

CHAPTER IV

CLEAVAGE OF THE EGG

WHEN the egg comes to rest in its membranes after fertilization has taken place, it will be found that the egg-axis assumes an oblique position with respect to the vertical. The degree of obliquity may be different for the eggs of different species of frogs, but in some species it is carried so far that, when the egg is looked at from above, a crescent of the white hemisphere can be seen on one side of the egg. Roux has stated that the declination of the egg-axis takes place only *after* the entrance of the spermatozoön, and *toward* that side into which the spermatozoön has penetrated.¹ He was able to determine this by artificially fertilizing the egg at definite points. By means of a small pipette, water containing spermatozoa was brought in contact with the jelly somewhere near the upper hemisphere of an egg. Presumably the spermatozoön will then take the shortest path to the egg. Roux found that the egg after a time *generally* rotated on its axis toward the point at which the artificial fertilization was supposed to have taken place.

NORMAL CLEAVAGE

The first furrow appears on the egg about two and one half to three hours after fertilization, the time depending in part on the temperature of the water. A rather wide furrow appears in the flattened area near the black pole, and rapidly extends over the upper surface of the egg, and then moves more slowly over the lower or white surface. The sides of the furrow are often wrinkled, probably a mechanical result of the

¹ Roux believes the obliquity to be a usual phenomenon *after* fertilization for some species; in others the obliquity is only occasionally seen. Schultze finds it to be as much as forty-five degrees in *Rana fusca*.

infolding of the outer harder crust of the egg. These wrinkles are best seen in the upper hemisphere; subsequently they disappear. It will be found on cutting in two an egg in the process of cleavage that the furrow is also extending *through*

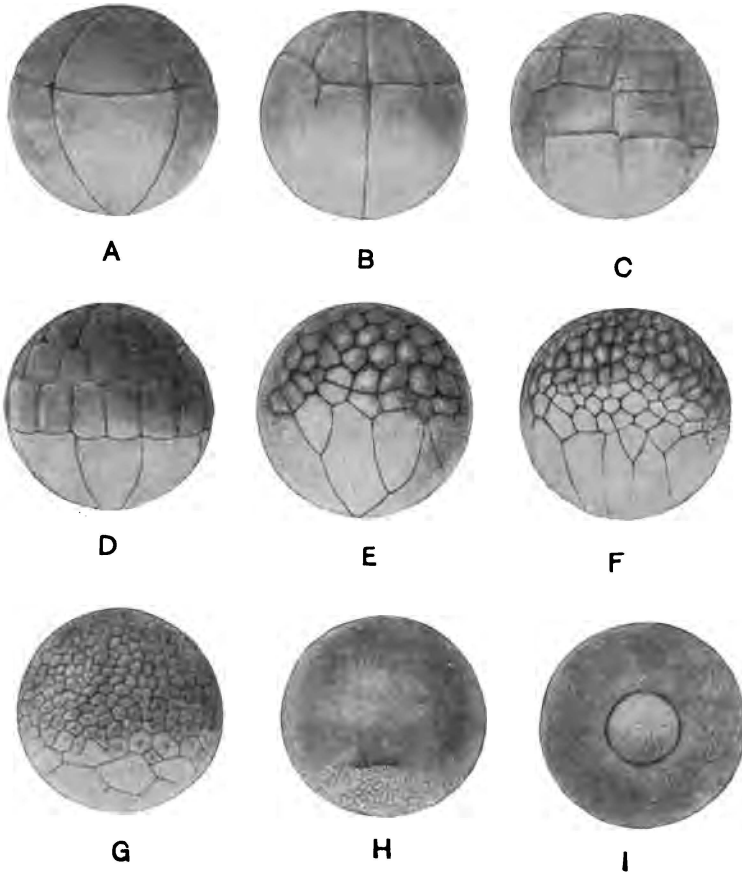


FIG. 12.—Segmentation of egg and formation of blastopore (H, I). A. Eight-cell stage. B. Beginning of sixteen-cell stage. C. Thirty-two-cell stage. D. Forty-eight-cell stage (unusually regular). E, F. Two sides of same egg in later cleavage. G. Still later cleavage. H. Dorsal lip of blastopore. I. Circular blastopore (with lower pole toward observer).

the protoplasm of the egg, *i.e.* dividing the contents into two parts. When the superficial furrow has encircled the egg, the substance also has been divided.

If a series of sections be made through the egg at different stages in the process of cleavage, we should see that prior to the division of each blastomere the nucleus had divided into two parts. This takes place by the ordinary process of indirect

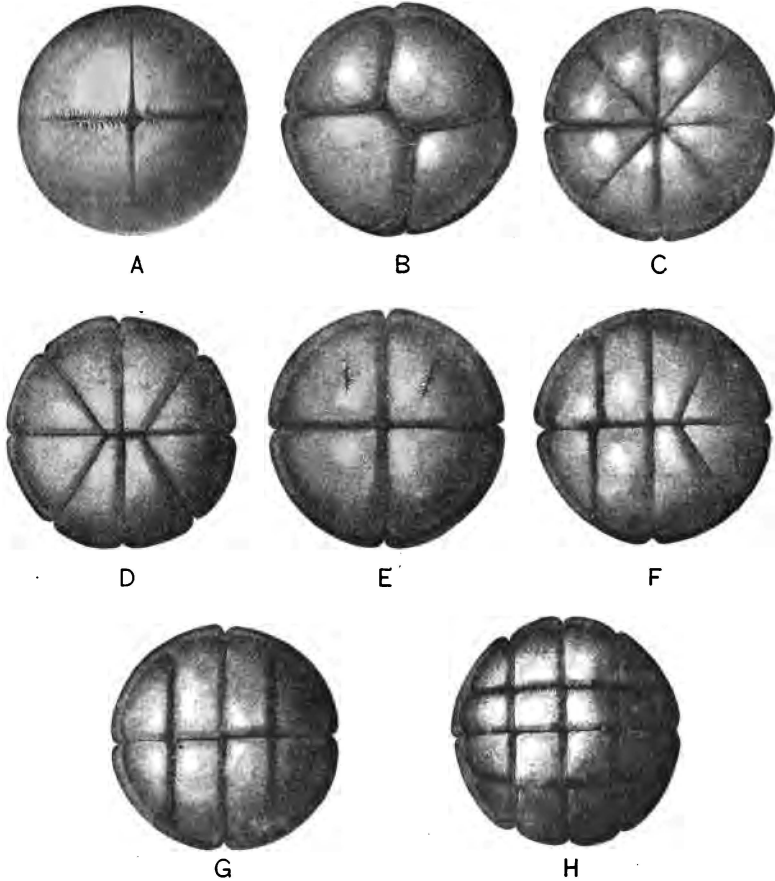


FIG. 13. — Segmentation of egg (two, eight, sixteen, and thirty-two cell stages, after M. Schultze), as seen from above. A. Two-cell stage; beginning of second furrows. B. Eight-cell stage, with cross-furrow. C, D, F, G. Sixteen-cell stages. E. Eight-cell stage (regular type). H. Thirty-two-cell stage.

or karyokinetic division. Half of the chromatin passes to one pole of the nuclear spindle, and the other half to the other pole. As the spindle elongates, it carries with it the surrounding pig-

ment. The first cleavage-plane always passes directly between the separating halves of the segmentation-nucleus.

There is an infinite number of possible planes through which the first cleavage might divide the egg into equal portions. What, then, determines the particular plane taken? We can think of this plane as determined by external conditions, or by the internal structure of the egg, or by a combination of the two. In the first place, it seems probable that at the first division of the segmentation-nucleus each resulting half will get half of the chromatin of the male and half of the chromatin of the female pronucleus. The first plane of division *must therefore pass at right angles to the plane of apposition* of the two pronuclei. That is to say, it will also pass through the path of penetration of the spermatozoön (the male pronucleus), and therefore approximately through the point at which the spermatozoön has entered. This, according to Roux, is what actually takes place. Moreover, since the egg has rotated as a whole in the direction of the point of entrance of the spermatozoön, the first cleavage will pass exactly through the highest point of the white crescent, as seen from above.

On the other hand, there is no direct evidence to show that the two apposed pronuclei retain throughout subsequent changes the position of *first apposition*, and there is much to show that in the frog's egg, as well as in other eggs, the dividing nucleus, or the direction of its spindle, is very susceptible to modifications in the surrounding conditions.

There is also some evidence to show that the declination of the axis of the frog's egg is not necessarily determined by the entrance of the spermatozoön, but by the arrangement of the internal constituents of the egg itself. If, therefore, it could be shown that the declination is present in unfertilized eggs, and that in fertilized eggs the plane of first cleavage passes more or less through the highest point of the white crescent, then we should conclude that the plane of first cleavage is pre-arranged in the egg. It would follow as a corollary that the nuclear spindle orients itself with *respect to the egg*.

There is direct evidence to show that in the newt some such process as this does take place. Jordan ('93) has shown that the spermatozoön may enter at any point of the surface of the

upper hemisphere, yet the plane of first division is always *across* the long axis of the egg. Hence, it is fair to assume that the segmentation-spindle does so orient itself after the fusion of the male and female pronuclei that half of the male and half of the female chromatin are carried apart in the direction of the long axis of the egg, whatever may have been at first the position of apposition of the two pronuclei. I have dwelt on this point at some length because it is one of great importance for our understanding of the relation between egg and embryo; and because it is much to be desired that the present state of doubt should be cleared away.

After the protoplasm has divided into two equal parts, the egg "rests" for a time. During the division-period the hemispheres or blastomeres round up to some extent; but as soon as the division is completed they flatten against each other, so that the cleavage-plane is not so distinctly seen on the surface of the egg. The same process of flattening generally takes place also when the dividing egg is brought into preserving fluids.

During the time of division we may speak of each blastomere as tending to become itself a sphere, but, owing to the lack of room, the rounding of the two parts is very imperfect. In other eggs (*e.g.* the eggs of the sea-urchin), where it is possible to remove the egg-membranes, it has been found that then each of the blastomeres approaches more nearly the spherical form, or even becomes a complete sphere. We see from this that the external conditions may at least modify the form of cleavage of the egg.

It is sometimes said that during the division the two new parts or blastomeres tend to repel each other until after the division is completed, and to attract each other after the division is finished. Such a statement is, however, of little value, and may convey an entirely wrong impression of the changes taking place. One thing seems to be certain, that during the division of the egg the *spheres* or cells have an influence on one another. Whether unseen protoplasmic connections weld them together, or whether it is merely a question of *contact action*, has not yet been fully determined.¹

¹ See Roux's experiments on cytotaxis ('96).

The nucleus of each blastomere during the resting-period undergoes a series of changes, the so-called reconstructive process taking place. The chromatin-granules or chromosomes are again surrounded by a nuclear membrane, and the granules fuse into a thread or network. At the next division of the egg the nuclear chromatin is again set free in the protoplasm by the absorption of the nuclear membrane. A spindle is formed and the chromatin in each cell is again exactly halved.

The second cleavage-furrow appears about three-quarters of an hour after the appearance of the first. Each of the two blastomeres divides in a plane at right angles to the preceding division. The furrows begin, generally simultaneously, in the upper hemisphere of each of the first two blastomeres, and push toward the lower pole (Fig. 13, A). The upper and lower ends of these new cleavage-planes are sometimes exactly opposite to each other, so that the effect is as though the whole egg had been divided by a single furrow in a plane at right angles to the first. In many cases, however, the new planes of division are not quite opposite, but reach the upper and lower poles of the egg at different points along the first plane of division. A "cross-line" is thus formed. The same result may be brought about even subsequent to division by a shifting or readjustment of the blastomeres on one another. As a rule, when a cross-line occurs in the upper pole, another one is formed in the lower pole, and the two stand in space at right angles to each other, as is shown in the diagrammatic reconstruction in Fig. 14, A. The same result can be obtained by compressing four clay spheres together until a single sphere results. It will be found in such a model that the cross-lines above and below are generally at right angles to each other.

The third furrows come in at right angles to the preceding planes of division, and are therefore horizontal (Fig. 12, A). The third planes of division do not lie at the equator of the egg, but, taken together, form a small circle in the black hemisphere or on the border-line between the black and white areas. Above there are four smaller dark blastomeres and below four larger white blastomeres. The four upper blastomeres are of approximately the same size, but in some species of frogs it seems that one is a little smaller than the rest, one is somewhat

larger, and two are intermediate in size. The *smallest blastomeres of the upper four always lie nearest the summit of the white crescent*; the largest is its *vis-à-vis*. If we think of the third planes of cleavage as lying in a single plane not quite at right angles to the first and second, but tilted a little, we get a clearer conception of the conditions present. The fourth cleavage-period comes in from a half to three-quarters of an hour later. As an idealized form, we may think of the new planes as forming two great circles at right angles to each other, and lying vertically and between the planes of the first and second cleav-

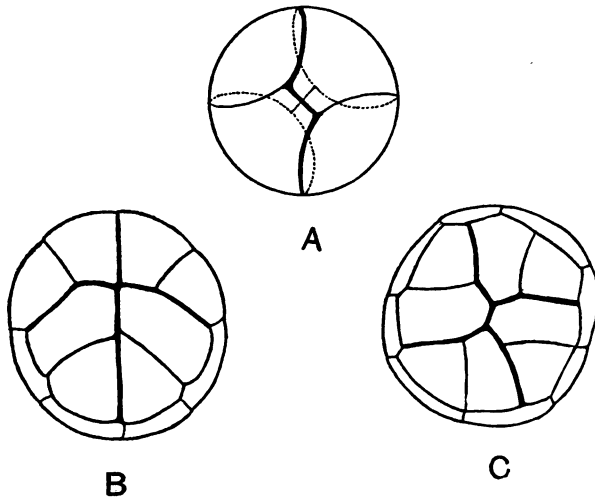


FIG. 14.—A. Diagram of four-cell stage to show cross-line. B, C. Sixteen-cell stage of two eggs. (After Rauber.)

ages (Fig. 13, C). This regular form is rarely if ever attained, and the greatest amount of variation is found to exist.

Remak said that frog's eggs divide much more *regularly* when carried in from places where they were normally laid. If allowed to stand quietly after being laid, they soon begin to divide irregularly. Vogt has also observed that those eggs of the salmon develop most regularly that have been kept in motion. It does not seem probable, however, that the motion itself could have anything to do directly with the matter; but if the egg be not supplied with a sufficient amount of fresh water,

etc., it might no doubt segment irregularly, or it may be that the motion equalizes the external conditions so that the eggs keep a more nearly spherical shape and hence divide more regularly.

Max Schultze ('63) and Rauber ('82) have made the most careful study of the variations in the planes of division of the fourth cleavage. In Figs. 13, D, F, G, and 14, B, C, are shown the upper hemispheres of several eggs. If we examine the position of the planes of the last (fourth) divisions, we see that in the upper hemisphere each new cleavage-plane fails generally to reach the black pole of the egg, but passes to one or to the other side. In the lower hemisphere the new planes fall far short of the white pole.

Occasionally we find eggs in the upper hemisphere of which one or more of the fourth planes reach the black pole itself, and, therefore, lie more nearly radial in position (Fig. 13, C). In other cases, however, one or more of the new fourth cleavage-lines may even be nearly in the horizontal plane. In the lower pole also there is much variation, and occasionally a blastomere is divided into a very small and a very large part, owing to the sudden turning aside of the new cleavage-line, so that it meets one of the first two cleavage-planes before it has extended far into the lower hemisphere. Other eggs at this same stage show a strictly bilateral arrangement of the cells in the upper hemisphere. In Fig. 13, D, F, G, we see that the fourth cleavage-planes have met the same furrow (first or second). Also in Fig. 14, B, a bilateral symmetry is present, formed in a somewhat different way, as the figure shows; and in this egg the lower hemisphere also is symmetrically divided.

During the fifth cleavage-period the irregularities in the division of the cells is generally so great that we cannot speak definitely of any special direction of the new planes. Nevertheless there is a tendency for some of the new furrows to come in at right angles to the last planes of division. Therefore, many and occasionally all of the new fifth cleavage-planes are horizontal (Fig. 12, C). The eight cells in the upper hemisphere divide into equal or nearly equal parts, but the eight blastomeres of the lower hemisphere divide unequally into eight upper smaller blastomeres containing pigment, and eight lower blastomeres which are the white blastomeres around the lower

pole. The division of the lower eight blastomeres is sometimes so regular that a circle of eight dark cells is formed around the equator of the egg (Fig. 12, C). After this division thirty-two cells are present. At this period the distribution of the cells over the dark and light regions of the egg is such that the cells on the side of the egg showing the light crescent above are smaller than the corresponding cells on the opposite side.

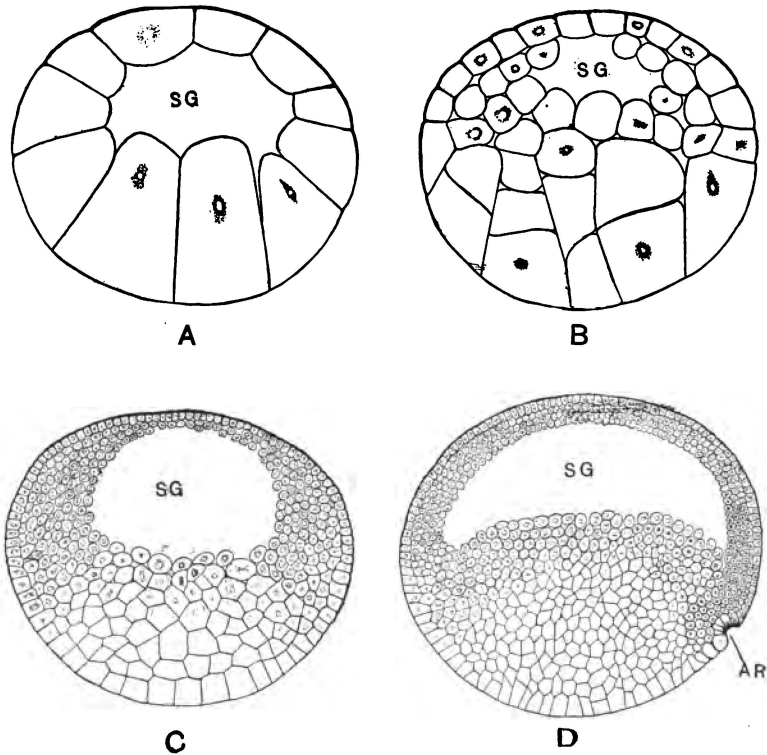


FIG. 15.—Stages in the segmentation (A, B, C) of the egg, and the beginning of gastrulation (D). AR. Beginning of archenteron. SG. Segmentation-cavity.

Up to the present time all the divisions of the cells started on the outside of the egg or blastomeres and progressed inward. As early as the eight-cell stage, a cavity appeared between the cells in the upper hemisphere of the egg. This is the "segmentation-cavity." It is filled with an albuminous fluid which

probably comes entirely, or in part, from the surrounding cells. This cavity gets larger and larger as development proceeds (Fig. 15, A). If an egg be cut open after the thirty-two-cell stage, it will be found that many, perhaps all, of the cells or blastomeres are undergoing division into outer and inner cells (Fig. 15, B). We may speak of this process as a *delamination*. Before the egg has divided into sixty-four cells, as seen on the surface, this delamination into inner and outer cells has in most cells taken place.

The cell-divisions now proceed more rapidly and with great irregularity. The rhythm also soon becomes lost, so that while some cells are dividing others are resting. Not only have the outer blastomeres continued to divide at the surface, but also below the surface of the egg new blastomeres are being cut off from the outer cells; the inner blastomeres also continue to divide. In the upper part of the egg a large segmentation-cavity forms. Its roof is covered by several layers of small deeply pigmented cells, its sides by larger cells, and its floor is formed by the large whitish yolk-bearing cells (Fig. 15, C).

If the surface of the egg be carefully examined during these later stages, it will be found that the cells over one side are distinctly smaller than those over the opposite side. We see that the side of the egg containing the most pigment is made up of larger cells. In Fig. 12, G, H, the opposite sides of an egg are shown, and here the less pigmented cells are seen to be smaller than the cells in the same position on the other side of the egg. Sections show, moreover, that this difference in size is not only found on the surface of the egg, but also in the interior as well. During the early periods of cleavage the egg has become neither more nor less pigmented on its surface, and has retained the same distribution of pigment as in the unsegmented egg.

Besides the variations in the cleavage noted above, others are more rarely found that depart much further from the usual typical forms. The first furrow, for instance, may divide the egg into very unequal parts. The second furrow may appear before the first has reached the lower pole. The third furrows may stand *vertically*, passing from near the upper pole into the lower hemisphere, *i.e.* the third furrows occupy the position of the fourth furrows of the usual type of cleavage.

CORRESPONDENCE OF THE FIRST CLEAVAGE-PLANE AND THE
MEDIAN PLANE OF THE EMBRYO

If the egg when in the two-cell stage be fixed¹ so that it cannot rotate in a horizontal plane, and if such an egg be carefully watched until the moment when the medullary folds have just appeared, it will be found that the position of the plane of first cleavage corresponds approximately, or even exactly, to the median plane of the body of the embryo. This experiment was first made by Newport in 1851, subsequently by Pflüger ('83), and Roux ('85), and later by other workers.² If, however, during the subsequent cleavage-periods, *i.e.* during the eight and sixteen cell stages, etc., the position of this plane be kept in mind, it will be found that the later blastomeres from one or the other side often pass over the imaginary plane that corresponds to the plane of first division. Striking, therefore, as is the coincidence of the first plane of cleavage and the middle plane of the embryo, it remains to be proved, I think, that there is any direct causal connection between the first cleavage-plane and the median line of the body. It may be that the two phenomena are coincident because the internal arrangement of the egg that determines one may also, but independently, determine the other. In the newt Jordan ('93) has shown that the first plane of cleavage corresponds approximately to the cross-plane of the body. That is, the first two blastomeres correspond to the anterior and posterior parts of the body respectively. He suggests that the shape of the egg-capsule of the newt may be the cause determining the plane of first division. Some other factor than that of the position of the first plane of cleavage seems to determine the position of the embryo on the egg, for in the teleost's egg, where the symmetry and bilaterality of the cleavage is even more sharply marked than in the frog or newt, there seems to be no relation at all between the first cleavage-planes and the planes of the adult body.³

¹ For method, see Pflüger ('83), Roux ('85), and Morgan ('91).

² Rauber ('86) has later contradicted these results, but it is probable that there is an error in his experiment.

³ Clapp ('91), Morgan ('93).

ROUX'S EXPERIMENTS WITH OIL-DROPS

The arrangement assumed by the blastomeres after each cleavage has attracted much attention. A system of soap-bubbles, or of balls of clay compressed into a sphere, gives somewhat similar figures. In this connection Roux has made a most instructive series of experiments. A small wine-glass is half filled with dilute alcohol and then sufficient oil is poured in to form a large drop. A stronger (lighter) alcohol is now poured on top of the oil, which assumes a spherical or nearly spherical shape. The drop lies suspended between the two

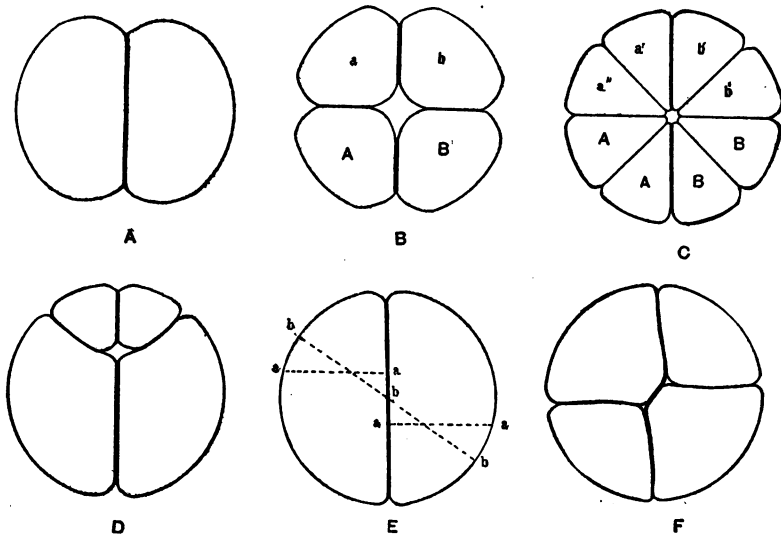


FIG. 16.—Systems of oil-drops. (After Roux.) In C, the lowest drops should be marked A', B'; and those next them A'', B''.

alcohols and its periphery just touches the walls of the glass.¹ It is possible to divide this sphere of oil into equal or unequal parts by means of a glass rod and, if precautions are taken, the drops will not for a time flow together. The drops tend each

¹ Roux recommends olive or paraffine oil. I find that thick cotton-seed oil gives as good or better results when suspended between fifty and seventy per cent. alcohols. A smaller drop is to be used when more than two divisions are to be made.

to become spherical, but the wine-glass holds them together and their surface-tensions cause them to assume definite relations to one another. When the drop is divided into two equal parts, the halves, if little compressed, arrange themselves as shown in Fig. 16, A, and if much compressed, as shown in Fig. 16, E.

If each drop is again divided,¹ the resulting four drops arrange themselves as shown in Fig. 16, B. A large central cavity, similar to the segmentation-cavity of many segmenting eggs, is present in the centre between the four drops.

If the drops had been first divided unequally, we should find that the smaller drop, having a stronger tendency to become round, caused the region of contact of the two drops to bend in toward the larger drop. If each of these two drops is again divided, the four parts arrange themselves as shown in Fig. 16, D. The same result is brought about if we divide the drop at first equally and then each of the products unequally (Fig. 16, D).

If we first divide a drop equally and then each of the two unequally, but at different ends of each drop, as shown by the dotted lines in Fig. 16, E, the resulting four drops arrange themselves as shown in Fig. 16, F. Moreover, and this is a point of much importance, it is a matter of indifference in what direction the smaller drops are cut off. For instance, if each of the first two drops is divided along the dotted lines, *a-a*, *a-a* (Fig. 16, E), the result is the same as when the division takes place along the line *b-b*, *b-b*. In either case the drops arrange themselves as shown in Fig. 16, F. The two larger drops come together at the centre of the system and flatten somewhat against each other, producing a cross-line. The two smaller drops are pushed out more toward the periphery of the system.

If we adopt the method of lettering shown in Fig. 16, B, we can follow more readily the further divisions. Dividing equally two of the four drops of Fig. 16, B, we find the

¹ In dividing the drops it is better to move the rod always from the centre toward the periphery. The plane of the first division is indicated in the figures by the heavier line.

arrangement of the six resulting drops to be that shown in Fig. 17, A. We can write out the arrangement in the form of equations: thus (in Fig. 16, B) $a = A = B = b$; and (in Fig. 17, A) $b' = b''$, $a' = a''$.

Dividing *unequally* a and b so that a' is less than a'' and b' is less than b'' , the drops arrange themselves as shown in Fig. 17, B. A large central cavity is present in the centre of the system.

If each of the four equal drops (Fig. 16, B) be equally divided, the resulting eight drops arrange themselves as shown

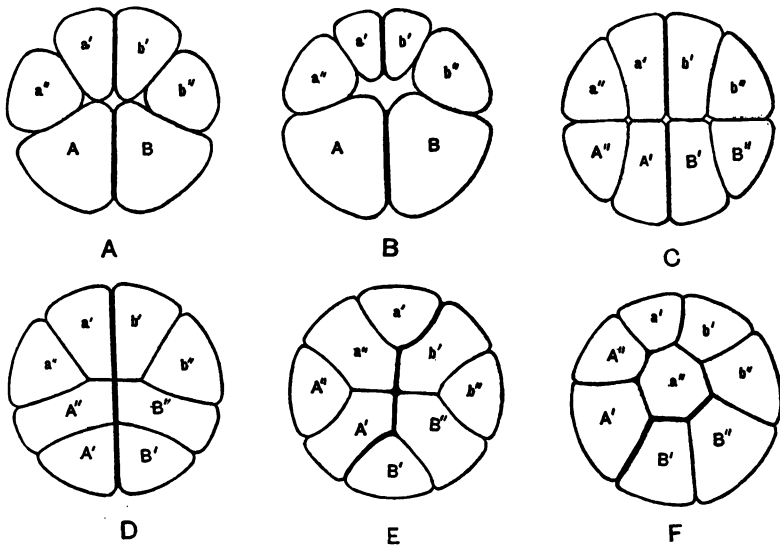


FIG. 17.—Systems of oil-drops. (After Roux.)

in Fig. 16, C. A central cavity is present, but *smaller* than when only four equal drops formed the system.

If we divide each of four equal drops (Fig. 16, B) *unequally* so that a'' is less than a' and b'' is less than b' , also A'' is less than A' and B'' is less than B' , the resulting eight drops arrange themselves as shown in Fig. 17, C. The four larger drops come together in the centre, pushing the smaller drops more toward the periphery of the system.

If we divide four equal drops (Fig. 16, B) so that a'' is less

than a' , b'' is less than b' , but A' is less than A'' and B' is less than B'' , then the drops assume the form shown in Fig. 17, D.

If we divide four equal drops (Fig. 16, B) so that a' is less than a'' , b'' is less than b' , A'' is less than A' , and B' is less than B'' , the resulting eight drops arrange themselves as shown in Fig. 17, E. In this system it is instructive to note how far the first division-plane is drawn out of its straight course as a result of the shifting of the drops on one another. It is not unusual for one of the drops to glide into the centre of the system, as shown in Fig. 17, F. This produces a more stable arrangement than when a large central cavity is present.

Most of these systems are found also in the segmenting frog's egg, as can be seen by comparing these figures of the oil-drops with the figures of the segmenting frog's egg (Fig. 13) by Max Schultze made in 1863. Rauber has also given figures showing arrangements of the upper eight blastomeres (Fig. 14), like the systems of oil-drops shown in Fig. 17, D and E.

A careful comparison between the systems of oil-drops and the arrangement of the blastomeres of the frog's egg shows, as Roux points out, that while in many cases the agreement is perfect, yet occasionally the blastomeres assume an arrangement that oil-drops of the same size would not assume. For instance, Roux figures an arrangement of the blastomeres like that of Fig. 17, C, but here the blastomere corresponding to a' is less than a'' and A' is less than A'' . In this egg the *smaller* blastomeres meet in the centre, but this never occurs in the system of oil-drops.

Roux removed a part of a blastomere so that it became suddenly smaller. A new arrangement ought now to have taken place among the blastomeres if they conformed entirely to the laws regulating the oil-drops. In one case where four blastomeres were present, the blastomere that had been reduced in size did move out more toward the periphery of the system, and the two neighboring blastomeres pushed in more toward the centre to form a cross-line. In other experiments, however, the blastomeres did not rearrange themselves in conformity with the systems of oil-drops. For instance, in one experiment in which material was drawn out of one of the first

four blastomeres, the inner end of the reduced blastomere retained its central position. In another instance material was taken out of that one of the four blastomeres that had already made a broad cross-line with its *vis-à-vis*. Although this blastomere was much reduced in size and made smaller than any other blastomere of the system, yet it retained the same cross-line as before; *i.e.* it was not pushed out to the periphery. Even when the experiment was made *at the time of appearance* of the second cleavage, the newly forming blastomeres did not in all cases adjust themselves in agreement with the laws regulating the oil-drops.

These results show that the conditions present in the frog's egg do not allow the blastomeres to assume always the arrangement shown by the same number of oil-drops having the same relative size. Roux points out several differences in the two cases. The walls of neighboring blastomeres seem to stick together, and this would prevent the blastomeres from gliding freely over one another should any change take place to disturb the equilibrium. Moreover, the blastomeres are living contractile bodies, and through their own internal activity may interfere with the mechanical tendencies of the system. The nature of the surface of each blastomere and the sort of changes taking place in the surface may also affect the arrangement.

It will be seen then, as has been said, that there may be factors present in the frog's egg that so influence the arrangement of the blastomeres that the systems do not always conform to those of the oil-drops. Nevertheless, the results from the latter give us an ideal scheme showing the effect produced by one set of factors, — that of surface-tension. It seems highly probable that surface-tension is also an important factor in the segmenting egg, but other conditions present prevent its free play.

HISTORICAL ACCOUNT OF THE CLEAVAGE OF THE FROG'S EGG

The earliest observations on the segmentation of the animal-ovum were made upon the frog's egg. Swammerdam ('37) saw, but did not understand, the first cleavage-furrow of the egg. Spallanzani, in 1785, observed the first two furrows cross-

ing each other at right angles. Prévost and Dumas, in 1824, gave for the first time a definite description of the cleavage of the frog's egg. They described the first furrow beginning in the black hemisphere and stretching out into the white hemisphere. They saw, moreover, the small lateral creases or folds along the edges of the first cleavage-furrow. The second furrow, they said, cuts the first at right angles. When the dark hemisphere is divided into four segments, they saw that then a third equatorial furrow forms near the boundary of the two hemispheres. The next furrows, they said, appear parallel to the first.

Rusconi ('26) observed that the furrows were not simply surface-lines, but cut up the yolk into separate parts, producing finally a large number of small pieces, which he believed were the elements from which the different parts of the body developed. Von Baer's description of the process, in 1834, is much more exact than the accounts of his predecessors. His interpretation, too, is much clearer and nearer to the truth. He said that the advance of the first furrow into the lower hemisphere goes on as though it were overcoming great difficulty. The tearing apart of the yolk into halves is brought about as a result of a living activity, and the power to divide the ovum does not reside only in the surface of the ovum, but extends throughout the whole mass. Von Baer noticed that after the division the cross-diameter of the egg is greater than the vertical diameter in the proportion of six to five, and he said that the difference would be greater were it not for the egg-membrane. The tendency, he said further, is to form two spheres which are, however, compressed against each other by the membrane. Since the division of the white hemisphere progresses more slowly, and since the third division is nearer to the upper hemisphere, we can understand why the dark portions are always smaller than the white portions. When the surface appears again smooth (owing to the smallness of the portions into which the ovum has divided), the egg is very distinctly larger than at first. Von Baer concluded that material is taken up from the outside to form the albumen, and hence to enlarge the ovum. He interpreted the process of cleavage as the self-division of the individual to form innumerable smaller units. In the later

stages these smaller bodies fuse by a vital process into a new whole, and a new individual is thus produced from the fragments of the first.

Schwann and Schleiden promulgated the cell-theory in 1838-1839. This produced an effect on all subsequent interpretations of the segmentation of the frog's egg. The main points to settle were: first, whether the process of cleavage is a process of cell-division, *i.e.* whether the egg is a cell that divides; second, whether the bodies that result from the segmentation of the egg pass over into the cells of the embryo. The search for the nucleus, before and after the process, also occupied the attention of workers on the subject. Bergmann ('41) was the first to treat the process of cleavage from the cell standpoint. The first divisions of the egg did not produce true cells, he said; yet as the results of these divisions went over directly into the cells of the embryo, therefore the division of the batrachian egg is the introduction of cell-formation into the yolk. Later, he said that the yolk may be thought of as strongly disposed to form cells, but that nuclei are wanting. Reichert's interpretation ('46) was a step backwards. Kölliker, in 1843, described the segmentation-spheres as without a membrane and containing spore-like bodies which multiplied endogenously. When these bodies are set free, he thought, they become the cells from which the tadpole is built up. Cramer ('48) thought that the early cleavage-spheres formed membranes (cell-walls) and were the progenitors of the true cells of the body. Remak ('50-'55) argued that the cleavage-process was the beginning of cell-division, and that the products resulting from division formed the cells of the embryo. This statement marked a distinct advance and is the standpoint taken at the present time. Moreover, Remak thought it highly probable that there was a continuity of the original egg-nucleus with the cleavage-nuclei. Max Schultze, in 1863, described admirably the process of cleavage of the frog's egg. He spoke of the egg as a cell with protoplasm and nucleus, and of the process of cleavage as cell-division. Ordinary cell-division depends, he said, on the contractility of the protoplasm. The same property belongs to the egg-yolk, since it divides like a true cell.