ON THE LAWS AND PRINCIPLES

CONCERNED IN THE

AGGREGATION

OF

BLOOD-CORPUSCLES

BOTH

WITHIN AND WITHOUT THE VESSELS.

BY RICHARD NORRIS, M.D.

PROFESSOR OF PHYSIOLOGY, QUEEN'S COLLEGE, BIRMINGHAM.

Read to Royal Society, May 27th, 1869.

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In 1827, or forty-one years ago, the phenomenon which forms the subject of this paper was first observed by Mr. Joseph Jackson Lister, and the late Dr. Hodgkin.

To these observers the microscope revealed the fact that if a minute drop of human blood was placed between two plates of glass, the red corpuscles apply themselves to each other by their concave surfaces in such a manner as to form long cylindrical masses, which resemble piles of coin, and that very frequently these piles are so arranged as to form with each other a complete network of rouleaux with clear intervening spaces occupied by liquor sanguinis. Vide Plate i.

Simple as this observation may appear, its importance in a pathological point of view can scarcely be overrated; for upon its correct interpretation depends our knowledge of the exact nature of one of the most marked characteristics of inflammation, viz. the phenomenon of inflammatory or homogeneous stasis.

During the forty years which have elapsed since the discovery of this fact, many theories have been advanced to explain its nature; but all of them, without exception, have laboured under the disadvantage of being purely hypothetical in their character, and quite incapable of demonstration by an appeal to experiment. Thus, while some writers have attributed the effect to an imaginary law of vital attraction, others have more correctly referred it to the operation of some unexplained physical cause.

Professor Lister (son of the original observer already mentioned), who has devoted much attention to this subject, says, in a paper submitted to the Royal Society, June 18, 1857, and published in the Philosophical Transactions for 1858, p. 648:—"For my own part, I am satisfied that the rouleaux are simply the result of the biconcave form of the red disks, together with a certain, though not very great degree of *adhesiveness*, which retains them pretty firmly attached together when in the position most favourable for its operation, viz. when the margins of their concave surfaces are applied accurately together, but allows them to slip upon one another when in any other position. *There is never to be seen anything indicating the existence of an attractive force drawing the corpuscles towards each other: they merely stick together when brought into contact by accidental causes.* Their adhesiveness does not affect themselves alone, but other substances also, as may be seen when blood is in motion in an extremely thin film between two plates of glass, when they may be observed sticking for a longer or shorter time to one of the surfaces of the glass, each one dragging behind it a short tail-like process."

Again, at the end of section I., p. 652 of the same paper, Lister says, "From the facts detailed in this section, it appears that the aggregation of the corpuscles of blood removed from the body *depends on their possessing a certain degree of mutual adhesiveness,* which is much greater in the colourless globules than in the red disks, and that in the latter, this property, though apparently not dependent upon vitality, is capable of remarkable variations *in consequence of very slight chemical changes in the liquor sanguinis.*"

From these quotations it is apparent that Lister ignores altogether the idea of the aggregation of the corpuscles being due to an *attractive force or energy*, and refers it to *adhesiveness or stickiness* of the corpuscles; in his own words, "they merely stick together when brought into contact by accidental causes." At the same time he states that this adhesiveness is liable to great variations, both in the way of increase and diminution, by very slight changes in the chemical qualities of the plasma.

Dipping deeper into the writings of Lister, we find that this idea of adhesiveness or stickiness of the corpuscles is retained in his explanation of the nature of inflammatory stasis. And his views upon the subject generally may be summed up in three propositions:—

1. The blood-corpuscles exhibit no tendency to unite together in healthy blood within the vessels, although such blood may be in a state of rest.

2. The corpuscles become suddenly adhesive (10 seconds) when, by being shed, the blood is brought into contact with ordinary matter.

3. That irritation, by reducing the vitality of the surrounding tissues, causes them to bear the same relation to the blood within the vessels in their immediate vicinity as ordinary matter does to that which has been shed, inducing adhesiveness of the corpuscles, and thus bringing about inflammatory stasis.

These effects upon the blood-corpuscles are assumed by Lister to depend upon *chemical* changes induced by ordinary matter or by vitally degraded tissues upon the plasma of the blood; but inasmuch as chemical changes cannot occur without corresponding physical modifications, it is quite as rational to refer the increased aggregating tendency displayed by the corpuscles to physical as to chemical changes in the liquor sanguinis; and this view has the advantage of not requiring us to believe that the functional activity of the tissues is depressed by mild forms of irritation, an idea which is opposed to all we know of the increased nutritive and formative changes which follow in the wake of irritation.

Having now briefly reviewed the existing position of the subject, we will proceed to consider the real causes at work in the production of the phenomenon under consideration.

Many years since, having familiarized myself with the behaviour of, and the appearances presented by blood-corpuscles under almost every conceivable condition, both within and without the vessels, I became profoundly impressed with the conviction that these phenomena had their origin in *some physical law of attraction*, and at the same time felt not the less certain that, if this view proved to be correct, the behaviour of the blood-corpuscles would be found to be no isolated exhibition of this law, and that, provided conditions similar to those which exist in the case of the blood-corpuscles could be obtained, many illustrative examples of the operation of the law would be immediately forthcoming.

That such attractive force did not exert its influence through distances readily appreciable was obvious, and this fact at once indicated that it must be sought for among those forms of attraction which have been designated molecular.

After much experiment and reflection I came in 1862 to the conclusion that these phenomena were due to no less universal a law than that of *cohesive attraction*, and I embodied the views I then held upon the subject in a paper which was read before the Royal Society, and published in the Proceedings, entitled "The causes of various Phenomena of Attraction and Adhesion as exhibited in Solid Bodies, Films, Vesicles, Liquid Globules, and Blood-corpuscles." Since that time other departments of physiology have occupied my attention, and I have only been induced to recur to the old theme because I find that, in some recent references to the history of this subject, my observations have not been mentioned, from which I am led to infer, either that my views have not been pressed with suitable earnestness, or that my experiments have failed to produce conviction in others. I therefore now present the result of a renewed investigation, in which I believe I have established, by conclusive experiments, the correctness of my explanation of the phenomena. Among the various modes of aggregation which the blood-corpuscles undergo, two typical forms stand prominently forward of which all others are merely modifications. The one appears to be dependent upon the normal disk shape, the other upon the globular or spherical form which the corpuscles assume on the addition of various substances to the blood, such as gum, gelatine, linseed mucilage, potash, etc.

With the first of these modes of aggregation, viz. into rouleaux, we are all sufficiently familiar, (plate i.) and an excellent notion of the character of the second form may be obtained by a careful examination of the microphotographs of the blood-corpuscles which accompany this paper, and which have been obtained instantaneously by exploding magnesium in heated oxygen. Vide Plate i. Fig. ii.

In order to leave as little as possible to hypothesis, it was desirable as a preliminary step to make sure that these differences in form of the corpuscles were the real cause of the diverse modes of arrangement; whether, in fact, we could safely predicate that disk-shaped bodies having an attraction for each other would arrange themselves so as to form rolls or cylindrical masses, and whether, on the other hand, attracting spheres of soft material would attach themselves together in such a fashion as to cause plane surfaces to be opposed to each other—

in a word, to convert themselves by mutual attraction into polyhedral bodies just as they might do under mutual compression.

In the first place, we had to ascertain experimentally how disk-shaped bodies, having the utmost freedom of movement, and possessing an attraction for each other, would arrange themselves.

In casting about for the conditions to make such an experiment, I remembered a very familiar phenomenon which had often excited my curiosity, viz. the rapidity with which a bubble or a small floating fragment upon the surface of a cup of tea or other liquid, rushes to the side of the containing vessel, or with which two such bubbles or fragments rush together the moment they approach within a certain range. I determined to see if I could not make use of this attraction, the true nature of which I at the time imperfectly understood, and with this object prepared a number of circular disks of cork, which I accurately poised so that they should assume and maintain the vertical position when partially immersed in liquid. On throwing these disks into liquid, I had the satisfaction of seeing them run together and form themselves into the most perfect rouleaux after the fashion of the blood-disks. Vide Plate ii.

This experiment has the value of demonstrating that if the blood-disks possessed an attraction for each other, *their shape* would determine the formation of rouleaux.

I next sought to ascertain how spherical vesicles or globules, which possess the property of attracting each other, would arrange and group themselves.

In thinking over the probable relations which delicate and plastic films might bear to each other, I was again helped out by the recollection of an observation made some years previously upon fine films of collodion. It was found that if one of these films, while still in the wet condition, was detached from the glass plate upon which it had been formed, it immediately, in opposition to gravity, sprang back to its former situation into contact with the glass plate, precisely as if it were electric.

This phenomenon of attraction may be witnessed in a somewhat less energetic degree by simply spreading upon a glass plate a thoroughly wetted piece of thin cambric paper, taking care that the contact is perfect throughout. On separating the paper from the glass to nearly its whole extent, and allowing it to hang down at a right angle from the plate, which is held in the horizontal position, it will be found to gradually raise itself upwards and reassume its old position of contact with the surface of the glass plate. Vide Plate viii.

This is an example of a kind of action which may be very properly designated *progressive cohesive attraction.*

The consideration of this experiment led me to study the behaviour of *convex plastic* films upon each other; these films were obtained by dipping the mouths of wine-glasses into a solution of albumen, and it was found that when two such films were made to touch each other at their centres or highest points of convexity, they became immediately attracted in the progressive manner before explained, and so flattened as to make two adherent planes. This attraction from *a central point in every direction* is of course only possible with highly plastic films.

My next step was to experiment with soap-bubbles, which not only present delicate and plastic films, but films forming the walls of vesicles.

If we allow a soap-bubble to fall upon an irregular surface, such as a piece of flannel or cloth, it retains its spherical form; but if we bring it into contact at any point with a smooth surface, such as a plate of glass, the wall of the bubble will be immediately attracted to the glass and *flattened out* upon it. Vide Plates v. and vi.

On the same principle, two bubbles will exert a flattening action upon each other the moment any point in their convex surfaces is made to touch, consequently bubbles in a group will convert each other into polyhedral-shaped bodies. This effect is not due to compression, but to a *progressive mutual attraction* of the sufaces of these bodies for each other. Vide Plate vii.

As soap-bubbles are vesicles with aërial contents, and are therefore physically unlike the blood-corpuscles, it became desirable to ascertain how vesicles with liquid contents would behave in regard to each other. This was accomplished by placing in a large test-tube a solution of soap, and upon its surface a stratum of petroleum an inch or so in depth; the petroleum does not mix with or injure the soap solution, which is the case with most other substances. A glass tube is now passed through the petroleum into the solution of soap below. On blowing down the tube, we succeed in forming innumerable small bodies or corpuscles of a spherical form, which are very plastic, and the contents of which consist of petroleum; and the external envelope or vesicle of soap. Corpuscles so produced float in the upper stratum of petroleum, and are found to unite themselves into groups and masses in precisely the manner of the air-bubbles, although they are entirely submerged in liquid.

These experiments show that disk-shaped bodies, having an attraction for each other, will arrange themselves in rolls or cylindrical masses, and that spherical bodies of a plastic character and vesicular structure, be their contents aërial or liquid, will attach themselves together in such a fashion as to cause plane surfaces to be opposed to each other—in a word, convert themselves by a progressive attraction, which commences at their points of mutual contact, into groups of polyhedral bodies.

The question now remaining is, do the blood-corpuscles possess such attractions for each other as those displayed by the objects with which we have been dealing? The reply is that their physical nature being analogous, if the same conditions exist, they cannot escape the influence of this law. An examination of the photographs and of the drawings of blood-corpuscles exhibited will serve to show that these bodies are amenable to the law which is concerned in grouping together the bubbles and liquid vesicles.

At this stage of the inquiry an objection may be justly urged that the disks, bubbles, and films of these experiments are not in precisely the same conditions as the blood-corpuscles—the former being only partially, or not at all submerged in liquid, while the latter are entirely so, and nevertheless they run together into rouleaux and groups. It may fairly be asked if the artificial bodies will do the same. The answer obtained by experiment is, that the moment these disks or bubbles are entirely submerged, they lose at once their attraction for each other and fall apart. Vide Plate iii.

For several years I unceasingly asked myself the cause of this difference in behaviour. I found that when small bodies, such as disks of cork or gelatine, are first wetted with water, and then submerged in a liquid with which water will not mix, such as oil of turpentine or petroleum, they will run together in piles or rouleaux, very much in the same way as the blood-disks. Vide Plate iv.

To understand this result, a few simple primary principles must be called to mind. In the first place, the particles which compose any liquid have a mutual attraction for each other, but between the particles which compose different liquids a mutual repulsion may exist, *e. g.* water and oil, or chloroform and water. It is likewise true that there is a mutual attraction between certain liquid and rigid bodies, and also a mutual repulsion between others. Any rigid body which can be wetted by a liquid is regarded as having a cohesive attraction for it, while one which cannot be wetted is said to have no such attraction, or to exert a repulsive influence, as the case may be.

Now this attractive power between rigid and liquid substances is exerted through appreciable distances. In a small glass pan filled with water two pieces of glass are placed so as to stand up vertically parallel to each other, and having a space between them of about one-eighth of an inch. On the outside of these plates of glass the water is seen to be piled up, and between the two pieces it is raised still more above the water-line. Now, if these two perpendicular plates of glass were free to move, they would approach each other just as the cork disks do which are partially submerged.

In what way can these raised portions of water occasion movement in these rigid bodies? It has been referred to the tendency which the water exerts to resume its level; but this is clearly not the case, for this action must be the same on both sides of the glass plate, and therefore would produce equilibrium. It may be observed that the water between the two plates has a concave surface.

Now, suppose for another experiment we take two globules of liquid, say, mercury or water. If we approximate such globules, the moment they touch at any point in their convexities they will leap, as it were, into each other, and satisfy their tendency to arrange their particles around a common centre.

Another modification of these experiments may be made by supporting two sheets of microscopic glass so as to form an acute angle like the letter V. On placing a drop of water in the angle, the plates will be drawn together and cohere by their surfaces. It is observed that the form of the upper surface of the water is in this case also concave. The same thing may be observed by suspending two sheets of wetted paper as in Plate viii.

All these phenomena therefore depend upon what might be justly termed *double cohesion*—cohesion in the first place between the rigid body and the liquid, and in the second place between the particles of the liquid itself.

If, now, we examine into the cases in which we have complete submergence, viz. the blood-rolls, the gelatine disks, and the loaded cork disks, we find the same law to be in operation. These bodies must all be regarded as *localizers of liquids*, either by their cohesive attraction for liquids, or, as in the case of the blood-corpuscles, by being receptacles containing liquids, which can exude through their coats.

If the cork disks, bubbles, or V-shaped glasses are entirely submerged in water, all attraction ceases, and this because a cohesive equilibrium is established; there is no longer any differentiation such as exists between water and air. If, however, after having wetted these bodies in water, we completely submerge them in a liquid which has a cohesive antagonism to water, or even a liquid which has simply no cohesion for water, which may be known by the insolubility and immiscibility of one liquid in the other, such as turpentine or petroleum, we get the phenomena of attraction precisely as in the atmosphere. This fact is illustrated by taking the cork disks from the water in which they are non-adherent, and placing them in the vessel of petroleum, in which they become instantly attractive of each other, or the converse, as the case may be.

This principle is further illustrated by the gelatine disks, which are first made to absorb as much water as possible, and are then submerged in petroleum.

In all these cases there are present, therefore, two dissimilar or antagonistic liquids, and upon the presence of these the phenomena depend.

My idea of the blood-corpuscle is that its contents are something essentially different, so far as cohesive attraction is concerned, from the liquor sanguinis, that is to say, not readily miscible with liquor sanguinis. This is of course self-evident, if, according to some modern views, we regard the corpuscles "as tiny lumps of a uniformly viscous matter," inasmuch as such matter must be insoluble in, and immiscible with the liquor sanguinis. The explanation is equally easy, if we accept the old and, I believe, the true view of the vesicular character of these bodies, as we have only to assume that the envelope is so saturated with the corpuscular contents as practically to act as such contents would themselves act, *i. e.* to exhibit a greater cohesive attraction for their own particles than for those of the contiguous liquid.

The cohesive power of the blood-corpuscles varies with varying conditions of the liquor sanguinis, and this is doubtless due to the law of osmosis; for we can readily imagine that when the exosmotic tendency was in excess, the corpuscles would become more adhesive, and on the contrary, when the endosmotic current prevailed, less so. In any case the increased cohesiveness will be due to the increased extrusion upon the surface of the corpuscular contents.

All, then, that is required in the case of the blood-corpuscles, is a difference between their liquid contents and the plasma in which they are submerged. That this difference is not so great as between the liquids used in these experiments is probable, but it must also be remembered that the attraction is not so powerful. The power required to attach the blood-corpuscles together is, on account of their exceeding minuteness, extremely small, as they are thus so much more removed from the influence of gravitation, and brought under that of molecular attraction.

I shall conclude this paper by a brief reference to inflammatory stasis. In one of my papers to the Royal Society in 1862, I described no less than four distinct forms of stasis. I proposed to designate that induced by irritation *homogeneous* stasis, because the blood-corpuscles become so blended together as to entirely lose their outlines, and present the appearance of a uniform and continuous plug filling up the capillaries.

This peculiar blending of the corpuscles is dependent upon the law I have been describing, viz. that of double cohesion, and is brought about by diminished quantity of liquor sanguinis in a part in proportion to the corpuscles, and by loss of fluidity in that which remains.

One of the primary effects of irritation is neural paralysis of the minute arteries which supply capillary tracts, and this paralysis gives rise to increased diosmotic action, in fact to exudation of liquor sanguinis, consequently there is a lagging behind of the corpuscles, and an increase of their numbers in the capillaries; the plasma, too, which still surrounds the corpuscles in the capillaries, is modified, and when a certain relation has been reached between the corpuscles and the plasma, the former blend together precisely in the same manner as the soap-bubbles, or as the blood-corpuscles exhibited in the photographs. This completely arrests the passage of blood through the capillaries, which become as much occluded as if blocked up by solid fibrin.

I have frequently had opportunities of watching in the transparent webs of frogs the mode in which this homogenous stasis is resolved. In these creatures the restoration of the circulation commences some hours after the application of the irritant. When the circulation is about to be resumed, the stagnation in the vessel appears to thaw as it were. The corpuscles are not pushed onwards in the mass as a coherent plug; but the homogeneity of appearance is suddenly lost by the resumption of their normal form by the corpuscles and the reappearance of their differentiating outlines, which were previously obscured by their blending with one another and with the walls of the vessels. Before this takes place, the vessel very gradually assumes a lighter tint, passing in some instances from a deep red to a pale orange. This appears to be due to a washing away of extruded colouring-matter.

When this change from homogeneity to heterogeneity commences, although sufficiently progressive in its character as it traverses the vessel, it nevertheless takes place with considerable rapidity. It is evidently brought about by the gradual permeation of the new liquor sanguinis among the corpuscles, and the contemporaneous abolition of their cohesive attraction for each other in accordance with the principles previously established.

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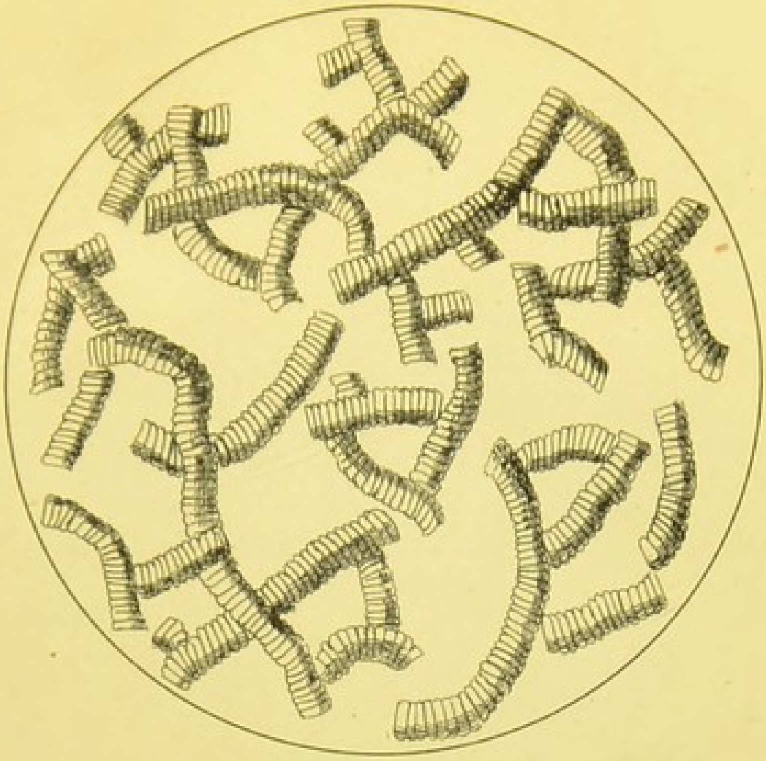
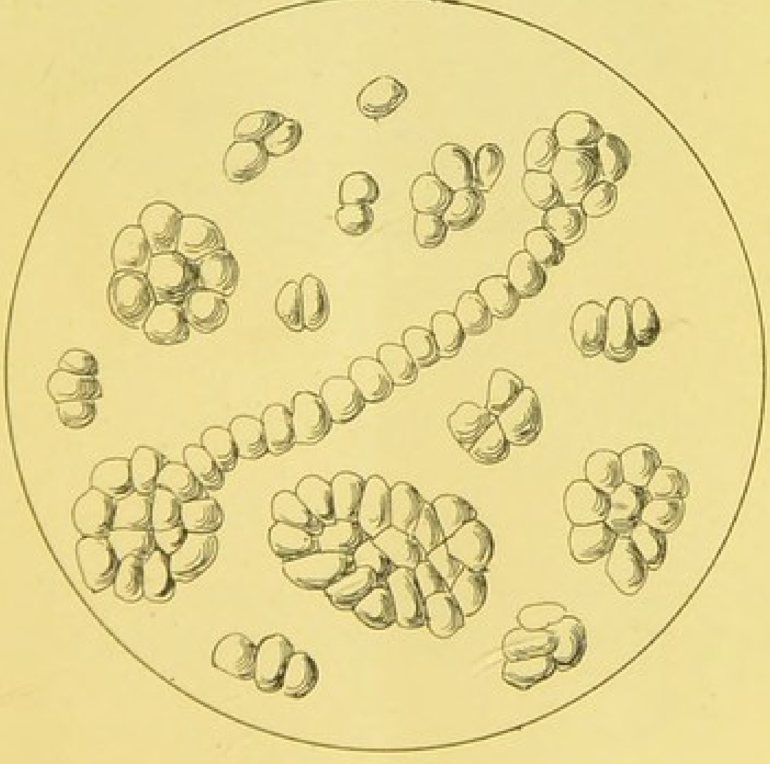
PLATE 1.

FIG 1.



APPEARANCE PRESENTED BY HUMAN RED CORPUSCLES WHEN ARRANGED IN ROULEAUX.

FIG 2.



MODE OF AGGREGATION OF THE HUMAN RED BLOOD CORPUSC
AFTER BEING RENDERED SPHERICAL BY CHANGES IN THE LIQU

PLATE 2.

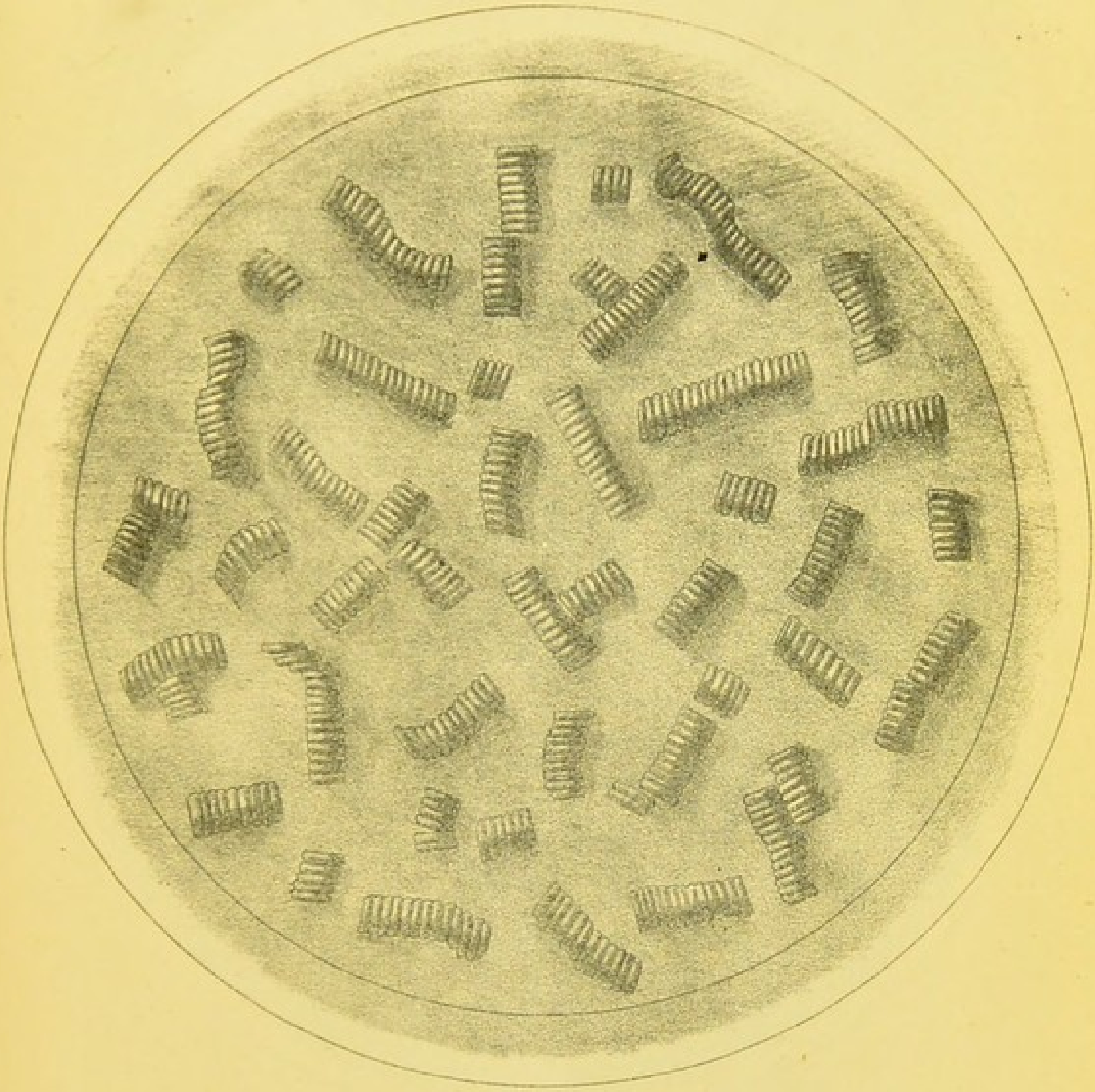
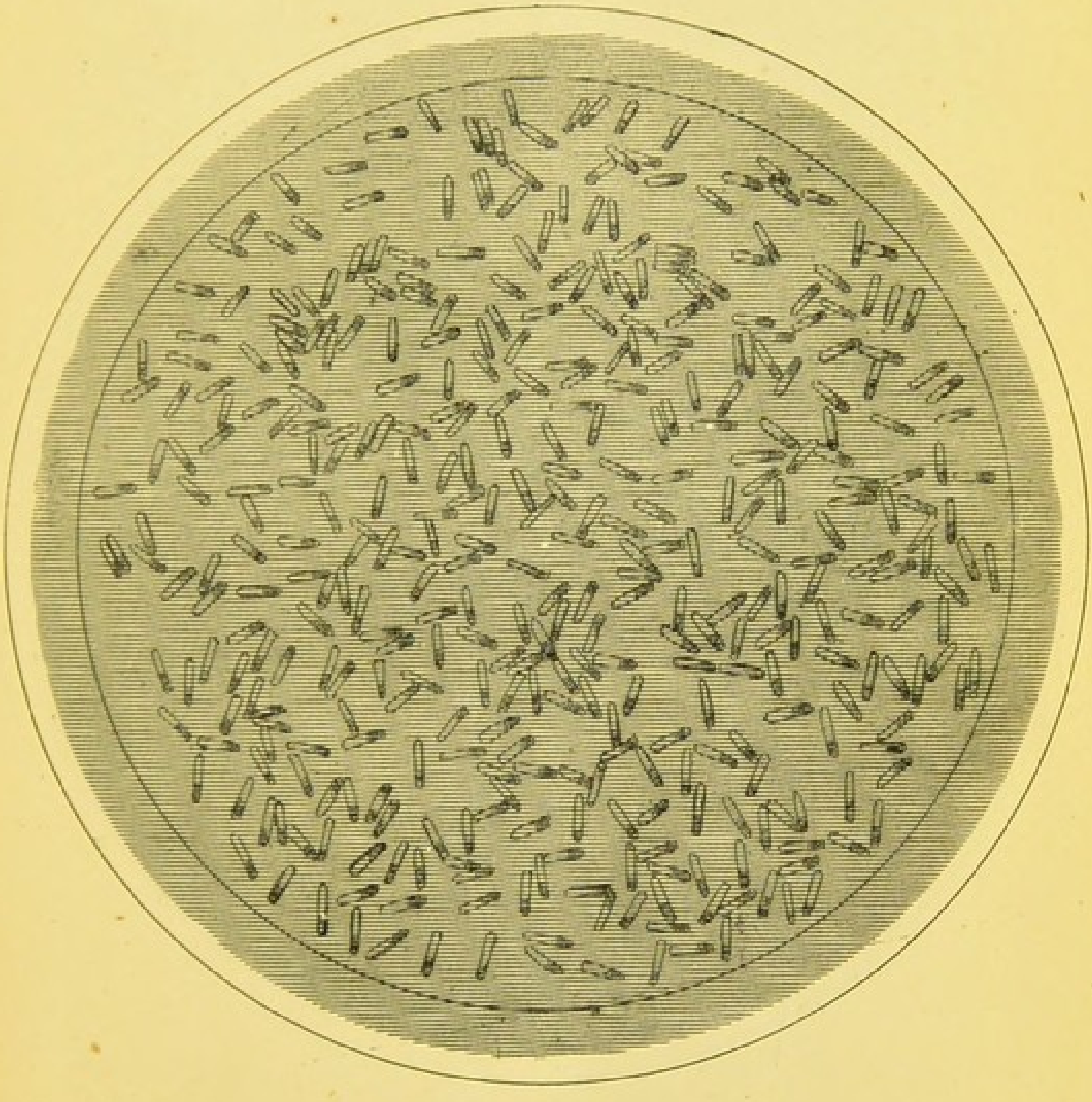


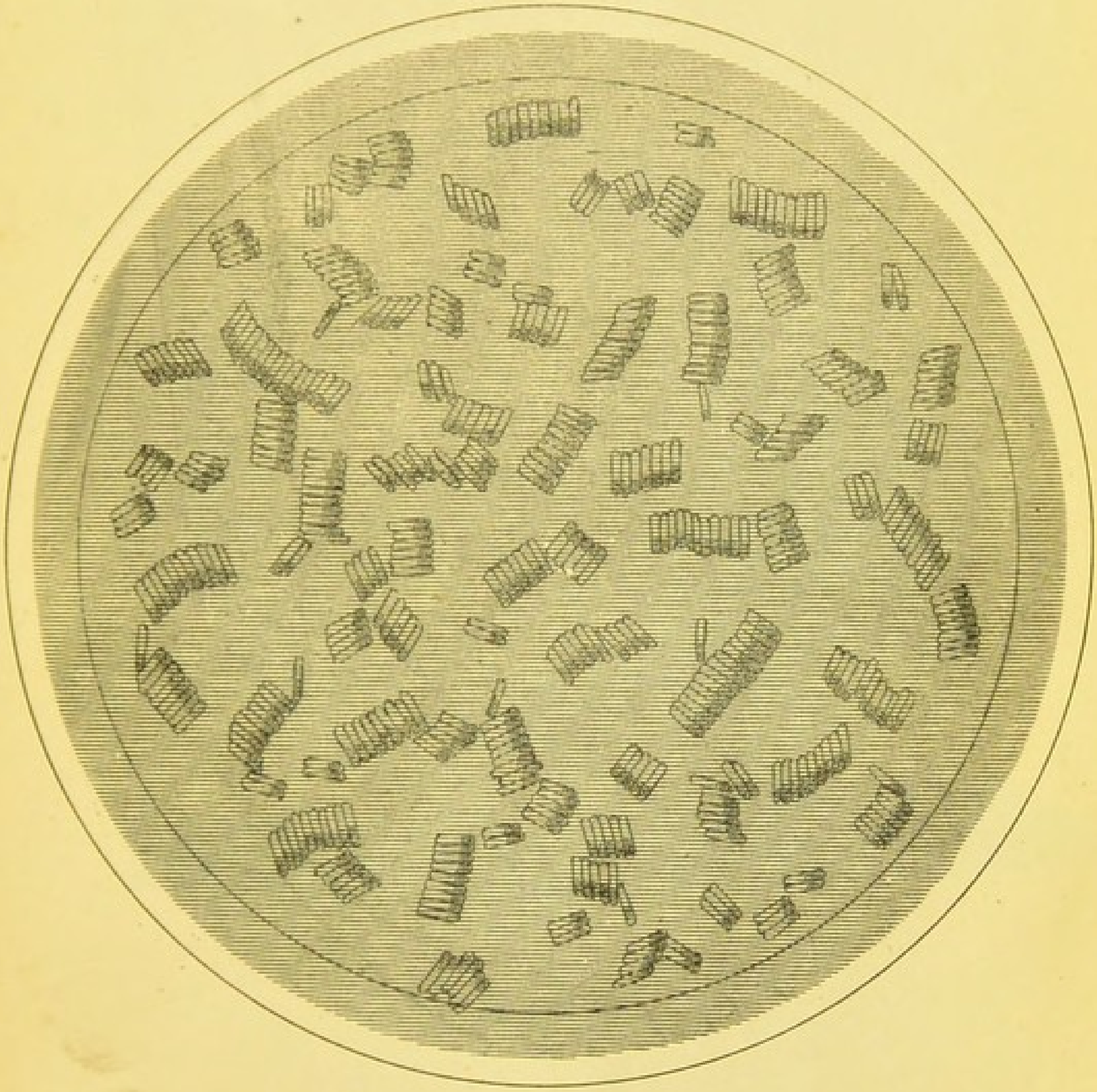
ILLUSTRATION OF THE MODE IN WHICH POISED CORK DISCS PARTIALLY IMMERSED IN LIQUID ARRANGE THEMSELVES

PLATE 3



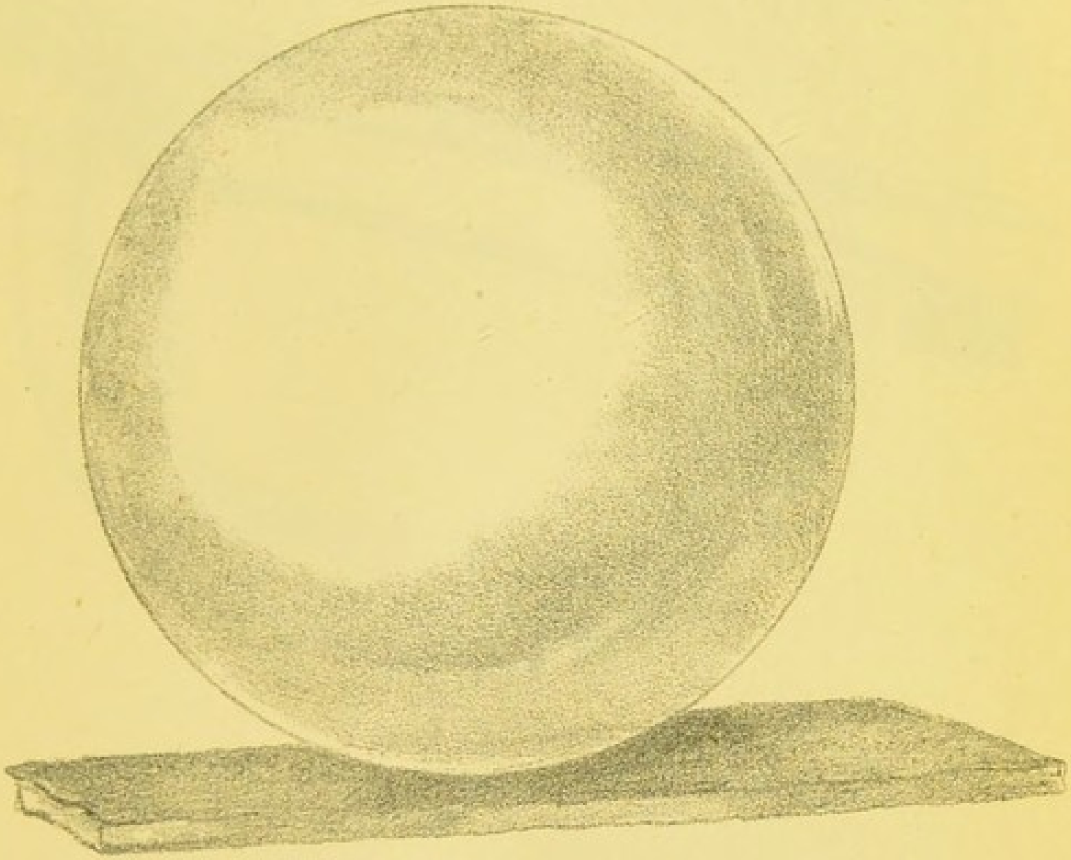
THIS DIAGRAM SHOWS THAT THE ATTRACTION IS DESTROYE[D] BY ENTIRE SUBMERGENCE OF THE CORK DISCS — IT WILL B[E] SEEN THAT THEY REMAIN ISOLATED AND DO NOT FORM ROULEAUX AS IN PLATE 2

PLATE 4



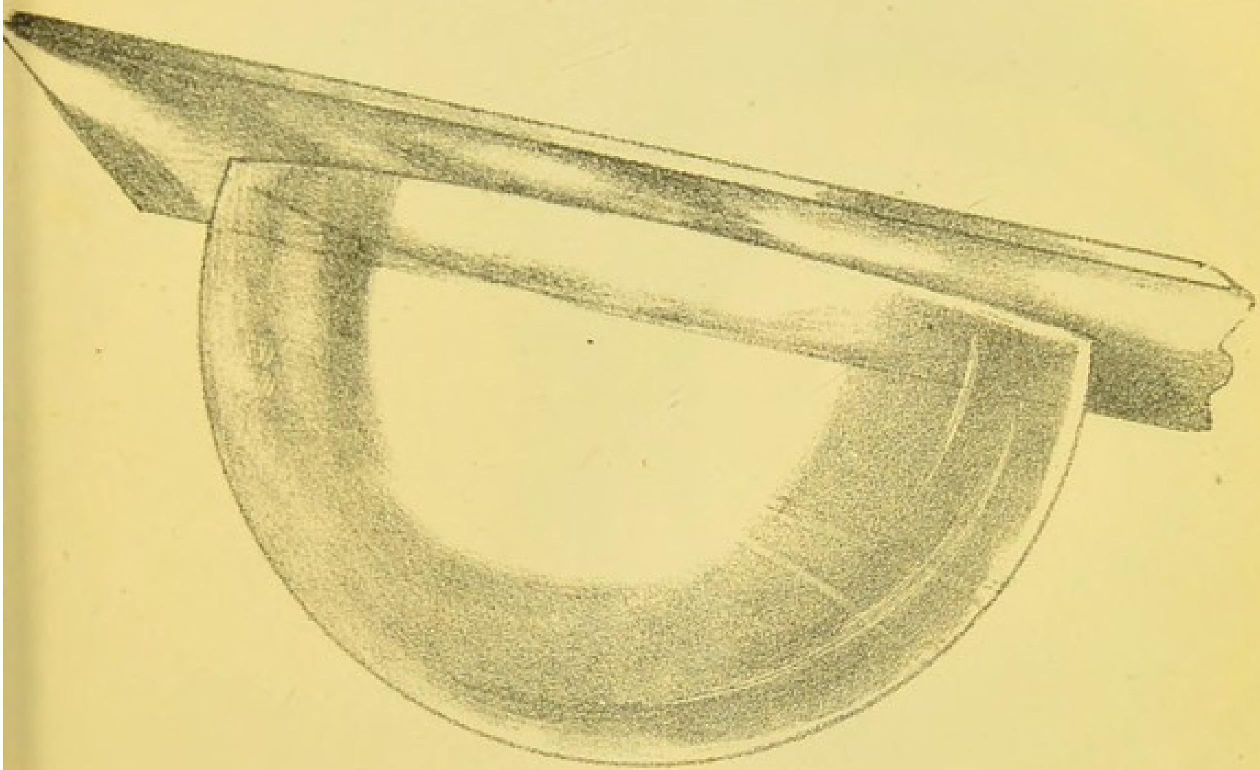
CORK DISCS WHICH PREVIOUSLY TO ENTIRE SUBMERGENCE HAVE BEEN WETTED WITH SOME LIQUID ANTAGONISTIC TO OR IMMISCIBLE WITH THE ONE IN WHICH THEY ARE SUBMERGED THEY ARE SEEN TO FORM ROLLS AS IN PLATE 2

PLATE, 5,



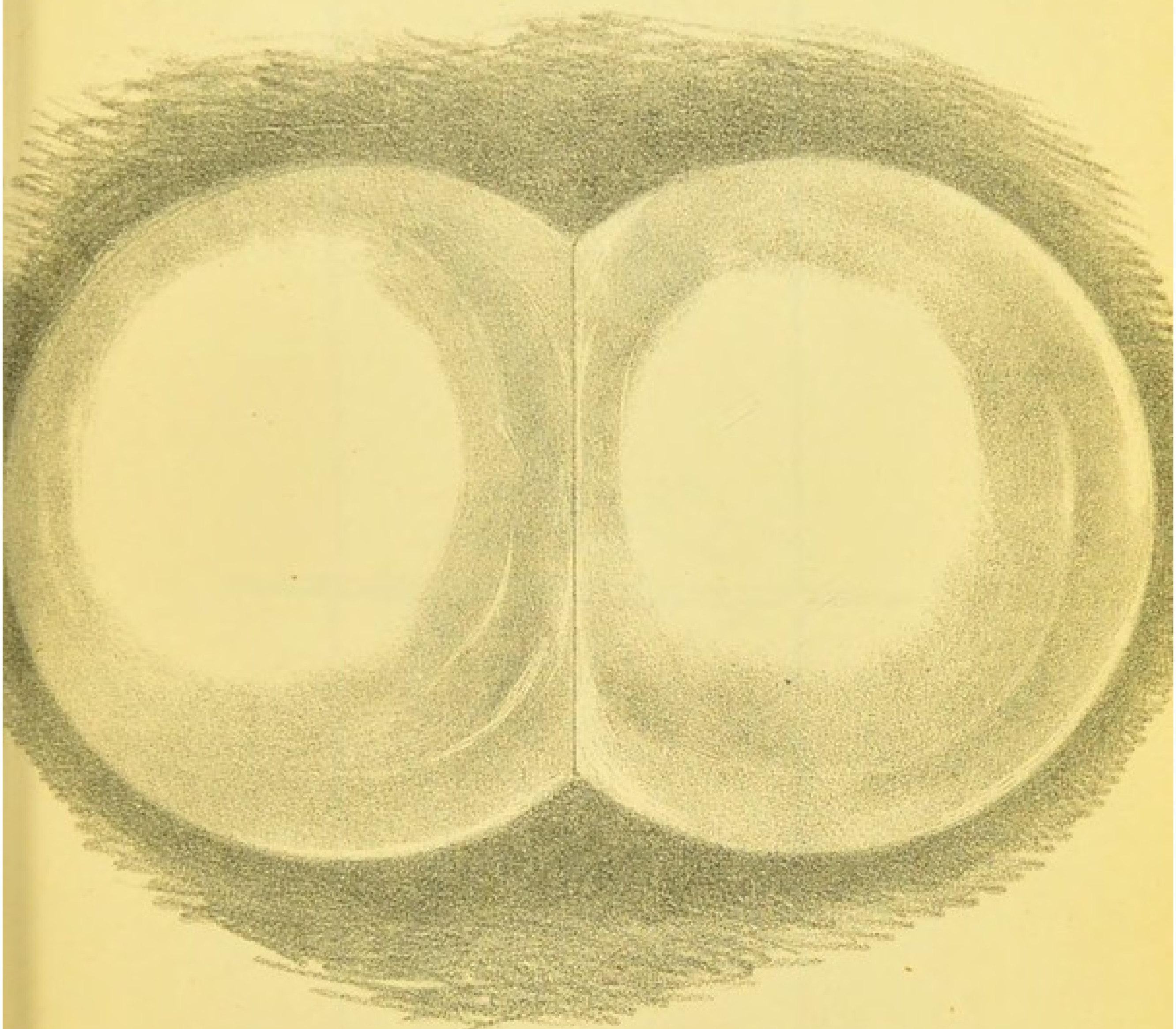
THIS FIGURE SHOWS THAT A BUBBLE RETAINS ITS SPHERICAL SHAPE WHEN IN CONTACT WITH A DRY ROUGH SURFACE VIZ, A PIECE OF CLOTH,

PLATE, 6,



PROGRESSIVE ATTRACTIVE ACTION EXERTED UPON A BUBBLE WHEN ANY POINT OF ITS CONVEXITY IS ALLOWED TO TOUCH THE SURFACE OF A WETTED PLATE OF GLASS

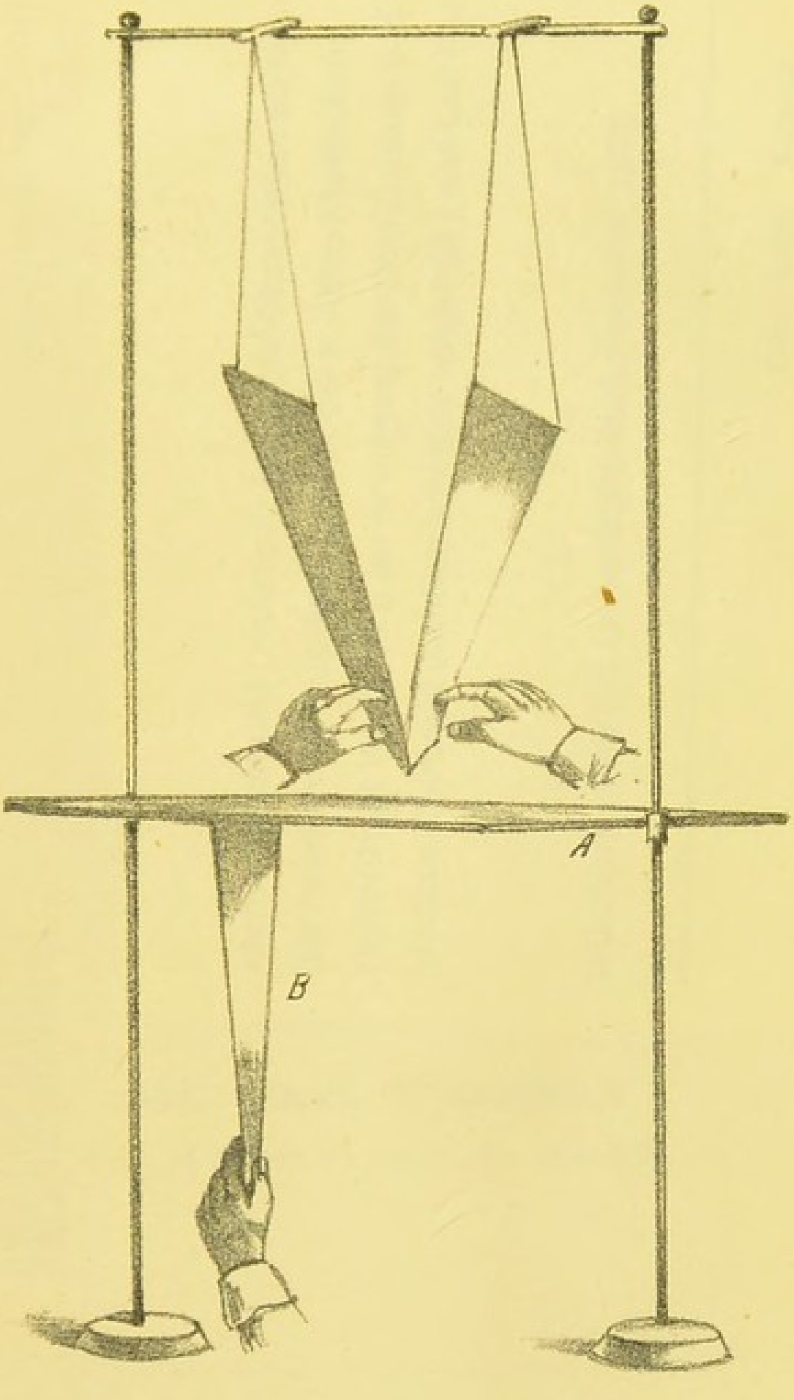
PLATE . 7.



PROGRESSIVE ATTRACTIVE ACTION EXERTED BY BUBBLES UPON EAC
OTHER WHEN TWO POINTS OF THEIR CONVEXITIES ARE ALLOWED TO
COME INTO CONTACT.

PLATE , 8 ,

DIAGRAM OF AN ARRANGEMENT ILLUSTRATIVE OF THE PHENOMENON DESIGNATED BY THE AUTHOR, PROGRESSIVE COHESIVE ATTRACTION.



A REPRESENTS A WELL CLEANED GLASS PLATE THE UNDER SURFACE OF WHICH IS UNIFORML WETTED.- IN CONTACT WITH THIS IS LAID EVENLY A PIECE OF THIN CAMBRIC PAPER B ALSO WETTED - IF THE PAPER BE NOW DRAWN DOWN FROM THE GLASS AS DEPICTED THEN LIBERATED IT WILL PROGRESSIVELY ASCEND & REAPPLY ITSELF TO THE SURFA OF THE GLASS - IF A TRIANGULAR FORM BE GIVEN TO THE PAPER WE GET AN INCREASE OF ATTRACTIVE POWER IN RELATION TO THE WEIGHT & MORE EASY MANIPULATION - THE UPPER PART OF THE DIAGRAM EXHIBITS THE SAME PRINCIPLE IN ACTION BETWEEN TWO WETTED PIECES OF SUSPENDED PAPER THE EXTREME POINTS BEING BROUGHT INTO CONTACT, THE SHEETS OF PAPER BECOME GRADUALLY APPLIED TO EACH OTHER THROUGHOUT THEIR EN TIRE EXTENT.