

CHAPTER I

GENERAL SKETCH OF THE CELL

“Wir haben gesehen, dass alle Organismen aus wesentlich gleichen Theilen, nämlich aus Zellen zusammengesetzt sind, dass diese Zellen nach wesentlich denselben Gesetzen sich bilden und wachsen, dass also diese Prozesse überall auch durch dieselben Kräfte hervorgebracht werden müssen.”
SCHWANN.¹

In the passage quoted above Schwann expressed a truth which subsequent research has established on an ever widening basis; and we have now more than ever reason to believe that despite unending diversity of form and function all cells may be brought into definite relation to a common morphological and physiological type. We are, it is true, still unable to specify all its essential features, and hence can give no adequate brief definition of the cell. For practical purposes, however, no such definition is needed, and we may be content with the simple type that has been familiar to histologists since the time of Leydig and Max Schultze.

It should from the outset be clearly recognized that the term “cell” is a biological misnomer; for cells only rarely assume the form implied by the word of hollow chambers surrounded by solid walls. The term is merely an historical survival of a word casually employed by the botanists of the seventeenth century to designate the cells of certain plant-tissues which, when viewed in section, give somewhat the appearance of a honeycomb.² The cells of these tissues are, in fact, separated by conspicuous solid walls which were mistaken by Schleiden, followed by Schwann, for their essential part. The living substance contained within the walls, to which Hugo von Mohl gave the name *protoplasm*³ (1846), was at first overlooked or was regarded as a waste-product, a view based upon the fact that in many important plant-tissues such as cork or wood it may wholly disappear, leaving only the lifeless walls. The researches of Bergmann, Kölliker, Bischoff, Cohn, Max Schultze, and many others

¹ *Untersuchungen*, p. 227, 1839.

² The word seems to have been first employed by Robert Hooke, in 1665, to designate the minute cavities observed in cork, a tissue which he described as made up of “little boxes or cells distinct from one another” and separated by solid walls.

³ The same word had been used by Purkinje some years before (1840) to designate the formative material of young animal embryos.

showed, however, that most living cells are not hollow but solid bodies, and that in many cases—for example, the colourless corpuscles of blood and lymph—they are naked masses of protoplasm not surrounded by definite walls. Thus it was proved that neither the vesicular form nor the presence of surrounding walls is an essential character, and that the cell-contents, *i.e.* the *protoplasm*, must be the seat of vital activity.

Within the protoplasm (Figs. 6-8) lies a body, usually of definite rounded form, known as the *nucleus*,¹ and this in turn often contains

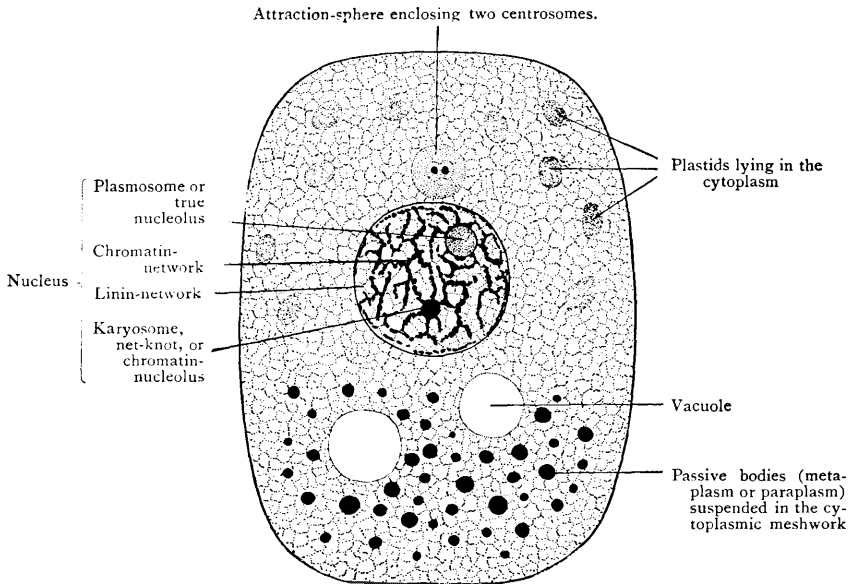


Fig. 6.—Diagram of a cell. Its basis consists of a meshwork containing numerous minute granules (*microsomes*) and traversing a transparent ground-substance.

one or more smaller bodies or *nucleoli*. By some of the earlier workers the nucleus was supposed to be, like the cell-wall, of secondary importance, and many forms of cells were described as being devoid of a nucleus (“cytodes” of Haeckel). Nearly all later researches have indicated, however, that the characteristic nuclear material, whether forming a single body or scattered in smaller masses, is always present, and that it plays an essential part in the life of the cell.

Besides the presence of protoplasm and nucleus, no other structural features of the cell are yet known to be of universal occurrence.

¹ First described by Fontana in 1781, and recognized as a normal element of the cell by Robert Brown in 1833.

We may therefore still accept as valid the definition given more than thirty years ago by Leydig and Max Schultze, that a cell is *a mass of protoplasm containing a nucleus*,¹ to which we may add Schultze's statement that *both nucleus and protoplasm arise through the division of the corresponding elements of a preëxisting cell*. Nothing could be less appropriate than to call such a body a "cell"; yet the word has become so firmly established that every effort to replace it by a better has failed, and it probably must be accepted as part of the established nomenclature of science.²

A. GENERAL MORPHOLOGY OF THE CELL

The cell is a rounded mass of protoplasm which in its simplest form is approximately spherical. The form is, however, seldom realized save in isolated cells such as the unicellular plants and animals or the egg-cells of the higher forms. In vastly the greater number of cases the typical spherical form is modified by unequal growth and differentiation, by active movements of the cell-substance, or by the mechanical pressure of surrounding structures, but true angular forms are rarely if ever assumed save by cells surrounded by hard walls. The protoplasm which forms its active basis is a viscid, translucent substance, sometimes apparently homogeneous, more frequently finely granular, and as a rule giving the appearance of a meshwork, which is often described as a spongelike or netlike "reticulum."³ Besides the active substance or protoplasm proper the cell almost invariably contains various lifeless bodies suspended in the meshes of the network; examples of these are food-granules, pigment-bodies, drops of oil or water, and excretory matters. These bodies play a relatively passive part in the activities of the cell, being either reserve food-matters destined to be absorbed and built up into the living substance, or by-products formed from the protoplasm as waste-matters or in order to play some *rôle* subsidiary to the actions of the protoplasm itself. The passive inclusions in the protoplasm may be collectively designated as *metaplasm* (Hanstein) or *paraplasm* (Kupffer), in contradistinction to the active *protoplasm*.

¹ Leydig, *Lehrbuch der Histologie*, p. 9, 1857; Schultze, *Arch. Anat. u. Phys.*, p. 11, 1861.

² Sachs has proposed the convenient word *energid* (*Flora*, '92, p. 57) to designate the essential living part of the cell, *i.e.* the nucleus with that portion of the active cytoplasm that falls within its sphere of influence, the two forming an organic unit both in a morphological and in a physiological sense. It is to be regretted that this convenient and appropriate term has not come into general use. (See also *Flora*, '95, p. 405, and *cf.* Kupffer ('96), Meyer ('96), and Kölliker ('97).)

³ Such meshworks are sometimes plainly visible in the living protoplasm (p. 44). It is always more or less an open question how far the appearances seen in fixed (coagulated) material correspond with the conditions existing in life. See pp. 42-46.

It is often difficult to distinguish between such metaplasmic bodies and the granules commonly supposed to be elements of the active protoplasm; indeed, as will appear beyond (p. 29), there is reason to believe that "protoplasmic" and "metaplasmic" granules cannot be separated by any definite limit, but are connected by various gradations. Among the lifeless products of the protoplasm must be reckoned also the *cell-wall* or *membrane* by which the cell-body may

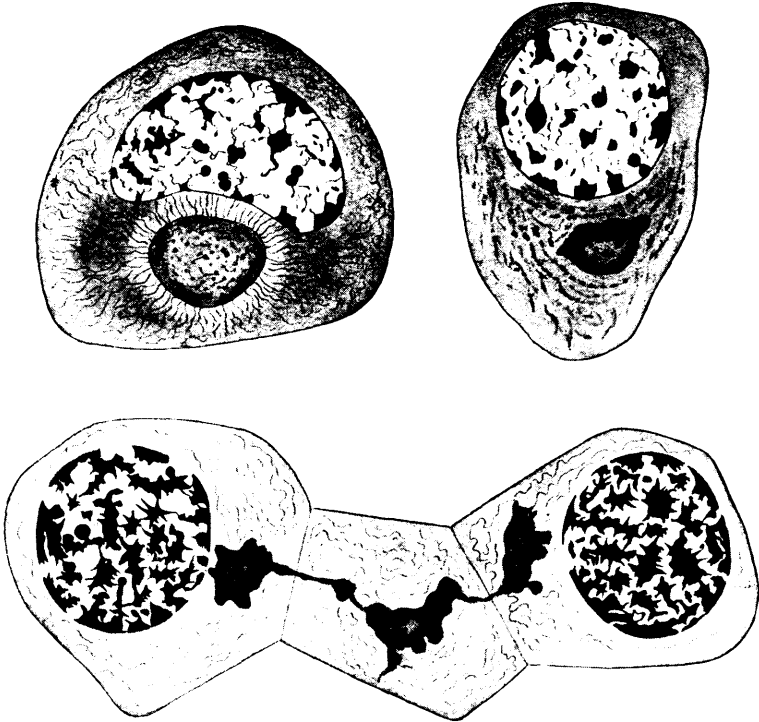


Fig. 7—Spermatogonia of the salamander. [MEVES.]

Above, two cells showing large nuclei, with linin-threads and scattered chromatin-granules; in each cell an attraction-sphere with two centrosomes. Below, three contiguous spermatogonia, showing chromatin-reticulum, centrosomes and spheres, and sphere-bridges.

be surrounded; but it must be remembered that the cell-wall in some cases arises by a direct transformation of the protoplasmic substance, and that it often retains the power of growth by intussusception like living matter.

It is unfortunate that some confusion has arisen in the use of the word *protoplasm*. When Leydig, Schultze, Brücke, De Bary, and other earlier writers spoke of "protoplasm," they had in mind only the substance of the cell-body, not that of the nucleus. Strasburger,

however, in 1882, extended the term so as to denote the entire active cell-substance, including the nuclear material, suggesting that the latter be called *nucleoplasm*, and that of the cell-body *cytoplasm*.

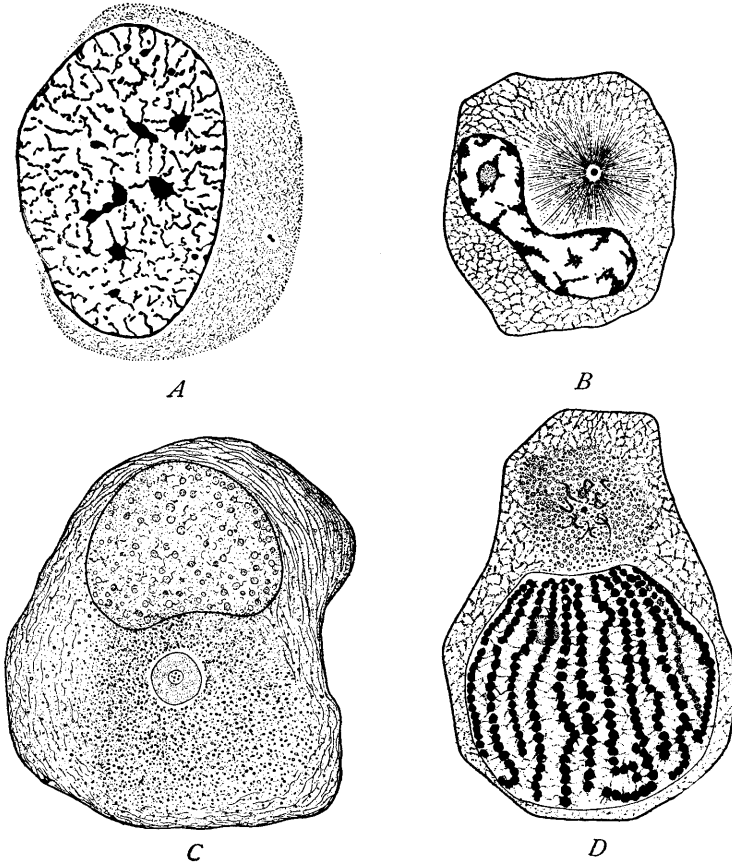


Fig. 8 — Various cells showing the typical parts.

A. From peritoneal epithelium of the salamander-larva. Two centrosomes at the right. Nucleus showing net-knots. [FLEMMING.]

B. Spermatogonium of frog. Attraction-sphere (aster) containing a single centrosome. Nucleus with a single plasmosome. [HERMANN.]

C. Spinal ganglion-cell of frog. Attraction-sphere near the centre, containing a single centrosome with several centrioles. [LENHOSSÉK.]

D. Spermatocyte of *Proteus*. Nucleus in the spireme-stage. Centrosome single; attraction-sphere containing rod-shaped bodies. [HERMANN.]

These terms have been adopted by many, but not all, later writers, the hybrid word *nucleoplasm* having, however, at Flemming's suggestion, been changed to *karyoplasm*. At the present time, therefore, the word *protoplasm* is used by some authors (Bütschli, Hertwig,

Kölliker, etc.) in its original narrower sense (equivalent to Strasburger's *cytoplasm*), while perhaps the majority of writers have accepted the terminology of Strasburger and Flemming. On the whole, the terms *cytoplasm* and *karyoplasm* seem too useful to be rejected, and, without attaching too much importance to them, they will be employed throughout the present work. It must not, however, be supposed that either of the words denotes a single homogeneous substance; for, as will soon appear, both cytoplasm and karyoplasm consist of several distinct elements.

The nucleus is usually bounded by a definite membrane, and often appears to be a perfectly distinct vesicular body suspended in the cytoplasm—a conclusion sustained by the fact that it may move actively through the latter, as often occurs in both vegetable and animal cells. Careful study of the nucleus during all its phases gives, however, reason to believe that its structural basis is similar to that of the cell-body; and that during the course of cell-division, when the nuclear membrane usually disappears, cytoplasm and karyoplasm come into direct continuity. Even in the resting cell there is good evidence that both the intranuclear and the extranuclear material may be structurally continuous with the nuclear membrane¹ and among the Protozoa there are forms (some of the flagellates) in which no nuclear membrane can at any period be seen. For these and other reasons *the terms "nucleus" and "cell-body" should probably be regarded as only topographical expressions denoting two differentiated areas in a common structural basis.* The terms *karyoplasm* and *cytoplasm* possess, however, a specific significance owing to the fact that there is on the whole a definite chemical contrast between the nuclear substance and that of the cell-body, the former being characterized by the abundance of a substance rich in phosphorus known as *nuclein*, while the latter contains no true nuclein and is especially rich in albuminous substances such as nucleo-albumins, albumins, globulins, and the like, which contain little or no phosphorus.

Both morphologically and physiologically the differentiation of the active cell-substance into nucleus and cell-body must be regarded as a fundamental character of the cell because of its universal, or all but universal, occurrence, and because there is reason to believe that it is in some manner an expression of the dual aspect of the fundamental process of metabolism, constructive and destructive, that lies at the basis of cell life. The view has been widely held that a third essential element is the *centrosome*, discovered by Flemming and Van Beneden in 1875–76, and since shown to exist in a large number of other cells (Figs. 7, 8). This is an extremely minute body which

¹ Conklin ('97, 1), Obst ('99), and some others have described a direct continuity in the resting cell between the intranuclear and extranuclear meshworks.

is concerned in the process of cell-division and in the fertilization of the egg, and has been characterized as the "dynamic centre" of the cell. Whether it has such a significance, and whether it is in point of morphological persistence comparable with the nucleus, are questions still *sub judice*, which will be discussed elsewhere.¹

B. STRUCTURAL BASIS OF PROTOPLASM

As ordinarily seen under moderate powers of the microscope, protoplasm appears as a more or less vague granular substance which shows as a rule no definite structure organization. More precise examination under high powers, especially after treatment by suitable fixing and staining reagents, often reveals a highly complex structure in both nucleus and cytoplasm. Since the fundamental activities of protoplasm are everywhere of the same nature, investigators have naturally sought to discover a corresponding fundamental morphological organization common to all forms of protoplasm and underlying all of its special modifications. Up to the present time, however, these attempts have not resulted in any *consensus* of opinion as to whether such a common organization exists. In many forms of protoplasm, both in life and after fixation by reagents, the basis of the structure is a more or less regular framework or *meshwork*, consisting of at least two substances. One of these forms the substance of the meshwork proper; the other, often called the *ground-substance* (also cell-sap, enchylema, hyaloplasma, paramitome, interfilar substance, etc.),² occupies the intervening spaces. To these two elements must be added minute, deeply staining *granules* or "microsomes" scattered along the branches of the meshwork, sometimes quite irregularly, sometimes with such regularity that the meshwork seems to be built of them. Besides the foregoing three elements, which we may provisionally regard as constituting the active substance, the protoplasm almost invariably contains various passive or metaplasmic substances in the form of larger granules, drops of liquid, crystalloid bodies, and the like. These bodies, which usually lie in the spaces of the meshwork, are often difficult to distinguish from the microsomes lying in the meshwork proper—indeed, it is by no means certain that any adequate ground of distinction exists.³

From the time of Frommann and Arnold ('65-'67) onwards, most of the earlier observers regarded the meshwork as a fibrillar structure, either forming a continuous network or *reticulum* somewhat like the fibrous network of a sponge ("reticular theory" of Klein, Van Beneden, Carnoy, Heitzmann), or consisting of disconnected threads,

¹ Cf. pp. 304, 354.

² Cf. Glossary.

³ Cf. p. 29.

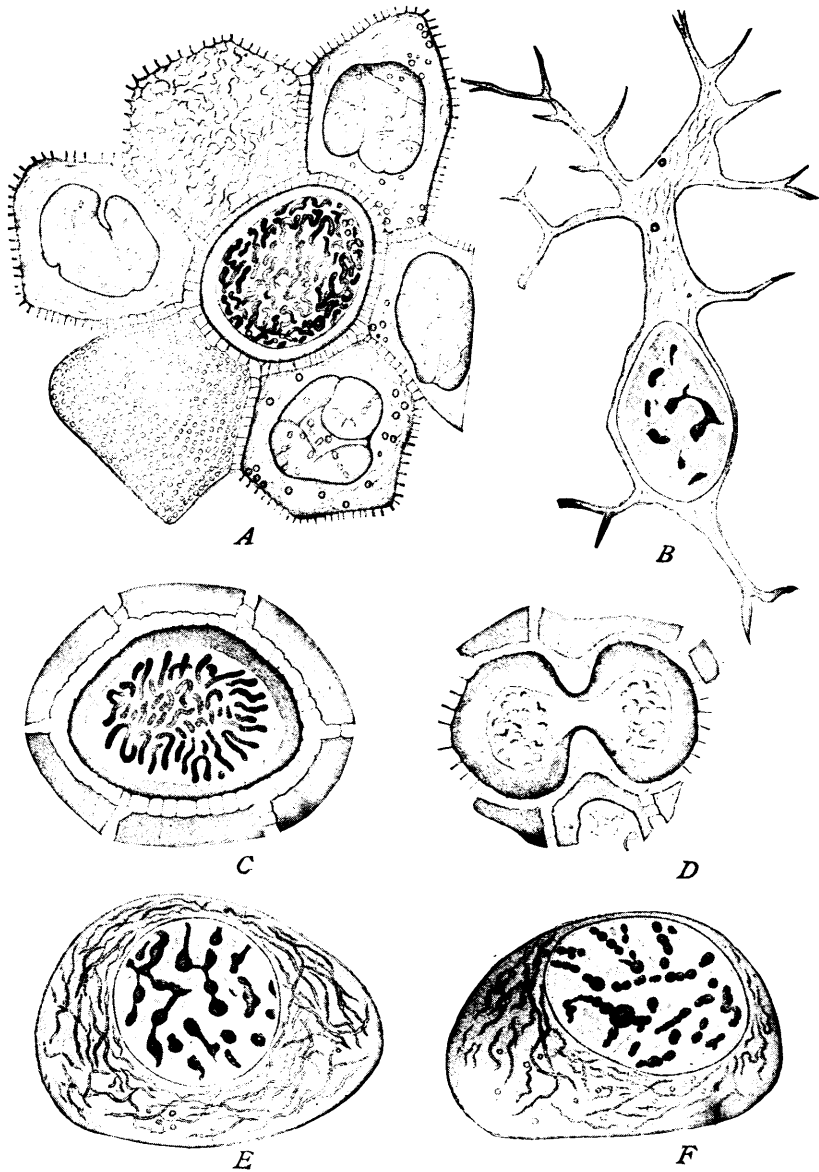


Fig. 9. — Living cells of salamander-larva. [FLEMMING.]

A. Group of epidermal cells at different foci, showing protoplasmic bridges, nuclei, and cytoplasmic fibrillæ; the central cell with nucleus in the spireme-stage. *B.* Connective tissue cell. *C.* Epidermal cell in early mitosis (segmented spireme) surrounded by protoplasmic bridges. *D.* Dividing cell. *E, F.* Cartilage-cells with cytoplasmic fibrillæ (the latter somewhat exaggerated in the plate).

whether simple or branching ("filar theory" of Flemming), and the same view is widely held at the present time. The meshwork has received various names in accordance with this conception, among which may be mentioned *reticulum*, *thread-work*, *spongioplasm*, *mitome*, *filar substance*,¹ all of which are still in use. Under this view the "granules" described by Schultze, Virchow and still earlier observers have been variously regarded as nodes of the network, optical sections of the threads, or as actual granules ("microsomes") suspended in the network as described above.

Widely opposed to these views is the "alveolar theory" of Bütschli, which has won an increasing number of adherents. Bütschli regards protoplasm as having a foam-like alveolar structure ("Wabenstruktur"), nearly similar to that of an emulsion (Fig. 10), and he has shown in a series of beautiful experiments that artificial emulsions, variously prepared, may show under the microscope a marvelously close resemblance to living protoplasm, and further that drops of oil-emulsion suspended in water may even exhibit amœboid changes of form. To restate Bütschli's view, protoplasm consists of separate, closely crowded minute drops² of a liquid *alveolar substance* suspended in a continuous *interalveolar substance*, likewise liquid, but of different physical nature. The latter thus forms the walls of closed chambers or *alveoli* in which the alveolar drops lie, just as in a fine emulsion the emulsifying liquid surrounds the emulsified drops. The appearance of a network in protoplasm is illusory, being due to optical section of the interalveolar walls or partitions as viewed at any given focus of the microscope. As thus seen, the walls themselves appear as fibres, while the "spaces of the network" are in like manner optical sections of the alveoli, the alveolar substance that fills them corresponding to the "ground substance." As explained beyond,³ Bütschli interprets in like manner the radiating systems or asters formed during cell-division, the astral rays (usually considered as fibres) being regarded as merely the septa between radially arranged alveoli (Fig. 10).

The two (three) general views above outlined may be designated respectively as the *fibrillar* (reticular or filar) and *alveolar* theories of protoplasmic structure; and each of them has been believed by some of its adherents to be universally applicable to all forms of protoplasm. Beside them may be placed, as a third general view, the *granular* theory especially associated with the name of Altmann, by whom it has been most fully developed, though a number of earlier writers have held similar views. According to Altmann's view, which apart from its theoretical development approaches in

¹ See Glossary.

² Measuring on an average about .001 mm. in diameter.

³ Cf. p. 110.

some respects that of Bütschli, protoplasm is compounded of innumerable minute granules which alone form its essential active basis; and while fibrillar or alveolar structures may occur, these are of only secondary importance.

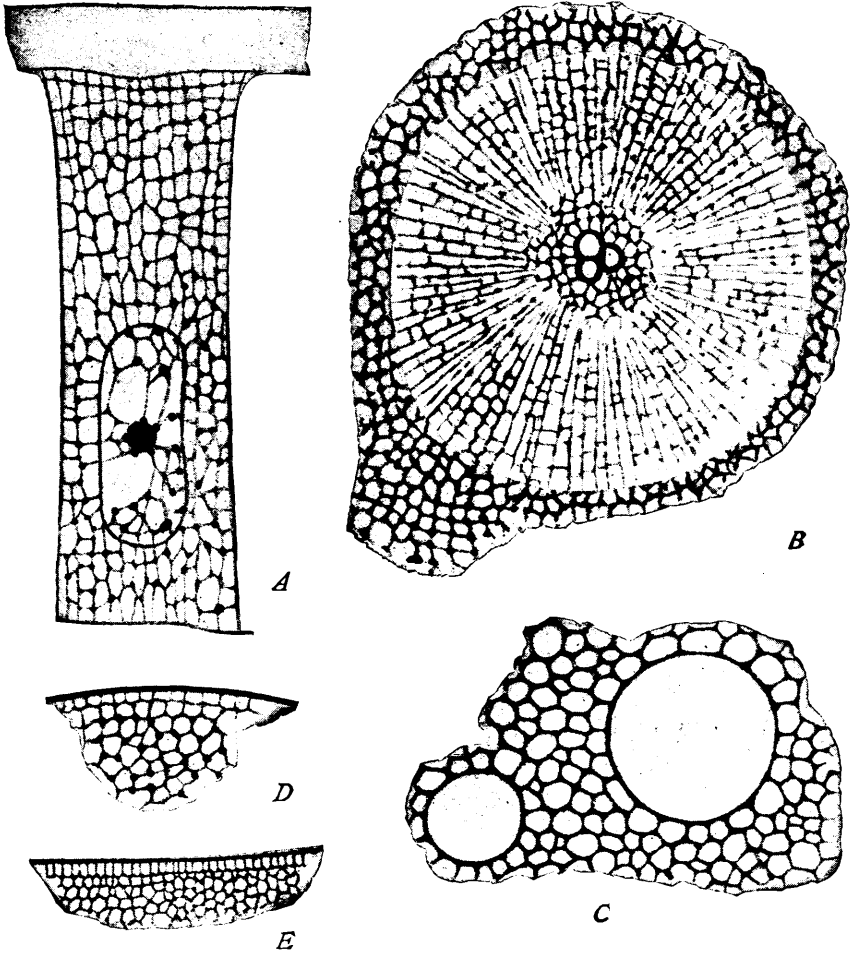


Fig. 10. — Alveolar or foam-structure of protoplasm, according to Bütschli. [BÜTSCHLI.]

A. Epidermal cell of the earthworm. B. Aster, attraction-sphere, and centrosome from sea-urchin egg. C. Intracapsular protoplasm of a radiolarian (*Thalassicolla*) with vacuoles. D. Peripheral cytoplasm of sea-urchin egg. E. Artificial emulsion of olive-oil, sodium chloride, and water.

It is impossible here adequately to review the many combinations and modifications of these views which different investigators have

made.¹ On the whole, the present drift of opinion is toward the conclusion that none of the above interpretations has succeeded in the attempt to give a universal formula for protoplasmic structure; and many recent observers have reached the conclusion, earlier advocated by Kölliker ('89), that the various types described above are connected by intermediate gradations and may be transformed one into another, in different phases of cell-activity. Unna ('95), for example, endeavours to show how an alveolar structure may pass into a sponge-like or reticular one by the breaking down of the inter-

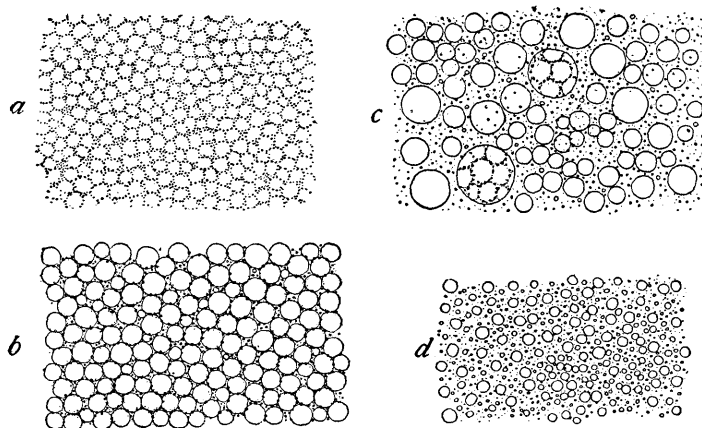


Fig. 11.—(a) Protoplasm of the egg of the sea-urchin (*Toxopneustes*) in section showing meshwork of microsomes; (b) protoplasm from a living star-fish egg (*Asterias*) showing alveolar spheres with microsomes scattered between them; (c) the same in a dying condition after crushing the egg; alveolar spheres fusing to form larger spheres; (d) protoplasm from a young ovarian egg of the same. (All the figures magnified 1200 diameters.)

alveolar walls. Flemming, for many years the foremost and most consistent advocate of the fibrillar theory, now admits that protoplasm may be fibrillar, alveolar, granular, or sensibly homogeneous,² and that we cannot, therefore, regard any one of these types of structure as absolutely diagnostic of the living substance. In plant-cells Strasburger³ and a number of his pupils maintain that the “kino-plasm” (p. 322) or filar plasm, from which the spindle-fibres and astral rays are formed, is fibrillar, while the “trophoplasm” or alveolar plasm forming the main body of the cell is alveolar, the former, however, assuming the fibrillar structure, as a rule, only during the mitotic activity of the cell. My own long-continued studies on various forms of protoplasm have likewise led to the conclusion that no universal formula for protoplasmic structure can be

¹ For full discussion, with literature list, see Flemming, '82, '97, 1, '97, 2, and Bütschli, '92, 2, '99.

² '97, 1, p. 260.

³ '95, '97, 3, '98.

given.¹ In that classical object, the echinoderm-egg, for example, it is easy to satisfy oneself, *both in the living cell and in sections*, that the protoplasm has a beautiful alveolar structure, exactly as described by Bütschli in the same object (Fig. 11). This structure is here, however, entirely of secondary origin; for its genesis can be traced step by step during the growth of the ovarian eggs through the deposit of minute drops in a homogeneous basis, which ultimately gives rise to the interalveolar walls. In these same eggs the astral systems formed during their subsequent division (Fig. 12) are, I

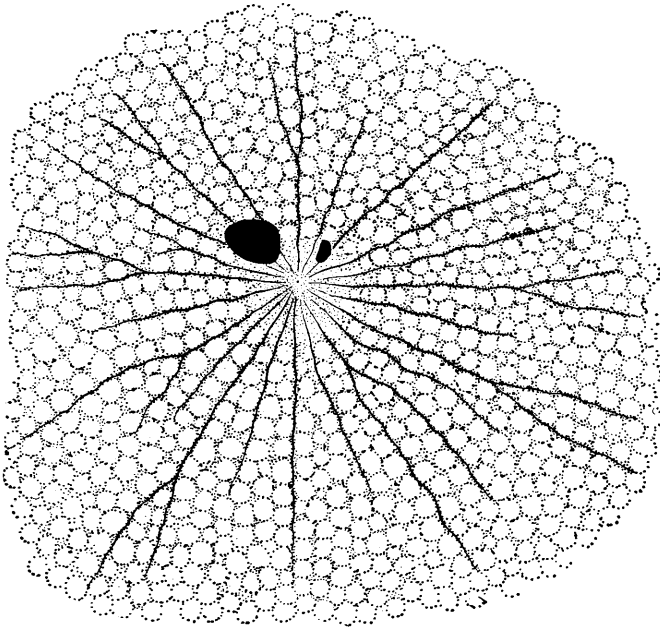


Fig. 12.—Section of sea-urchin egg (*Toxopneustes*), 1½ minutes after entrance of the spermatozoön, showing alveoli and microsomes, sperm-nucleus, middle piece, and aster (about 2000 diameters).

believe, no less certainly fibrillar; and thus we see the protoplasm of the same cell passing successively through homogeneous, alveolar, and fibrillar phases, at different periods of growth and in different conditions of physiological activity. There is good reason to regard this as typical of protoplasm in general. Bütschli's conclusions, based on researches so thorough, prolonged, and ingenious, are entitled to great weight; yet it is impossible to resist the evidence that fibrillar and granular as well as alveolar structures are of wide occurrence; and while each may be characteristic of certain kinds of

¹ Wilson, '99.

cells, or of certain physiological conditions,¹ none is common to all forms of protoplasm. If this position be well grounded, we must admit that the attempt to find in visible protoplasmic structure any adequate insight into its fundamental modes of physiological activity has thus far proved fruitless. We must rather seek the source of these activities in the ultramicroscopical organization, accepting the probability that apparently homogeneous protoplasm is a complex mixture of substances which may assume various forms of visible structure according to its modes of activity.

Some of the theoretical speculations regarding the essential nature of that organization are discussed in Chapter VI., but one *quasi*-theoretical point must be here considered. Much discussion has been given to the question as to which of the visible elements of the protoplasm should be regarded as the "living" substance proper; and the diversity of opinion on this subject may be judged by the fact that although many of the earlier observers identified the "reticulum" as the living element, and the ground-substance as lifeless, others, such as Leydig and Schäfer, held exactly the reverse view, while Altmann insisted that only the "granules" were alive. Later discussions have shown the futility of this discussion, which is indeed largely a verbal one, turning as it does on the sense of the word "living." In practice we continually use the word "living" to denote various degrees of vital activity. Protoplasm deprived of nuclear matter has lost, wholly or in part, one of the most characteristic vital properties, namely, the power of synthetic metabolism; yet we still speak of it as "living," since it still retains for a longer or shorter period such properties as irritability and the power of coördinated movement; and, in like manner, various special elements of protoplasm may be termed "living" in a still more restricted sense. In its fullest meaning, however, the word "living" implies the existence of a group of coöperating activities more complex than those manifested by any one substance or structural element. I am therefore entirely in accord with the view urged by Sachs, Kölliker, Verworn, and other recent writers, that life can only be properly regarded as a property of the cell-system as a whole; and the separate elements of the system would, with Sachs, better be designated as "active" or "passive," rather than as "living" or "lifeless." Thus regarded, the distinction

¹ Thus the alveolar structure seems to be characteristic of Protozoa in general, and of the protoplasm of plant-cells when in the vegetative state, the fibrillar of nerve-cells and muscle-cells. The granular type is characteristic of some forms of leucocytes and gland-cells; but many of the granules in these cells are no doubt metaplastic, and it is further very doubtful whether such a granular or "pseudo-alveolar" structure can be logically distinguished from an alveolar (*cf.* Wilson, '99). In the pancreas-cell granular and fibrillar structures alternate with the varying phases of secretory activity (*cf.* Mathews, '99).

between "protoplasmic" and "metaplasmic" substances, while a real and necessary one, becomes after all one of degree. I believe that we are probably justified in regarding the continuous substance as the most constant and active element, and that which forms the fundamental basis of the system, transforming itself into granules, drops, fibrillæ, or networks in accordance with varying physiological needs.¹

Thus stated, the question as to the relative activity of the various elements becomes a real and important one. It now seems probable that the substance of the meshwork (fibrillar or interalveolar structure) is most active in the processes of cell-division, in contractile organs such as cilia and muscle-fibres, and in nerve-cells; but the ground-substance, while apparently the most frequent seat of metaplasmic deposits, is certainly also the seat of active chemical changes. This subject has, however, not yet been sufficiently investigated.

C. THE NUCLEUS

A fragment of a cell deprived of its nucleus may live for a considerable time and manifest the power of coördinated movement without perceptible impairment. Such a mass of protoplasm is, however, devoid of the powers of assimilation, growth, and repair, and sooner or later dies. In other words, those functions that involve destructive metabolism may continue for a time in the absence of the nucleus; those that involve constructive metabolism cease with its removal. There is, therefore, strong reason to believe that the nucleus plays an essential part in the constructive metabolism of the cell, and through this is especially concerned with the formative processes involved in growth and development. For these and many other reasons, to be discussed hereafter, the nucleus is generally regarded as a controlling

¹ Wilson, '99. Cf. Sachs ('92, '95), Kölliker ('97), Meyer ('96), and Kupffer ('96) on energids. Sachs sharply distinguishes between the *energid* (nucleus and protoplasm), which forms a living unit, and the passive *energid-products*, placing in the former the nucleus, nucleolus, general cytoplasm, centrosome and plastids (chloroplasts and leucoplasts), and in the latter the starch-grains, aleurone-crystals, and membrane. Meyer carries the analysis further, classifying the active energid-elements into *protoplasmatic* and *alloplasmatic* organs, the former (nucleus cytoplasm, chromatophores, and perhaps the centrosomes) arising only by division, the latter (cilia, and according to Kölliker, also the muscle- and nerve-fibrillæ) formed by differentiation from the protoplasmatic elements. The passive energid-products (*ergastic* structures or "formed material" of Beale) are formed as *enclosures* (starch-grains, etc.), or excretions (membranes). These general views are accepted by Kölliker; but none of these writers has undertaken to show how "alloplasmatic" structures are to be distinguished from metaplasmic or ergastic. I believe Sachs' view to be in principle not only true but of high utility. Practically, however, it involves us in considerable difficulty, unless the terminology adopted above — itself directly suggested by and nearly agreeing with the usage of Sachs and Kölliker — be employed.

centre of cell-activity, and hence a primary factor in growth, development, and the transmission of specific qualities from cell to cell, and so from one generation to another.

I. *General Structure*

The cell-nucleus passes through two widely different phases, one of which is characteristic of cells in their ordinary or vegetative condition, while the other only occurs during the complicated changes involved in cell-division. In the first phase, falsely characterized as the "resting state," the nucleus usually appears as a rounded sac-like body surrounded by a distinct membrane and containing a conspicuous irregular network (Figs. 6, 7, 13), which is in some cases plainly visible in the living cell (Fig. 9). The form of the nucleus, though subject to variation, is on the whole singularly constant, and as a rule shows no very definite relation to that of the cell-body, though in elongated cells such as muscle-cells, in certain forms of parenchyma, and in epithelial cells (Fig. 49), the nucleus is itself often elongated. Typically spherical, it may, in certain cases, assume an irregular or amœboid form, may break up into a group of more or less completely separated lobes (polymorphic nuclei, Fig. 49), sometimes forming an irregular ring ("ring-nuclei" of leucocytes, giant-cells, etc., Fig. 14, *D*). It is usually very large in gland-cells and others that show a very active metabolism, and in such cases its surface is sometimes increased by the formation of complex branches ramifying through the cell (Fig. 14, *E*).

These forms seem in general to be fairly constant in a given species of cell, but in a large number of cases the nucleus has been seen in the living cell (cartilage-cells, leucocytes, ova) to undergo more or less active changes of form, sometimes so marked as to merit the name of amœboid (Fig. 77). Perhaps the most remarkable deviations from the usual type of nucleus occur among the unicellular forms. In the ciliate Infusoria the nuclei are massive bodies of two kinds, viz. a large *macronucleus* and one or more smaller *micronuclei*, both of which are present in the same cell, the former kind being generally regarded as the active nucleus, the latter as a reserve nucleus from which at certain periods new macronuclei arise (p. 224). The macronuclei show a remarkable diversity of form and structure in different species. Still more interesting are the so-called scattered or distributed nuclei, described by Bütschli in flagellates and Bacteria, by Gruber in certain rhizopods and Infusoria, and by several authors in the Cyanophyceæ (Figs. 15, 16). The nuclear material is here apparently scattered through the cell in the form of numerous minute, deeply stained granules, which, if this identification is correct, represent the most primi-

tive known types of nucleus; but this subject is still *sub judice* (p. 39). A transition from this condition to nuclei of the ordinary type appears to be given in the nuclei of certain flagellates (e.g. *Chilomonas* and *Trachelomonas*), where the chromatin-granules are aggregated about a nucleolus-like body, but are not enclosed by a membrane.¹

In considering the structure of the nucleus, as seen in sections, we must, as in the case of the cytoplasm, bear in mind the possibility, or

rather probability, that some of the elements described may be coagulation-products; for the nucleus is in life composed of liquid or semi-liquid substance, and Albrecht ('99) has recently shown that nuclei isolated in the fresh condition will flow together to form a single body. Most of the main features of the nucleus, both in the resting and in the dividing phases, have, however, been seen in life (Fig. 9), and the principal danger of mistaking artifacts for normal structures relates to the finer elements, considered beyond.

In the ordinary forms of nuclei in their resting state the following structural elements may as a rule be distinguished (Figs. 6, 7, 10):—

a. The *nuclear membrane*, a well-defined delicate wall which gives the nucleus a sharp contour and differentiates it clearly from the surrounding cytoplasm. This wall sometimes stains but very slightly, and can scarcely be differentiated from the outlying



Fig. 13.—Two nuclei from the crypts of Lieberkühn in the salamander. [HEIDENHAIN.]

The character of the chromatin-network (*basichromatin*) is accurately shown. The upper nucleus contains three plasmosomes or true nucleoli; the lower, one. A few fine *linin*-threads (*oxychromatin*) are seen in the upper nucleus running off from the chromatin-masses. The clear spaces are occupied by the ground-substance.

cytoplasm. In other and perhaps more frequent cases, it approaches in staining capacity the chromatin.

b. The *nuclear reticulum*. This, the most essential part of the nucleus, forms an irregular branching network or *reticulum* which consists of two very different constituents. The first of these, forming the general protoplasmic basis of the nucleus, is a substance known as *linin*

¹ Calkins, '98, 1.

(Schwarz), invisible until after treatment by reagents, which in sections shows a finely granular structure and stains like the cytoplasmic substance, to which it is nearly related chemically (Figs. 7, 49). The second constituent, a deeply staining substance known as *chromatin* (Flemming), is the nuclear substance *par excellence*, for in many cases it appears to be the only element of the nucleus that is directly handed on by division from cell to cell, and it seems to have the power to produce all the other elements. The chromatin often appears in the form of scattered granules and masses of differing size and form, which are embedded in and supported by the linin-substance (Figs. 7, 19). In some cases the entire chromatin-content of the nucleus appears to be condensed into a single mass which simulates a nucleolus; for example, in *Spirogyra* and in various flagellates and rhizopods (e.g. *Actinosphaerium*, *Arcella*); or there may be several such chromatin-masses, as in some of the Foraminifera and in *Noctiluca*. More commonly the chromatin forms a more or less regular network intermingled with and more or less embedded in the linin, from which it is often hardly distinguishable until the approach of mitosis, when a condensation of the chromatin-substance occurs.

In contradistinction to the other nuclear elements, chromatin is not acted upon, or is but slowly affected, by peptic digestion. It may thus be easily isolated for chemical analysis, which shows it to consist mainly of *nuclein*, i.e. a compound in varying proportions of a complex phosphorus-containing acid known as *nucleinic acid*, with albuminous bodies such as histon, protamin, or in some cases albumin itself.¹ Upon this, as will be shown in Chapter VI., probably depends the pronounced staining capacity when treated with the so-called "nuclear stains" (e.g. hæmatoxylin, methyl-green, and the basic tar-colours generally) from which chromatin takes its name. This capacity always increases as the nucleus prepares for division, reaching a climax in the spireme- and chromosome-stages, and it is also very marked in condensed nuclei such as those of spermatozoa. These variations are almost certainly due to varying proportions in the constituents of the nuclein, the staining capacity standing in direct ratio to the amount of nucleinic acid.

c. The *nucleoli*, one or more larger rounded or irregular bodies, suspended in the network, and staining intensely with many dyes. In some nuclei they are entirely absent. When present the nucleoli vary in number from one to five or more; and the number is often inconstant in the same species of cell, and even varies in the same cell with varying physiological conditions. In the eggs of some animals, at certain periods of growth (e.g. lower vertebrates), the nucleus may contain hundreds of nucleoli. An interesting case is

¹ See p. 334.

that of the subcutaneous gland-cells of *Pisciola*, the nuclei of which contain in early phases of secretion but a single nucleolus. During growth of the cell the nucleolus fragments, finally giving rise to several hundred nucleoli which then appear to migrate out into the cytoplasm, leaving but a single nucleolus to repeat the cycle.¹

The bodies known as nucleoli are of at least two different kinds. The first of these, the so-called true nucleoli or *plasmosomes* (Figs. 6, 8, *B*, 13), are of spherical form, and are shown by the staining reactions to differ widely from chromatin, being in general sharply stained by dyes which, like eosin, orange or acid fuchsin, stain the linin and the general cytoplasm. The plasmosomes sometimes seem to have no envelope, but in many cases (*e.g.* in leucocytes) are surrounded by a thin layer that stains like chromatin. Nucleoli of a quite different type are the "net-knots" (Netzknöten), chromatin-nucleoli, or *karyosomes*, which agree in staining reaction with chromatin and are doubtless to be regarded as merely a portion of the chromatin-network (Figs. 8, 49). These are sometimes spherical, more often irregular (Fig. 8), and often are hardly to be distinguished, except in size, from nodes of the chromatin-reticulum.² The relations between these two forms of nucleoli are far from certain, and the variations in staining reaction shown by true nucleoli render it not improbable that intermediate forms exist which may represent an actual transition from one to the other.³ In many of the Protozoa, as described beyond, the "nucleolus" is shown by its behaviour during mitosis to be comparable with an attraction-sphere or centrosome ("nucleolo-centrosome," Keuten); and even in higher forms there are some cells in which the centrosome is intranuclear (Fig. 148).

There is good reason to believe that the chromatin-nucleoli are merely more condensed portions of the chromatin-network, since during cell-division they have the same history as the remaining portion of the chromatin-substance.⁴ The nature of the true nucleoli is still imperfectly known. By some observers, including Flemming, O. and R. Hertwig, and Carnoy, they have been regarded as store-houses of material (para-nuclein, plastin) which contributes to the

¹ Montgomery, '98, 2.

² Flemming first called attention to the chemical difference between the true nucleoli and the chromatic reticulum ('82, pp. 138, 163) in animal-cells, and Zacharias soon afterward studied more closely the difference of staining reaction in plant-cells, showing that the former are especially coloured by alkaline carmine solutions, the latter by acid solutions. Other studies by Carnoy, Zacharias, Ogata, Rosen, Schwarz, Heidenhain, and many others show that the medullary substance (pyrenin) of true nuclei is coloured by acid tar-colours and other plasma stains, while the chromatin has a special affinity for basic dyes. *Cf.* p. 337.

³ For very full review of the literature of the nucleoli see Montgomery ('98, 2).

⁴ *Cf.* p. 67.

formation of chromosomes during division, and hence may play an active rôle in the nuclear activity. Strasburger ('95) likewise believes them to contain a store of active material which, however, has no direct relation to the chromosomes but consists of "kinoplasm"

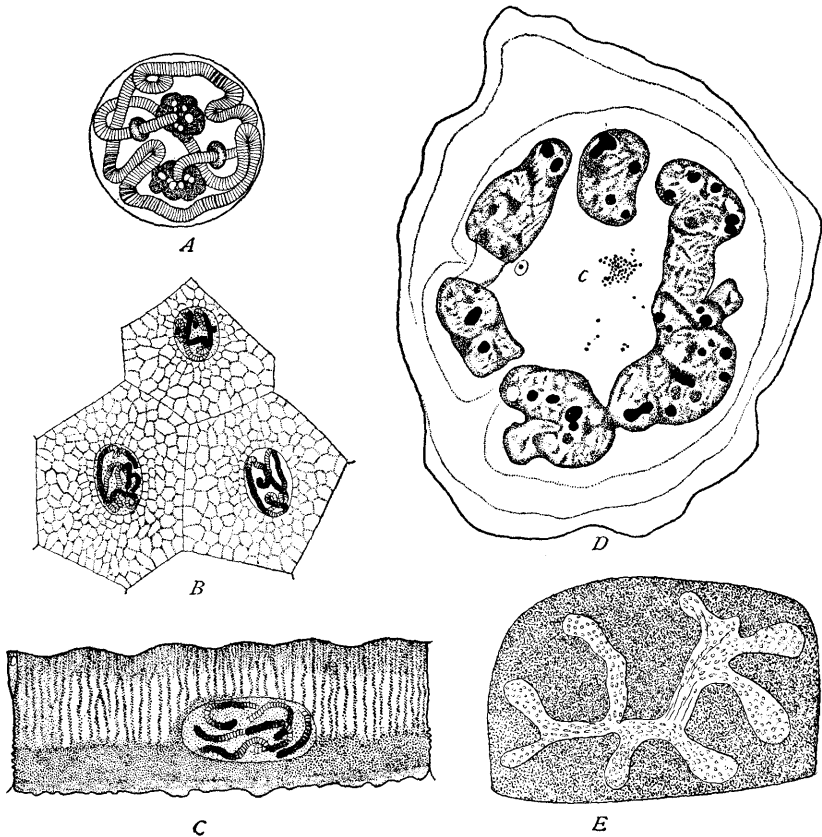


Fig. 14.—Special forms of nuclei.

A. Permanent spireme-nucleus, salivary gland of *Chironomus* larva. Chromatin in a single thread, composed of chromatin-discs (chromomeres), terminating at each end in a true nucleolus or plasmosome. [BALBIANI.]

B. Permanent spireme-nuclei, intestinal epithelium of dipterous larva *Phychoptera*. [VAN GEHUCHTEN.] *C.* The same, side view.

D. Polymorphic ring-nucleus, giant-cell of bone-marrow of the rabbit; *c.* a group of centrosomes or centrioles. [HEIDENHAIN.]

E. Branching nucleus, spinning gland of butterfly-larva (*Pieris*). [KORSCHULT.]

(p. 322), from which arises the achromatic part of the division-figure (p. 82). On the other hand, Häcker ('95, '99) and other observers regard the nucleolar material as a passive by-product of the chromatin-activity destined to be absorbed by the active sub-

stances. This is supported by the fact that in some forms of mitosis the nucleolus is at the time of division actually cast out of the nucleus into the cytoplasm, where it degenerates without further apparent function. This seems to constitute decisive evidence in support of Häcker's view as applied to certain cases; but without further evidence it must remain doubtful whether it applies to all.¹

d. The *ground-substance*, *nuclear sap*, or *karyolymph*, a clear substance occupying the interspaces of the network and left unstained by most of the dyes that colour the chromatin, the linin, or the plasmosomes. By most observers the ground-substance is regarded as a liquid filling a more or less completely continuous space traversed by the nuclear network. By Bütschli, however, and some of his followers the nucleus is regarded as an alveolar structure, the walls of which represent the "network," while the ground-substance corresponds to the alveolar material. Nearly related with this is the view of Reinke ('94) that the ground-substance consists of large pale granules of "lanthanin" or "œdematin."

The configuration of the chromatic network varies greatly in different cases. It is sometimes of a very loose and open character, as in many epithelial cells (Fig. 1); sometimes extremely coarse and irregular, as in leucocytes (Fig. 49); sometimes so compact as to appear nearly or quite homogeneous, as in the nuclei of spermatozoa and in many Protozoa. In some cases the chromatin does not form a network, but appears in the form of a thread closely similar to the spireme-stage of dividing nuclei (*cf.* p. 65). The most striking case of this kind occurs in the salivary glands of dipterous larvæ (*Chironomus*), where, as described by Balbiani, the chromatin has the form of a single convoluted thread, composed of transverse discs and terminating at each end in a large nucleolus (Fig. 14, *A*). Somewhat similar nuclei (Fig. 14, *B*) occur in various epithelial cells of other insects (Van Gehuchten, Gilson), and also in the young ovarian eggs of certain animals (*cf.* p. 273). In certain gland-cells of the marine isopod *Anilocra* it is arranged in regular rosettes (Vom Rath). Rabl, followed by Van Gehuchten, Heidenhain, and others, has endeavoured to show that the nuclear network shows a distinct polarity, the nucleus having a "pole" toward which the principal chromatin-threads converge, and near which the centrosome lies.² In many nuclei, however, no trace of such polarity can be discerned.

The network may undergo great changes both in physical configuration and in staining capacity at different periods in the life of the same cell, and the actual amount of chromatin fluctuates, sometimes to an enormous extent. Embryonic cells are in general

¹ *Cf.* pp. 126-130.

² *Cf.* the polarity of the cell, p. 55.

characterized by the large size of the nucleus; and Zacharias has shown in the case of plants that the nuclei of meristem and other embryonic tissues are not only relatively large, but contain a larger percentage of chromatin than in later stages. The relation of these changes to the physiological activity of the nucleus is still imperfectly understood.¹

2. *Finer Structure of the Nucleus*

A considerable number of observers have raised the question whether the nuclear structures may not be regarded as aggregates of more elementary morphological bodies, though there is still no general agreement regarding their nature and relationships. The most definite evidence in this direction relates to the chromatic network. In the stages preparatory to division this network resolves itself into a definite number of rod-shaped bodies known as *chromosomes* (Fig. 21), which split lengthwise as the cell divides. These bodies arise as aggregations of minute rounded bodies or *microsomes* to which various names have been given (*chromomeres*, Fol; *ids*, Weismann). They are as a rule most clearly visible and most regularly arranged during cell-division, when the chromatin is arranged in a thread (*spireme*), or in separate *chromosomes* (Figs. 8, D, 53, B); but in many cases they are distinctly visible in the reticulum of the "resting" nucleus (Fig. 54). It is, however, an open question whether the chromatin-granules of the reticulum are individually identical with those forming the chromosomes or the spireme-thread. The larger masses of the reticu-

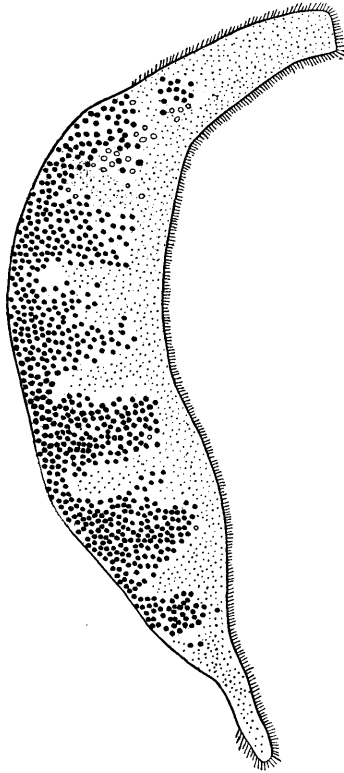


Fig. 15.—An infusorian, *Trachelocerca*, with diffused nucleus consisting of scattered chromatin-granules. [GRUBER.]

¹ Both chromatin-granules and nucleoli have been seen in a considerable number of living cells (Fig. 9). Favourable objects for this purpose are according to Korschelt ('96) the silk-glands of caterpillars, where the whole nucleus may be seen to be filled with fine granules ("microsomes"), among which are scattered many larger granules ("macrosomes"). The later studies of Meves ('97, 1) make it probable that the latter are true nucleoli and the former chromatin-granules. Korschelt, however, regards the "macrosomes" as composed of chromatin and the "microsomes" as representing the so-called "achromatic substance."

lum undoubtedly represent aggregations of such granules, but whether the latter completely fuse or remain always distinct is unknown. Even the chromosomes at certain stages appear perfectly homogeneous, and the same is sometimes true of the entire nucleus, as in the spermatozoön. It is nevertheless possible that the chromatin-granules have a persistent identity and are to be regarded as morphological units of which the chromatin is built up.¹

Heidenhain ('93, '94), whose views have been accepted by Reinke, Waldeyer, and others, has shown that the "achromatic" nuclear network is likewise composed of granules, which he distinguishes as *lanthanin-* or *oxychromatin-*granules from the *basichromatin-*granules of the chromatic network. Like the latter, the oxychromatin-granules are suspended in a non-staining clear substance, for which he reserves the term *linin*. Both forms of granules occur in the chromatic network, while the achromatic network contains only oxychromatin. They are sharply differentiated by dyes, the basichromatin being coloured by the basic tar-colours (methyl-green, safranin, etc.) and other true "nuclear stains"; while the oxychromatin-granules, like many cytoplasmic structures, and like the substance of true nucleoli (pyrenin), are coloured by acid tar-colours (rubin, eosin, etc.) and other "plasma stains." This distinction, as will appear in Chapter VII., is possibly one of great physiological significance.

Still other forms of granules have been distinguished in the nucleus by Reinke ('94) and Schloter ('94). Of these the most important are the "œdematin-granules," which according to the first of these authors form the principal mass of the ground-substance or "nuclear sap" of Hertwig and other authors. These granules are identified by both observers with the "cyanophilous granules," which Altmann regarded as the essential elements of the nucleus. It is at present impossible to give a consistent interpretation of the morphological value and physiological relations of these various forms of granules. The most that can be said is that the basichromatin-granules are probably normal structures; that they play a principal rôle in the life of the nucleus; that the oxychromatin-granules are nearly related to them; and that not improbably the one form may be transformed into the other in the manner suggested in Chapter VII.

The nuclear membrane is not yet thoroughly understood, and much discussion has been devoted to the question of its origin and structure. The most probable view is that long since advocated by Klein ('78) and Van Beneden ('83) that the membrane arises as a condensation of the general protoplasmic substance, and is part of the same structure as the linin-network and the cytoplasmic meshwork. Like these, it is in some cases "achromatic," but in other cases

¹ Cf. Chapter VI.

it shows the same staining reactions as chromatin, or may be double, consisting of an outer achromatic and an inner chromatic layer. According to Reinke, it consists of oxychromatin-granules like those of the linin-network.

Interesting questions are raised by a comparison of these facts with the conditions observed in some of the lowest organisms, such as the flagellates and lower rhizopods among animals and the

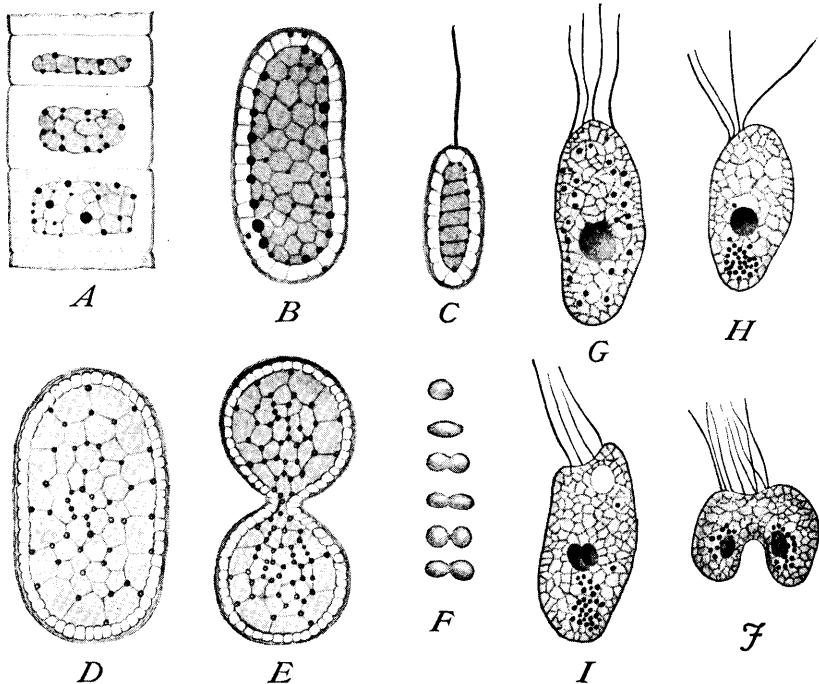


Fig. 16. — Forms of Cyanophyceæ, Bacteria, and Flagellates showing the so-called scattered or distributed nuclei. [A-C. BÜTSCHLI; D-F. SCHEWIAKOFF; G-J. CALKINS.]

A. *Oscillaria*. B. *Chromatium*. C. *Bacterium lineola*. D. *Achromatium*. E. The same in division. F. Fission of the granules. G. *Tetramitus*, with central sphere and scattered granules. H. Aggregation of the granules. I. Division of the sphere. J. Fission of the cell.

Cyanophyceæ and Bacteria among plants. In many of these forms (Fig. 16) no distinct nucleus can be demonstrated, the cell consisting of a mass of protoplasm in which are scattered numerous deeply staining granules. Many of these granules stain intensely with hæmatoxylin and other "nuclear" dyes; like chromatin, they resist the action of peptic digestion, and in at least one case (the bacterium-like *Achromatium*, according to Schewiakoff, '93) they have the power of division like the chromatin-granules of higher forms. For these