reasons most observers (Bütschli, Gruber, Schewiakoff, Nadson, etc.) regard them as true chromatin-granules which represent a scattered or distributed nucleus not differentiated as a definite morphological body. If this identification is correct, such forms probably give us the most primitive condition of the nuclear substance, which only in higher forms is collected into a distinct mass enclosed by a membrane; and the scattered granules are comparable to those forming the chromatin-reticulum and chromosomes in the higher types. The identification is, however, difficult, owing to the impossibility of actual chemical analysis; and Fischer ('97) has shown in the case of the Bacteria and Cyanophyceæ that we cannot safely trust either the staining reactions or the digestion test, since the former are variable, while the latter does not differentiate the granules from some other cytoplasmic constituents.[1] It is, however, certain that the staining power of chromatin in the higher forms varies with different conditions, and furthermore there is reason to believe that these granules may divide by fission. Besides these observations of Schewiakoff on *Achromatium* (see above), we have those of several authors on Infusoria, and more recently those of Calkins on flagellates, both pointing to the same conclusion. Balbiani, Gruber, Maupas, and others have described various Infusoria (*Urostyla, Trachelocerca, Holosticha, Uroleptus*), as well as some rhizopods (*Pelomyxa*), in which the body contains very numerous minute chromatin-granules of "nuclei" (Fig. 15), which Gruber ('87) showed to multiply by division. Balbiani ('61) long since showed that in *Urostyla* these bodies become concentrated toward the centre of the cell at the time of division, and Bergh ('89) demonstrated that they then fuse to form a macronucleus of the usual type, that elongates, assumes a fibrillar structure, and divides by fission. After division of the cell-body the macronucleus again fragments into minute scattered granules, which in this case certainly represent a distributed nucleus. In the flagellate *Tetramitus* Calkins ('98, 1) likewise finds numerous scattered chromatin-granules, which at the time of division become aggregated into a single dividing mass (p. 92); while in other forms the mass (nucleus) persists as such without (*Trachelomonas, Lagenella, Chilomonas*) or with (*Euglena, Synura*) a surrounding membrane.

Taken together, the foregoing facts, while certainly not conclusive, give good ground for the provisional acceptance of Bütschli's conception of the distributed nucleus, and indicate that nucleus and cytoplasm have arisen through the differentiation of a common protoplasmic mass. The nucleus, as Carnoy has well said,[2] is like a

[1] It should be remembered that we have no unerring "chromatin-stain." *Cf.* p. 335.
[2] '84, p. 251.

house built to contain the chromatic elements, and its achromatic elements (linin, etc.) were originally a part of the general cell-substance. Moreover, as Carnoy points out, the house periodically goes to pieces in the process of mitotic division, the chromatin afterward "building for itself a new dwelling."

3. *Chemistry of the Nucleus*

The chemical nature of the various nuclear elements will be considered in Chapter VII., and a brief statement will here suffice. The following classification of the nuclear substances, proposed by Schwarz in 1887, has been widely accepted, though open to criticism on various grounds.

1. *Chromatin.* The chromatic substance (basichromatin) of the network and of those nucleoli known as net-knots or karyosomes.
2. *Linin.* The achromatic network and the spindle fibres arising from it.
3. *Paralinin.* The ground-substance.
4. *Pyrenin* or *Parachromatin.* The inner mass of true nucleoli.
5. *Amphipyrenin.* The substance of the nuclear membrane.

Chromatin is probably identical with *nuclein* (p. 332), which is a compound of *nucleinic acid* (a complex organic acid, rich in phosphorus) and albuminous substances. In certain cases (nuclei of spermatozoa, and probably also the chromosomes at the time of mitosis) the percentage of nucleinic acid is very large (p. 333). The *linin* is supposed to be composed of "plastin"—a substance identified by Reinke and Rodewald ('81) and probably a nucleo-albumin or a related substance. "Pyrenin" is related to plastin; and Carnoy and Zacharias apply the latter word to the nucleolar substance, while O. Hertwig calls it paranuclein. "Amphipyrenin" has no very definite meaning; for the nuclear membrane sometimes appears to be of the same nature as the linin, while in other cases it stains like chromatin. For critique of the staining reactions see page 334.

D. The Cytoplasm

It has long been recognized that in the unicellular forms the cytoplasmic substance is often differentiated into two well-marked zones: viz. an inner medullary substance or *endoplasm* in which the nucleus lies, and an outer cortical substance or *exoplasm* (ectoplasm) from which the more differentiated products of the cytoplasm, such as cilia, trichocysts, and membrane, take their origin. Indications of a similar differentiation are often shown in the tissue-cells of higher plants and animals,[1] though it may take the form of a polar differentiation of the cell-substance, or may be wholly wanting. Whether the distinction is of fundamental importance remains to be seen; but it appears to be a general rule that the nucleus is surrounded by

[1] This fact was first pointed out in the tissue-cells of animals by Kupffer ('75), and its importance has since been urged by Waldeyer, Reinke, and others. The cortical layer is by Kupffer termed *paraplasm*, by Pfeffer *hyaloplasm*, by Pringsheim the *Hautschicht*. The medullary zone is termed by Kupffer *protoplasm, sensu strictu;* by Strasburger, *Körnerplasma;* by Nägeli, *polioplasm*.

protoplasm of relatively slight differentiation, while the more highly differentiated products of cell-activity are laid down in the more peripheral region of the cell, either in the cortical zone or at one end of the cell.[1] This fact is full of meaning, not only because it is an expression of the adaptation of the cell to its external environment, but also because of its bearing on the problems of nutrition.[2] For if, as we shall see reason to conclude in Chapter VII., the nucleus be immediately concerned with synthetic metabolism, we should expect to find the immediate and less differentiated products of its action in its neighbourhood, and on the whole the facts bear out this view.

The most pressing of all questions regarding the cytoplasmic structure is whether the sponge-like, fibrillar, or alveolar appearance is a normal condition existing during life. There are many cases, especially among plant-cells, in which the most careful examination has thus far failed to reveal the presence of a reticulum, the cytoplasm appearing, even under the highest powers and after the most careful treatment, merely as a finely granular substance. This and the additional fact that the cytoplasm may show active streaming and flowing movements, has led some authors, especially among botanists, to regard the reticulum as non-essential and as being, when present, either a secondary differentiation of the cytoplasmic substance specially developed for the performance of particular functions or a mere coagulation-product due to the action of fixatives. It has been shown that structureless proteids, such as egg-albumin and other substances, when coagulated by various reagents, often show a structure closely similar to that of protoplasm as observed in microscopical sections. Flemming ('82) long since called attention to the danger of mistaking such coagulation-products for normal structures as seen in fixed and stained material, and his warning has been emphasized by the later experiments of Berthold ('86), Schwarz ('87), and especially of Bütschli ('92, '98), Fischer ('94, '95, '99), and Hardy ('99). Bütschli's extensive studies of such coagulation-phenomena show that coagulated or dried albumin, starch-solutions, gelatin, gum arabic, and other substances show a fine alveolar structure scarcely to be distinguished from that which he believes to be the normal and typical structure of protoplasm. Fischer and Hardy have likewise made extensive tests of solutions of albumin, peptone, and related substances, in various degrees of concentration, fixed and stained by a great variety of the reagents ordinarily used for the demonstration of cell-structures. The result was to produce a marvellously close *simulacrum* of the appearances observed in the cell, alveolar, reticulated, and fibrillar structures being produced that often contain granules closely similar in every respect to those described as

[1] *Cf.* p. 55.

[2] See Kupffer ('90), pp. 473–476.

"microsomes" in sections of actual protoplasm. After impregnating pith with peptone-solution and then hardening, sectioning, and staining, the cells may even contain a central nucleus-like mass suspended in a network of anastomosing threads that extend in every direction outward to the walls, and give a remarkable likeness of a normal cell.

These facts show how cautious we must be in judging the appearances seen in preserved cells, and justify in some measure the hesita-

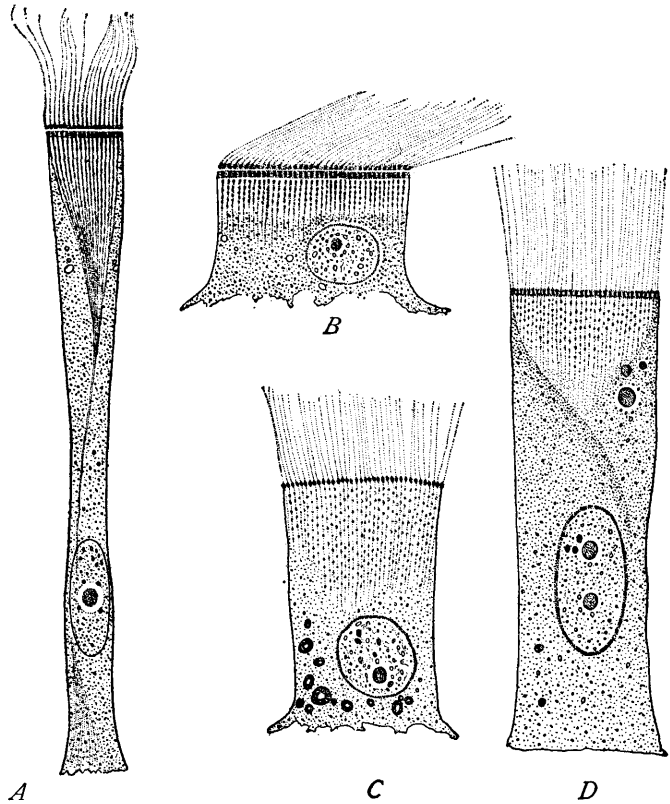

Fig. 17. — Ciliated cells, showing cytoplasmic fibrillæ terminating in a zone of peripheral microsomes to which the cilia are attached. [ENGELMANN.]

A. From intestinal epithelium of *Anodonta*. *B.* From gill of *Anodonta*. *C.D.* Intestinal epithelium of *Cyclas*.

tion with which many existing accounts of cell-structure are received. The evidence is nevertheless overwhelmingly strong, as I believe, that not only the fibrillar and alveolar formations, but also the microsomes observed in cell-structures, are in part normal structures. This evidence is derived partly from a study of the living cell, partly from the regular and characteristic arrangement of the thread-work and

microsomes in certain cases. In many Protozoa, for example, a fine alveolar structure may be seen in the living protoplasm; and Flemming as well as many later observers has clearly seen fibrillar structures in the living cells of cartilage, epithelium connective-tissue, and some other animal cells (Fig. 9). Mikosch, also, has recently described *granular* threads in living plant-cells.

Almost equally conclusive is the beautifully regular arrangement of the fibrillæ in ciliated cells (Fig. 17, Engelmann), in muscle-fibres and nerve-fibres, and especially in the mitotic figure of dividing cells

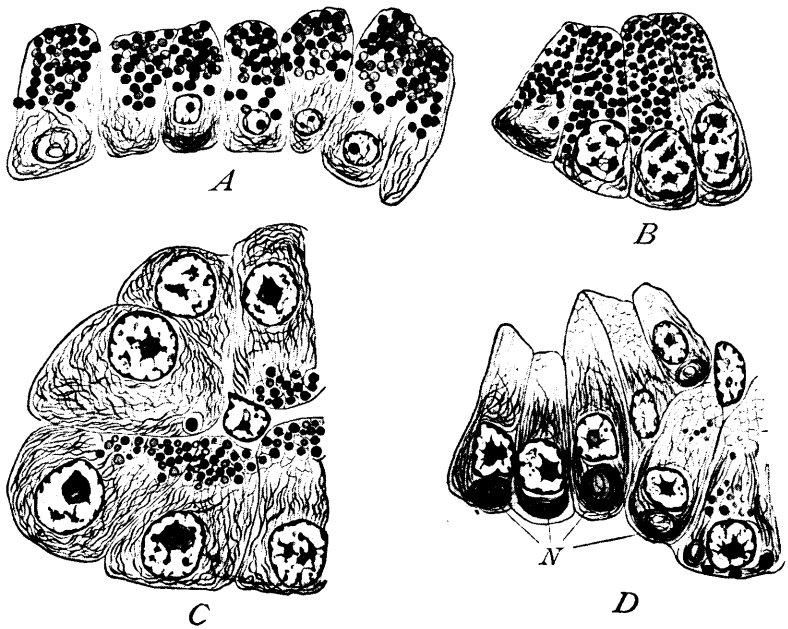

Fig. 18. — Cells of the pancreas in Amphibia. [MATHEWS.]

A-C. *Necturus;* D. *Rana.* A and B represent two stages of the "loaded" cell, showing zymogen-granules in the peripheral and fibrillar structures in the basal part of the cell. C shows cells after discharge of the granule-material and invasion of the entire cell by fibrillæ. In D portions of the fibrillar material are coiled to form the mitosome ("paranucleus" or "Nebenkern").

(Figs. 21, 31), where they are likewise more or less clearly visible in life. A very convincing case is afforded by the pancreas-cells of *Necturus*, which Mathews has carefully studied in my laboratory. Here the thread-work consists of long, conspicuous, definite fibrillæ, some of which may under certain conditions be wound up more or less closely in a spiral mass to form the so-called *Nebenkern*. In all these cases it is impossible to regard the thread-work as an accidental coagulation-product. In the case of echinoderm eggs, I have made ('99) a critical comparison of the living structure, as seen under powers

of a thousand diameters and upwards, with the same object stained in thin sections after fixation by picro-acetic, sublimate-acetic, and

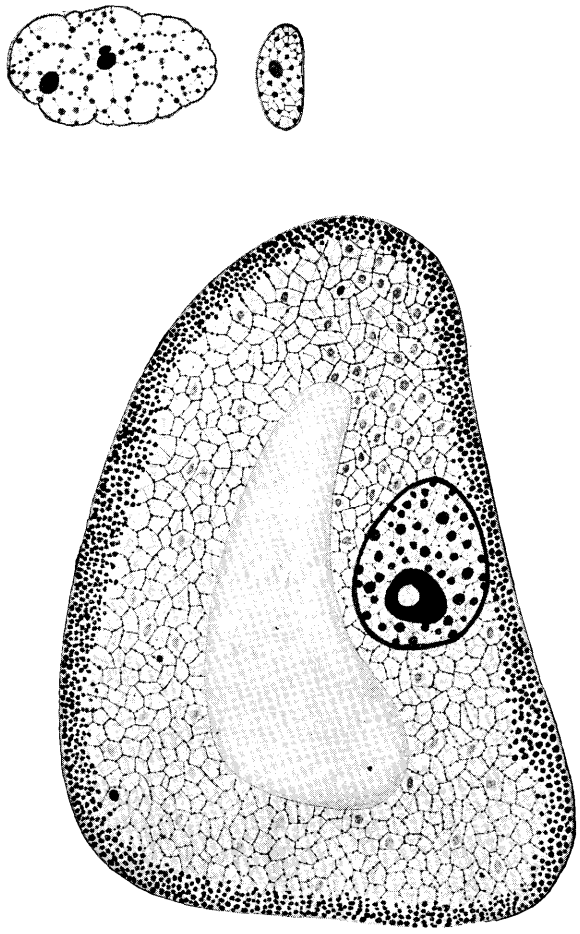

Fig. 19. — Section through a nephridial cell of the leech, *Clepsine* (drawn by Arnold Graf from one of his own preparations).

The centre of the cell is occupied by a large vacuole, filled with a watery liquid. The cytoplasm forms a very regular and distinct reticulum with scattered microsomes which become very large in the peripheral zone. The larger pale bodies, lying in the ground-substance, are excretory granules (*i.e.* metaplasm). The nucleus, at the right, is surrounded by a thick chromatic membrane, is traversed by a very distinct linin-network, contains numerous scattered chromatin-granules, and a single large nucleolus within which is a vacuole. Above are two isolated nuclei showing nucleoli and chromatin-granules suspended in the linin-threads.

other reagents. The comparison leaves no doubt that the normal structures are in this case very perfectly preserved, though the sections give at first sight an appearance somewhat different from that

of the living object, owing to differences of staining capacity. In these eggs the microsomes, thickly scattered through the alveolar walls, stain deeply (Figs. 11, 12), while the alveolar spheres hardly stain at all. When, therefore, the stained sections are cleared in balsam, the contours of the alveolar spheres almost disappear, and the eye is caught by the walls, which give at first sight quite the appearance of a granular reticulum, as it has been in fact described by many observers. Careful study of the sections shows, however, that *the form and arrangement of all the elements is almost identically the same as in life.*

This result shows that careful treatment by reagents in some cases at least gives a very faithful picture of the normal structure; and while it should never be forgotten that in sections we are viewing coagulated material, much of which is liquid or semi-liquid in life, we should not adopt too pessimistic a view of the results based on fixed material, as I think some of the experimenters referred to above have done. Wherever possible, the structures observed in sections should be compared with those in the living material. When this is impracticable we must rely on indirect evidence; but this is in many cases hardly less convincing than the direct.

It is a very interesting and important question whether living protoplasm that appears to the eye to be homogeneous does not really possess a structure that is invisible, owing to the extreme tenuity of the fibrillæ or alveolar walls (as was long since suggested by Heitzmann and Bütschli),[1] or to uniformity of refractive index in the structural elements. It is highly probable that such is often the case; indeed, Bütschli has shown that such "homogeneous" protoplasm in Protozoa may show a typical alveolar structure after fixation and staining. This explanation will not, however, apply to the young echinoderm eggs (already referred to at p. 28), where the genesis of the alveolar structure may be followed step by step in the living cell. The protoplasm here appears at first almost like glass, showing at most a sparse and fine granulation; but after fixing and staining it appears as a mass of fine, closely crowded granules. This may indicate the existence of an extremely fine alveolar structure in life; but on the whole I believe that these granules are for the most part coagulation-products, since they cannot be demonstrated by staining *intra vitam*, and they very closely resemble the coagulation-granules found in structureless proteids like egg-albumin after treatment by the same reagents. In common with many other investigators, therefore, I believe that protoplasm may in fact be homogeneous *down to the present limits of microscopical vision.*

One of the must beautiful forms of cyto-reticulum with which I

[1] *Cf.* Bütschli, '92, 2, p. 169.

am acquainted has been described by Bolsius and Graf in the nephridial cells of leeches as shown in Fig. 19 (from a preparation by Dr. Arnold Graf). The meshwork is here of great distinctness and regularity, and scattered microsomes are found along its threads. It

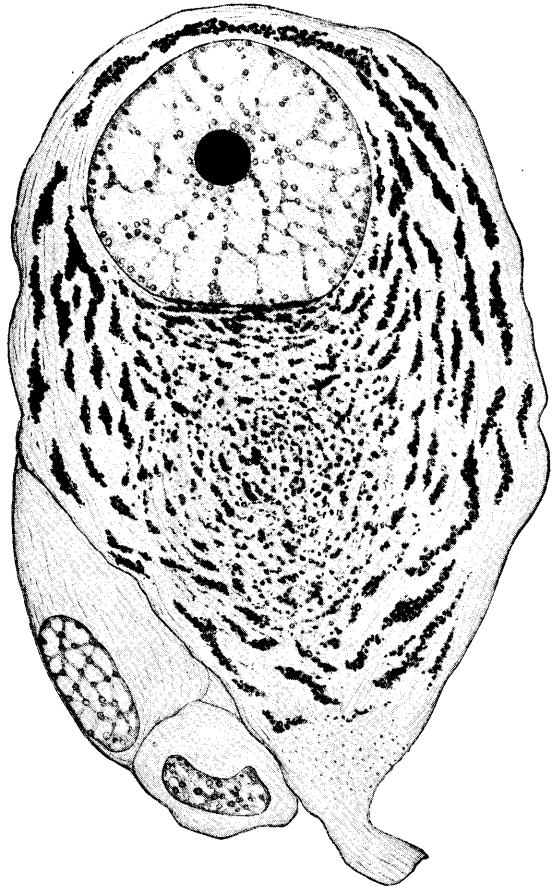

Fig. 20. — Spinal ganglion-cell of the frog. [LENHOSSÉK.]

The nucleus contains a single intensely chromatic nucleolus, and a paler linin-network with rounded chromatin-granules. The cytoplasmic fibrillæ are faintly shown passing out into the nerve-process below. (They are figured as far more distinct by Flemming.) The dark cytoplasmic masses are the deeply staining "chromophilic granules" (Nissl) of unknown function. (The centrosome, which lies near the centre of the cell, is shown in Fig. 8, *C*.) At the left, two connective tissue-cells.

appears with equal clearness, though in a somewhat different form, in many eggs, where the meshes are rounded and often contain food-matters or deutoplasm in the inter-spaces (Figs. 59, 60). In cartilage-cells and connective tissue-cells, where the threads can be plainly seen

in life, the network is loose and open, and appears to consist of more or less completely separate threads (Fig. 9). In the cells of columnar epithelium, the threads in the peripheral part of the cell often assume a more or less parallel course, passing outwards from the central region, and giving the outer zone of the cell a striated appearance. This is very conspicuously shown in ciliated epithelium, the fibrillæ corresponding in number with the cilia as if continuous with their bases (Fig. 17).[1] In nerve-fibres the threads form closely set parallel fibrillæ which may be traced into the body of the nerve-cell; here, according to most authors, they break up into a network in which are suspended numerous deeply staining masses, the "chromophilic granules" of Nissl (Fig. 20).[2] In the contractile tissues the threads are in most cases very conspicuous and have a parallel course. This is clearly shown in smooth muscle-fibres and also, as Ballowitz has shown, in the tails of spermatozoa. This arrangement is most striking in striped muscle-fibres where the fibrillæ are extremely well marked. According to Retzius, Carnoy, Van Gehuchten, and others, the meshes have here a rectangular form, the principal fibrillæ having a longitudinal course and being connected at regular intervals by transverse threads; but the structure of the muscle-fibre is probably far more complicated than this account would lead one to suppose, and opinion is still divided as to whether the contractile substance is represented by the reticulum proper or by the ground-substance.

Nowhere, perhaps, is a fibrillar structure shown with such beauty as in dividing cells, where (Figs. 21, 31) the fibrillæ group themselves in two radiating systems or *asters*, which are in some manner the immediate agents of cell-division. Similar radiating systems of fibres occur in amœboid cells, such as leucocytes (Fig. 49) and pigment-cells (Fig. 50), where they probably form a contractile system by means of which the movements of the cell are performed.

The views of Bütschli and his followers, which have been touched on at p. 25, differ considerably from the foregoing, the fibrillæ being regarded as the optical sections of thin plates or lamellæ which form the walls of closed chambers filled by a more liquid substance. Bütschli, followed by Reinke, Eismond, Erlanger, and others, interprets in the same sense the astral systems of dividing cells which are regarded as a radial configuration of the lamellæ about a central point (Fig. 10, *B*). Strong evidence against this view is, I believe,

[1] The structure of the ciliated cell, as described by Engelmann, may be beautifully demonstrated in the funnel-cells of the nephridia and sperm-ducts of the earthworm.

[2] The remarkable researches of Apathy ('97) on the nerve-cells of leeches have revealed the existence within the nerve-cell of networks far more complex and definite than was formerly supposed, and showing definite relations to incoming and outgoing fibrillæ within the substance of the nerve-fibres.

afforded by the appearance of the spindle and asters in cross-section. In the early stages of the egg of *Nereis*, for example, the astral rays are coarse anastomosing fibres that stain intensely and are therefore very favourable for observation (Fig. 60). That they are actual fibres is, I think, proved by sagittal sections of the asters in which the rays are cut at various angles. The cut ends of the branching rays appear in the clearest manner, not as plates but as distinct dots, from which in oblique sections the ray may be traced inwards toward the centrosphere. Drüner, too, figures the spindle in cross-section as consisting of rounded dots, like the end of a bundle of wires, though these are connected by cross-branches (Fig. 28, *F*). Again, the crossing of

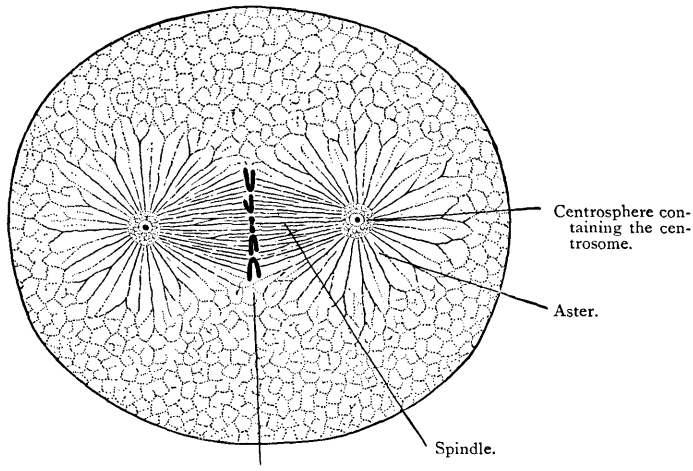

Fig. 21. — Diagram of the dividing cell, showing the mitotic figure and its relation to the cytoplasmic meshwork.

the rays proceeding from the asters (Fig. 128), and their behaviour in certain phases of cell-division, is difficult to explain under any other than the fibrillar theory.

We must admit, however, that the meshwork varies greatly in different cells and even in different physiological phases of the same cell; and that it is impossible at present to bring it under any rule of universal application. It is possible, nay probable, that in one and the same cell a portion of the meshwork may form a true alveolar structure such as is described by Bütschli, while other portions may, at the same time, be differentiated into actual fibres. If this be true the fibrillar or alveolar structure is a matter of secondary moment, and the essential features of protoplasmic organization must be sought in a more subtle underlying structure.[1]

[1] See Chapter VI.

Space would not suffice for a comparative account of the endless modifications shown by the cytoplasmic substance in different forms of cells. Many of these arise through special differentiations of the active substance, the character of the structure thus being sometimes so highly modified, as in the striated muscle-fibre, that it is difficult to trace its exact relation to the more usual forms. More commonly the cytoplasm is modified through the formation of passive or metaplasmic substances which often completely transform the original appearance of the cell. The most frequent of such modifications arise through the deposit of liquid drops and "granules" (many of the latter, however, being no doubt liquid in life). When the liquid drops are of watery nature the cavities in which they lie are known as *vacuoles*, which are especially characteristic of the protoplasm of plant-cells and of Protozoa. These may enlarge or run together to form extensive cavities in the cell, the protoplasm becoming reduced to a peripheral layer, or to strands and networks traversing the spaces; while in some forms of unicellular glands the spaces may form branching canals traversing the protoplasm.

The vacuolization or meshlike appearance arising through the formation of larger vacuoles or the deposit of other metaplasmic material is not to be confounded with the primary protoplasmic structure. When, however, smaller vacuoles or metaplasmic granules are evenly distributed through the protoplasm, a "pseudo-alveolar" structure (Reinke) arises that can often hardly be distinguished from the "true" alveolar structure of Bütschli.[1] Comparative study shows that all gradations exist between the "false" and the "true" alveolar structures and that no logical ground of distinction between the two exists.[2] We thus reach ground for the conclusion that the coarser secondary alveolar or reticular formations are to be regarded as only an exaggeration of the primary structure, and that the alveolar material of Bütschli's structure belongs in the same general category with the passive or metaplasmic substance.[3]

E. The Centrosome

The centrosome[4] is usually an extremely minute body, or more commonly a pair of bodies, staining intensely with hæmatoxylin and

[1] In the latter the alveolar spheres are, according to Bütschli, not more than one or two microns in diameter.

[2] This has been demonstrated in the cells of plants by *Crato* ('96), and more recently by the writer ('99), in the case of echinoderm and other eggs.

[3] *Cf.* p. 29.

[4] The centrosome was apparently first seen and described by Flemming in 1875, in the egg of the fresh-water mussel *Anodonta*, and independently discovered by Van Beneden, in

some other reagents, and surrounded by a cytoplasmic radiating aster or by a rounded mass known as the *attraction-sphere* (Figs. 8, 49, etc.). As a rule it lies in the cytoplasm, not far from the nucleus, and usually opposite an indentation or bay in the latter; but in a few cases it lies inside the nucleus (Fig. 148). In epithelia the centrosomes (usually double) lie as a rule near the free end of the cell (Fig. 23).[1]

There is still much confusion regarding the relation of the centrosome to the surrounding structures, and this has involved a corresponding ambiguity in the terminology. We will therefore only consider it briefly at this point, deferring a more critical account to Chapter VI. In its simplest form it is a single minute granule, which may, however, become double or triple (leucocytes, connective tissue-cells, some epithelial cells) or even multiple, as in certain giant-cells (Fig. 14, *D*), and as also occurs in some forms of cell-division (Fig. 52). In some cases (Figs. 8, *C*, 120, 148) the "centrosome" is a larger body containing one or more central granules or "centrioles" (Boveri); but it is probable that in some of these cases the central granule is itself the true centrosome, and the surrounding body is part of the attraction-sphere. During the formation of the spermatozoön the centrosome undergoes some remarkable morphological changes (p. 171), and is closely involved in the formation of the contractile structures of the tail.

The nature and functions of the centrosome have formed the subject of some of the most persistent and searching investigations of recent cytology. Van Beneden, followed by Boveri and many later workers, regarded the centrosome as a distinct and persistent cell-organ, which like the nucleus was handed on by division from one cell-generation to another. Physiologically it was regarded as being the especial organ of cell-division, and in this sense as the "dynamic centre" of the cell. In Boveri's beautiful development of this

the following year, in dycyemids. The name is due to Boveri ('88, 2, p. 68). Van Beneden's and Boveri's independent identification of centrosome in *Ascaris* as a permanent cell-organ ('87) was quickly supported by numerous observations on other animals and on plants. In rapid succession the centrosome and attraction-sphere were found to be present in pigment-cells of fishes (Solger, '89, '90), in the spermatocytes of Amphibia (Hermann, '90), in the leucocytes, endothelial cells, connective tissue-cells, and lung-epithelium of salamanders (Flemming, '91), in various plant-cells (Guignard, '91), in the one-celled diatoms (Bütschli, '91), in the giant-cells and other cells of bone-marrow (Heidenhain, Van Bambeke, Van der Stricht, '91), in the flagellate *Noctiluca* (Ishikawa, '91), in the cells of marine algæ (Strasburger, '92), in cartilage-cells (Van der Stricht, '92), in cells of cancerous growths (epithelioma, Lustig and Galeotti, '92), in the young germ-cells as already described, in gland-cells (Vom Rath, '95), in nerve-cells (Lenhossék, '95), in smooth muscle-fibres (Lenhossék, '99), and in embryonic cells of many kinds (Heidenhain, '97). Many others have confirmed and extended this list. Guignard's identification of the centrosomes in higher plants is open to grave doubt (*cf.* p. 82).

[1] *Cf.* p. 57.

view it was regarded further as the especial fertilizing element in the spermatozoön, which, when introduced into the egg, endowed the latter with the power of division and development. Van Beneden's and Boveri's hypothesis, highly attractive on account of its simplicity and lucidity, is supported by many facts, and undoubtedly contains an element of truth; yet recent researches have cast grave doubt upon its generality, and necessitate a suspension of judgment upon the entire matter. Many of the most competent recent workers on the cytology of higher plants have been unable to find centrosomes, whether in the resting-cells, in the apparatus of cell-division, or during the process of fertilization, notwithstanding the fact that undoubted centrosomes occur in some of the lower plants. Among zoölogists, too, an increasing number of recent investigators, armed with the best technique, have maintained the total disappearance of the centrosome at the close of cell-division or during the process of fertilization, agreeing that in such cases the centrosome is subsequently formed *de novo*. Experimental researches, also, have given strong ground for the conclusion that cells placed under abnormal chemical conditions may form new centrosomes (p. 306). If these strongly supported results be well founded, Van Beneden's hypothesis must be abandoned in favour of the view that the centrosome is but a subordinate part of the general apparatus of mitosis, and one which may be entirely dispensed with. Thus regarded, the centrosome would lose somewhat of the significance first attributed to it, though still remaining a highly interesting object for further research.[1]

F. Other Organs

The cell-substance is often differentiated into other more or less definite structures, sometimes of a transitory character, sometimes showing a constancy and morphological persistency comparable with that of the nucleus and centrosome. From a general point of view the most interesting of these are the bodies known as *plastids* or *protoplasts* (Fig. 6), which, like the nucleus and centrosome, are capable of growth and division, and may thus be handed on from cell to cell. The most important of these are the *chromatophores* or *chromoplastids*, which are especially characteristic of plants, though they occur in some animals as well. These are definite bodies, varying greatly in form and size, which possess the power of growth and division, and have in some cases been traced back to minute colourless plastids or

[1] *Cf.* pp. 111, 304. Eisen ('97) asserts that in the blood of a salamander, *Batrachoseps*, the attraction-sphere ("archosome") containing the centrosomes may separate from the remainder of the cell (nucleated red corpuscles) to form an independent form of blood-corpuscle or "plasmocyte," which leads an active life in the blood.

leucoplastids in the embryonic cells. By enlargement and differentiation these give rise to the starch-builders (amyloplastids), to the chlorophyll-bodies (chloroplastids), and to other pigment-bodies (chromoplastids), all of which may retain the power of division. The embryonic leucoplastids are also believed to multiply by division and to arise by the division of plastids in the parental organism; but it remains an open question whether this is their only mode of origin, and the same is true of the more highly differentiated forms of plastids to which they may give rise.

The contractile or pulsating vacuoles that occur in most Protozoa and in the swarm-spores of many Algæ are also known in some cases to multiply by division; and the same is true, according to the researches of De Vries, Went, and others, of the non-pulsating vacuoles of plant-cells. These vacuoles have been shown to have, in many cases, distinct walls, and they are regarded by De Vries as a special form of plastid ("tonoplasts") analogous to the chromatophores and other plastids. It is, however, probable that this view is only applicable to certain forms of vacuoles.

The plastids possess in some cases a high degree of morphological independence, and may even live for a time after removal from the remaining cell-substance, as in the case of the "yellow cells" of Radiolaria. This has led to the view, advocated by Brandt and others, that the chlorophyll-bodies found in the cells of many Protozoa and a few Metazoa (*Hydra*, *Spongilla*, some planarians) are in reality distinct Algæ living symbiotically in the cell. This view is probably correct in some cases, *e.g.* in the Radiolaria; but it may be doubted whether it is of general application. In the plants the plastids are almost certainly to be regarded as differentiations of the protoplasmic substance.

The existence of cell-organs which have the power of independent assimilation, growth, and division is a fact of great theoretical interest in its bearing on the general problem of cell-organization; for it is one of the main reasons that have led De Vries, Wiesner, and many others to regard the entire cell as made up of elementary self-propagating units.

G. The Cell-membrane

The structure and origin of the cell-wall or membrane form a subject somewhat apart from our general purpose, since the wall belongs to the passive or metaplasmic products of protoplasm rather than to the living cell itself. We shall therefore treat it very briefly. Broadly speaking, animal cells are in general characterized by the slight development and relative unimportance of the cell-walls, while

the reverse is the case in plants, where the cell-walls play a very important *rôle*. In the latter the wall sometimes attains a great thickness, usually displays a distinct stratification, and often has a complex sculpture. Such massive walls very rarely occur in the case of animal tissues, though the intercellular matrix of cartilage and bone is to a certain extent analogous to them, and the thick and often highly sculptured envelopes of some kinds of eggs and of various Protozoa may be placed in the same category.

It is open to question whether any cells are entirely devoid of an enclosing envelope; for even in such "naked" cells as leucocytes, rhizopods, or membraneless eggs, the boundary of the cell is usually formed by a more resistant layer of protoplasm or "pellicle" (Bütschli) which may be so marked as to simulate a true membrane, as is the case, for example, in the red blood-corpuscles (Ranvier, Waldeyer, etc.). Such pellicles probably differ from true membranes only in degree; but it is still an open question both in animals and in plants, how far true membranes arise by direct transformation of the peripheral protoplasmic layer (the "Hautschicht" of botanists), and how far as a secretion-product of the protoplasm. In the case of animal cells, Leydig long since proposed [1] to distinguish between "cuticular" membranes, formed as secretions and usually occurring only on the free surfaces (as in epithelia), from "true membranes" arising by direct transformation of the peripheral protoplasm. Later researches, including those of Leydig himself, have thrown so much doubt on this distinction that most later writers have used the term *cuticular* in a purely topographical sense to denote membranes formed only on one (the free) side of the cell,[2] leaving open the question of origin. The formation and growth of the cell-wall have been far more thoroughly studied in plants than in animals, yet even here opinion is still divided. Most recent researches tend to sustain the early view of Nägeli that the cell-wall is in general a secretion-product, though there are some cases in which a direct transformation of protoplasm into membrane-stuff seems to occur.[3] In the division of plant-cells the daughter-cells are in almost all cases cut apart by a cell-plate which arises in the protoplasm of the mother-cell as a transverse series of thickenings of the spindle-fibres in the equatorial region (Fig. 34). This fact, long regarded by Strasburger and others as a proof of the direct origin of the membrane from the protoplasmic substance, is shown by Strasburger's latest work ('98) to be open to a quite different interpretation, the actual wall being formed by a splitting of the cell-plate into two layers between which the wall appears as a secretion-product. Almost all observers further are agreed that the formation of new membranes on naked masses of

[1] *Cf.* '85, p. 12. [2] *Cf.* O. Hertwig, '93. [3] *Cf.* Strasburger, '98.

protoplasm produced by plasmolysis are likewise secretion-products, and that the secondary thickening of plant-membranes is produced in the same way. These facts, together with the scanty available zoölogical data, indicate that the formation of membranes by secretion is the more usual and typical process.[1]

The chemical composition of the membrane or intercellular substance varies extremely. In plants the membrane consists of a basis of *cellulose*, a carbohydrate having the formula $C_6H_{10}O_5$; but this substance is very frequently impregnated with other substances, such as silica, lignin, and a great variety of others. In animals the intercellular substances show a still greater diversity. Many of them are nitrogenous bodies, such as keratin, chitin, elastin, gelatin, and the like; but inorganic deposits, such as silica and carbonate of lime, are common.

H. Polarity of the Cell

In a large number of cases the cell exhibits a definite polarity, its parts being symmetrically grouped with reference to an ideal *organic axis* passing from pole to pole. No definite criterion for the identification of the cell-axis has, however, yet been determined; for the general conception of cell-polarity has been developed in two different directions, one of which starts from purely morphological considerations, the other from physiological, and a parallelism between them has not thus far been fully made out.

On the one hand, Van Beneden ('83) conceived cell-polarity as a primary morphological attribute of the cell, the organic axis being identified as a line drawn through the centre of the nucleus and the centrosome (Fig. 22, *A*). With this view Rabl's theory ('85) of nuclear polarity harmonizes, for the chromosome-loops converge toward the centrosome, and the nuclear axis coincides with the cell-axis. Moreover, it identifies the polarity of the egg, which is so important a factor in development, with that of the tissue-cells; for the egg-centrosome almost invariably appears at or near one pole of the ovum.

Heidenhain ('94, '95) has recently developed this conception of polarity in a very elaborate manner, maintaining that all the structures of the cell have a definite relation to the primary axis, and that this relation is determined by conditions of tension in the astral rays

[1] Strasburger ('97, 3, '98) believes membrane-formation in general to be especially connected with the activity of the "kinoplasm," or filar plasm of which he considers the "Hautschicht," as well as the spindle-fibres, to be largely composed. In support of this may be mentioned, besides the mode of formation of the partition-walls in the division of plant-cells, Harper's ('97) very interesting observations on the formation of the ascospores in *Erysiphe* (Fig. 33), where the spore-membrane appears to arise directly from the astral rays.

focussed at the centrosome. On this basis he endeavours to explain the position and movements of the nucleus, the succession of division-planes, and many related phenomena.[1]

Hatschek ('88) and Rabl ('89, '92), on the other hand, have advanced a quite different hypothesis based on physiological considerations. By "cell-polarity" these authors mean, not a predetermined morphological arrangement of parts in the cell, but a polar differentiation of the cell-substance arising secondarily through adaptation of the cell to its environment in the tissues, and having no necessary relation to the polarity of Van Beneden (Fig. 22, *B*, *C*). This is

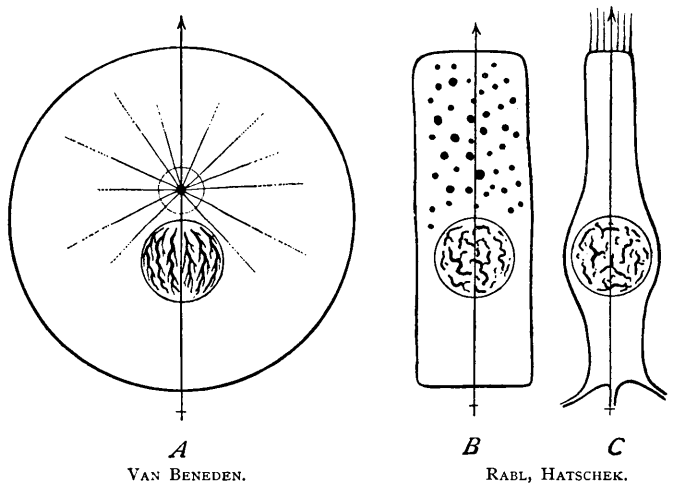

Fig. 22. — Diagrams of cell-polarity.

A. Morphological polarity of Van Beneden. Axis passing through nucleus and centrosome. Chromatin-threads converging toward the centrosome. *B.C.* Physiological polarity of Rabl and Hatschek, *B* in a gland-cell, *C* in a ciliated cell.

typically shown in epithelium, which, as Kölliker and Haeckel long since pointed out, is to be regarded, both ontogenetically and phylogenetically, as the most primitive form of tissue. The free and basal ends of the cells here differ widely in relation to the food-supply, and show a corresponding structural differentiation. In such cells the nucleus usually lies nearer the basal end, toward the source of food, while the differentiated products of cell-activity are formed either at the free end (cuticular structures, cilia, pigment, zymogen-granules), or at the basal end (muscle-fibres, nerve-fibres). In the non-epithelial tissues the polarity may be lost, though traces of it are often shown as a survival of the epithelial arrangement of the embryonic stages.

[1] *Cf.* p. 105.

But, although this conception of polarity has an entirely different point of departure from Van Beneden's, it leads, in some cases at least, to the same result; for the cell-axis, as thus determined, may coincide with the morphological axis as determined by the position of the centrosome. This is the case, for example, with both the spermatozoön and the ovum; for the morphological axis in both is also the physiological axis about which the cytoplasmic differentiations are grouped. Recent researches have further shown that the same is the case in many forms of epithelia, where the centrosomes lie in the outer end of the cell, often very near the surface.[1] (Fig. 23)

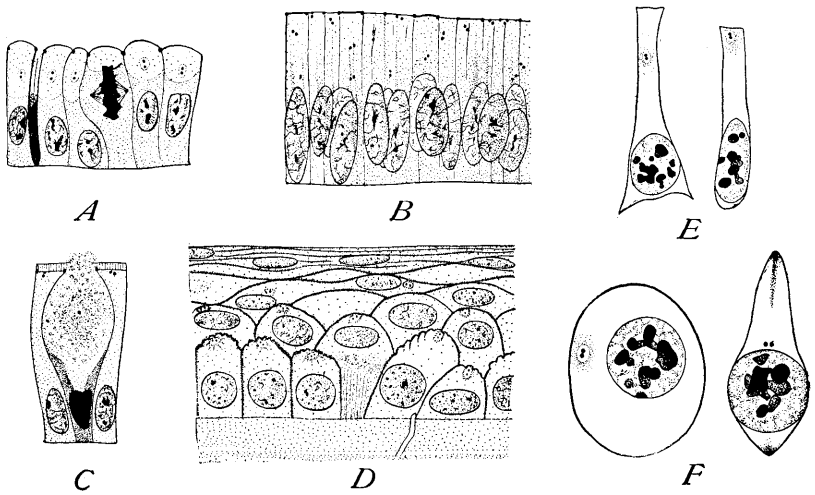

Fig. 23. — Centrosomes in epithelial and other cells. [*A*, *D*, ZIMMERMANN; *E*, HEIDENHAIN and COHN; *F*, HEIDENHAIN.]

A. From gastric glands of man; dead cell at the left. *B*. Uterine epithelium, man. *C*. From human duodenum; goblet-cell, with centrosome in the middle. *D*. Corneal epithelium of monkey. *E*. Epithelial cells from mesoblast-somites, embryo duck. *F*. Red blood-corpuscles from the duck-embryo. The centrosomes are double in nearly all cases.

and the recent observations of Henneguy ('98) and Lenhossék ('98,1) give reason to believe that the "basal bodies" to which the cilia of ciliated epithelium are attached may be the centrosomes.[2] These facts are of very high significance; for the position of the centrosome, and hence the direction of the axis, is here obviously related to the cell-environment, and it is difficult to avoid the conclusion that the latter must be the determining condition to which the intracellular relations conform. When applied to the germ-cells, this conclusion becomes of high interest; for the polarity of the egg is one of the

[1] Zimmermann, '98; Heidenhain and Cohn, '97.

[2] *Cf.* p. 356.

primary conditions of development, and we have here, as I believe, a clue to its determination.[1]

I. The Cell in Relation to the Multicellular Body

In analyzing the structure and functions of the individual cell we are accustomed, as a matter of convenience, to regard it as an independent elementary organism or organic unit. Actually, however, it is such an organism only in the case of the unicellular plants and animals and the germ-cells of the multicellular forms. When we consider the tissue-cells of the latter, we must take a somewhat different view. As far as structure and origin are concerned the tissue-cell is unquestionably of the same morphological value as the one-celled plant or animal; and *in this sense* the multicellular body is equivalent to a colony or aggregate of one-celled forms. Physiologically, however, the tissue-cell can only in a limited sense be regarded as an independent unit; for its autonomy is merged in a greater or less degree into the general life of the organism. From this point of view the tissue-cell must in fact be treated as merely a localized area of activity, provided it is true with the complete apparatus of cell-life, and even capable of independent action within certain limits, yet nevertheless a part and not a whole.

There is at present no biological question of greater moment than the means by which the individual cell-activities are coördinated, and the organic unity of the body maintained; for upon this question hangs not only the problem of the transmission of acquired characters, and the nature of development, but our conception of life itself. Schwann, the father of the cell-theory, very clearly perceived this; and after an admirably lucid discussion of the facts known to him ('39), drew the conclusion that the life of the organism is essentially a composite; that each cell has its independent life; and that "the whole organism subsists only by means of the reciprocal action of the single elementary parts."[2] This conclusion, afterward elaborated by Virchow and Haeckel to the theory of the "cell-state," took a very strong hold on the minds of biological investigators, and is even now widely accepted. It is, however, becoming more and more clearly apparent that this conception expresses only a part of the truth, and that Schwann went too far in denying the influence of the totality of the organism upon the local activities of the cells. It would of course be absurd to maintain that the whole can consist of more than the sum of its parts. Yet, as far as growth and development are con-

[1] *Cf.* pp. 384, 424. We should remember that the germ-cells are themselves epithelial products.

[2] *Untersuchungen*, Trans., p. 181.

cerned, it has now been clearly demonstrated that only in a limited sense can the cells be regarded as coöperating units. They are rather local centres of a formative power pervading the growing mass as a whole,[1] and the physiological autonomy of the individual cell falls into the background. It is true that the cells may acquire a high degree of physiological independence in the later stages of embryological development. The facts to be discussed in the eighth and ninth chapters will, however, show strong reason for the conclusion that this is a secondary result of development, through which the cells become, as it were, emancipated in a greater or less degree from the general control. Broadly viewed, therefore, the life of the multicellular organism is to be conceived as a whole; and the apparently composite character which it may exhibit is owing to a secondary distribution of its energies among local centres of action.[2]

In this light the structural relations of tissue-cells become a question of great interest; for we have here to seek the means by which the individual cell comes into relation with the totality of the organism, and by which the general equilibrium of the body is maintained. It must be confessed that the results of microscopical research have not thus far given a very certain answer to this question. Though the tissue-cells are often apparently separated from one another by a non-living intercellular substance, which may appear in the form of solid walls, it is by no means certain that their organic continuity is thus actually severed. Many cases are known in which division of the nucleus is not followed by division of the cell-body, so that multinuclear cells or *syncytia* are thus formed, consisting of a continuous mass of protoplasm through which the nuclei are scattered. Heitzmann long since contended ('73), though on insufficient evidence, that division is incomplete in nearly all forms of tissue, and that even when cell-walls are formed they are traversed by strands of protoplasm by means of which the cell-bodies remain in organic continuity. The whole body was thus conceived by him as a syncytium, the cells being no more than nodal points in a general reticulum, and the body forming a continuous protoplasmic mass.

This interesting view, long received with scepticism, has been to a considerable extent sustained by later researches, and though it still remains *sub judice*, has been definitely accepted in its entirety by some recent workers. The existence of protoplasmic cell-bridges between the sieve-tubes of plants has long been known; and Tangl's discovery, in 1879, of similar connections between the endosperm-cells was followed by the demonstration by Gardiner, Kienitz-Gerloff, A. Meyer, and many others, that in nearly all plant-tissues the cell-walls

[1] *Cf.* Chapters VIII., IX.

[2] For a fuller discussion see pp. 388 and 413.

are traversed by delicate intercellular bridges. Similar bridges have been conclusively demonstrated by Ranvier, Bizzozero, Retzius, Flemming, Pfitzner, and many later observers in nearly all forms of epithelium (Fig. 1); and they are asserted to occur in the smooth muscle-fibres, in cartilage-cells and connective tissue-cells, and in some nerve-cells. Dendy ('88), Paladino ('90), and Retzius ('89) have endeavoured to show, further, that the follicle-cells of the ovary are connected by protoplasmic bridges not only with one another, *but also with the ovum;* and similar protoplasmic bridges between germ-cells and somatic cells have been also demonstrated in a number of plants, *e.g.* by Goroschankin ('83) and Ikeno ('98) in the cycads and by A. Meyer ('96) in *Volvox*. On the strength of these observations some recent writers have not hesitated to accept the probability of Heitzmann's original conception, A. Meyer, for example, expressing the opinion that both the plant and the animal individual are continuous masses of protoplasm, in which the cytoplasmic substance forms a morphological unit, whether in the form of a single cell, a multinucleated cell, or a system of cells.[1] Captivating as this hypothesis is, its full acceptance at present would certainly be premature; and as far as adult animal tissues are concerned, it still remains undetermined how far the cells are in direct protoplasmic continuity. It is obvious that no such continuity exists in the case of the corpuscles of blood and lymph and the wandering leucocytes and pigment-cells. In case of the nervous system, which from an *a priori* point of view would seem to be above all others that in which protoplasmic continuity is to be expected, its occurrence and significance are still a subject of debate. When, however, we turn to the embryonic stages we find strong reason for the belief that a material continuity between cells here exists. This is certainly the case in the early stages of many arthropods, where the whole embryo is at first an unmistakable syncytium; and Adam Sedgwick has endeavoured to show that in *Peripatus* and even in the vertebrates the entire embryonic body, up to a late stage, is a continuous syncytium. I have pointed out ('93) that even in a total cleavage, such as that of *Amphioxus* or the echinoderms, the results of experiment on the early stages of cleavage are difficult to explain, save under the assumption that there must be a structural continuity from cell to cell that is broken by mechanical displacement of the blastomeres. This conclusion is supported by the recent work of Hammar ('96, '97), whose observations on sea-urchin eggs I can in the main confirm.

Among the most interesting observations in this direction are those of Mrs. Andrews ('97),[2] who asserts that during the cleavage

[1] '96, p. 212. *Cf.* also the views of Hanstein, Strasburger, Russow, and others there cited.

[2] *Cf.* also E. A. Andrews, '98, 1, '98, 2.

of the echinoderm-egg the blastomeres "spin" delicate protoplasmic filaments, by which direct protoplasmic continuity is established between them subsequent to each division. These observations, if correct, are of high importance; for if protoplasmic connections may be broken and re-formed at will, as it were, the adverse evidence of the blood-corpuscles and wandering cells loses much of its weight. Meyer ('96) adduces evidence that in *Volvox* the cell-bridges are formed anew after division; and Flemming has also shown that when leucocytes creep about among epithelial cells they rupture the protoplasmic bridges, which are then formed anew behind them.[1]

We are still almost wholly ignorant of the precise physiological meaning of the cell-bridges; but the facts indicate that they are not merely channels of nutrition, as some authors have maintained, but paths of subtler physiological impulse. Beside the facts determined by the isolation of blastomeres, referred to above, may be placed Townsend's recent remarkable experiments on plants, described at page 346. If correct, these experiments give clear evidence of the transference of physiological influences from cell to cell by means of protoplasmic bridges, showing that the nucleus of one cell may thus control the membrane-forming activity in an enucleated fragment of another cell. The field of research opened up by these and related researches seems one of the most promising in view; but until it has been more fully explored, judgment should be reserved regarding the whole question of the occurrence, origin, and physiological meaning of the protoplasmic cell-bridges.

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[1] '95, pp. 10–11; '97, p. 261.

[2] See also Introductory list, p. 14.

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