patterns, but some differences are nutritional. Yeast cells absorb exogenous nutrients directly across the cell membrane while *Amoeba* engulfs solid food. Contractile vacuole changes in *Amoeba* introduce extraneous perturbations into cell mass measurements. Furthermore, a diminishing growth rate and a period of constancy at the end of *Amoeba* growth reflect a decline in feeding before division.

Mechanisms Involved in Cell Growth

In most cases, the kinetics of mass increase is usually matched by parallel synthesis of RNA, protein and membrane. The synthesis of DNA, being discontinuous, is not directly related to the kinetics of cell growth. It is however, involved in controlling the cell size.

1. RNA synthesis and cell growth. Generally, ribosomal RNA and tRNA are synthesized continuously throughout the eukaryotic cell cycle. The rate of synthesis may increase during cell cycle; in mammalian cells rate of rRNA synthesis becomes double after S phase. The pattern for mRNA is not known since different species of mRNA are synthesized at different periods of the cycle

and at different rates. The correlation between overall cell growth patterns and rRNA synthesis suggests that the production of ribosomes might be an important site for growth regulation. Evidently, the total number of ribosomes in a bacterial cell controls the rate of synthesis of all proteins during growth, *i.e.*, the number of ribosomes per DNA genome is proportional to the rate of growth and protein synthesis (**O. Maaloe**). In eukaryotic cells, growth rate depends on total number of cytoplasmic ribosomes per cell and these are controlled by the nucleolus, the seat of ribosome synthesis.

2. Nucleolus and cell growth. Nucleolus shows cyclic changes during the cell cycle and is somehow related to cell growth. During interphase, when cells are actively growing, nucleoli are prominent and synthesize ribosomal RNA at a high rate. In prophase, when growth stops, nucleoli disappear, emptying their contents into the nucleoplasm. Nucleoli are absent in metaphase and anaphase but reappear early in telophase at twice their original number, as new nucleoli organize at nucleolar organizer sites in each daughter nucleus. The combined growth rate of the daughter cells increase to twice the rate of the original mother cell though total protoplasmic mass has not changed. The transition from a state of physiological "oneness" to that of physiological "twoness" is most closely coordinated with duplication of nucleolar organizers and formation of nucleoli. Thus, growth rate doubles after the nucleolar organizers are replicated during the S phase when twice the number of ribosomal RNA genes start to transcribe rRNA.

In fact, the nucleolus is a dynamic organelle, attuned to metabolic demands, responding rapidly to changing needs for new patterns and rates of growth. It becomes large and metabolically active in most growing and proliferating cells, such as tumor, and disappears in cells not active in protein synthesis. When there is a heavy demand for ribosomes, as in maturing oocytes, nucleolar function is greatly amplified by making many additional nucleoli (up to 1000 in some species), each equipped with a segment of DNA containing many copies of the rRNA genes.

Thus, growth regulation seems to hinge upon the nucleolus and its control over ribosome synthesis. Ribosome production and turnover may determine cell growth, with the nucleolus as the principal "flow-through" centre or "valve" regulating the entire process.

3. Protein synthesis and cell growth. Most eukaryotic cell growth results from total protein accumulation—the net balance between total protein synthesis and protein degradation. Both processes are subject to different modes of regulation, the former largely dependent upon the availability of the ribosomes. Further, though total cell protein may seem to increase continuously through the cell cycle, some individual proteins may be constant, others may be decreasing and still others may be increasing in a stepwise fashion. For example, during cell cycle the enzymes exhibit the following three patterns of their synthesis: 1. Synthesis may be periodic like the DNA synthesis and increase rapidly during one phase of the cycle, *e.g.*, enzymes involved in DNA synthesis, such as thymidine kinase do show a stepwise pattern of its synthesis. 2. Continuous synthesis of enzymes, either linear or exponential, is typical of many respiratory enzymes in mouse fibroblasts. 3. Some enzymes show a peak pattern. They increase rapidly during the cycle, and disappear, presumably as a result of degradation and turnover. Within the same cell, each protein may be regulated independently of others. However, some sets of proteins may be coordinately regulated, particularly those proteins that characterize a cell phenotype.

Two hypotheses or models have been proposed to explain various patterns of protein synthesis which are meant for cell growth:

1. Oscillatory repression model. According to this model, periodic enzyme production initiates end product repression by negative feedback. When the enzyme pool is high, enzyme synthesis is repressed; when low, enzyme synthesis is increased. This pattern will lead to stable

oscillations which need not correspond in frequency to other events in the cell cycle, such as DNA synthesis.

2. Sequential gene expression model. According to this model, a chromosome is itself programmed for sequential gene expression of genes at different stages in the cell cycle. Here an ordered reading of genes is emphasized. The RNA polymerase moves along the genome transcribing genes in sequence. Hence, genes are available for transcription only at specific periods of the cell cycle. For example, linear reading of genes has been reported for synchronized growing yeast. The time of synthesis of 12 different enzymes in yeast corresponds to the position of their respective genes in the chromosomes. Each enzyme is synthesized in a stepwise manner with the position of gene seemingly dictating the order of its expression during the cell cycle.

REVISION QUESTIONS

1. Write an essay on the growh of living organisms.
2. What is growth? Describe the process of cell growth.