Osmosis and life according to Dutrochet

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***Figure 1:* Henri Dutrochet on a medal** *(by David d'Angers)*

The years 1820-1840 saw the rapid development of cellular theories, the premises of which had been formulated by Henri Dutrochet (1776-1847), and whose essence is attributed, rightly or wrongly, to a German, Theodor Schwann (1810-1882). Yet Dutrochet's name will always be remembered for the discovery of the phenomenon of osmosis. We are going to evoke this discovery, its consequences for the development of general physiology in the 19th century, and its recent interpretation on the level of molecular mechanisms.

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In 1827, at the age of 51, Dutrochet published in *Annales de Chimie et de Physique* (text BibNum) an article analysing the phenomenon of osmosis. In this article, entitled 'New observations on endosmosis and exosmosis, and on the cause of this double phenomenon,' Dutrochet provides details on the mechanisms of osmosis, and develops remarkable conclusions on vital processes.

In several lines of the introduction, he starts by precising the results of a memoir published eight months earlier:

> *When two fluids differing in density and chemical properties are separated by a thin and permeable membrane, there are formed across this membrane two currents of opposite directions and of unequal force. It follows that the fluid accumulates in greater quantity at the side towards which the strongest current is directed. These two currents exist in the*

hollow organs which form organic textures, and it is there where I have described them under the names of endosmose *and* exosmose.

Osmosis, a phenomenon of diffusion

Osmosis is a physical phenomenon of diffusion. Liquid diffusion corresponds to the harmonisation of a solute (dissolved substance) in a solvent. Osmosis is a special case of liquid diffusion, which occurs when two solutions of different concentrations are placed on either side of a membrane that is semi-permeable, thus allowing the passage of a solvent (generally water) but not a solute.

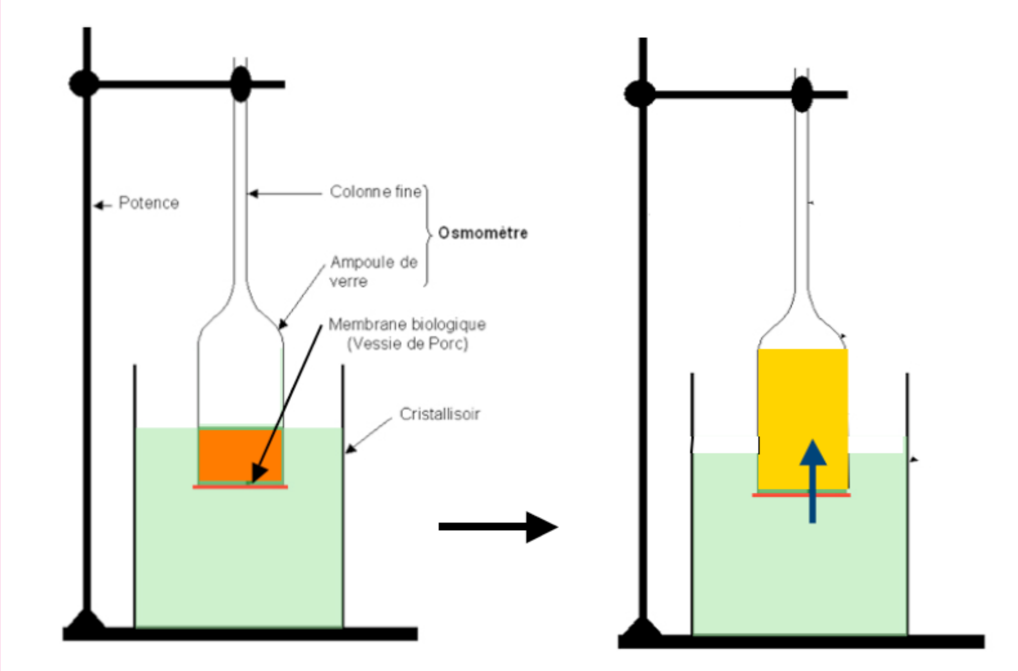

***Figure 2:* diagram of osmometer; (left) a glass ampoule with solute (orange) plunged in a beaker containing solvent (water, light green)**. *A semi-permeable membrane (here a pig bladder) separates the two compartments; (right) the solvent has diffused across the cellular membrane and diluted the solution until the hydrostatic pressure of the tube balances the osmotic pressure (this is the minimum pressure needed to stop the passage of the solvent from a solution less concentrated towards one more concentrated).*

The difference in concentration causes a difference in osmotic pressure, which entails displacement of the solvent across the membrane and dilution of the more concentrated solution. It is important to understand that the solvent (water) diffuses in *two* directions[1] (likewise, diffusion takes place in all directions), but that the most important flow (the final flow) takes place towards the more concentrated solution, and dilutes it.

1. Dutrochet indicates: 'There are formed across this membrane two currents of opposite directions and of unequal force'. *Op. cit.* p. 107.

The solvent, penetrating into the ampoule, causes the solution in the tube to rise until the osmotic pressure and the hydrostatic pressure equalise (which results, in particular, from the weight of the column of water). This balance reached, the hydrostatic pressure makes as many water molecules pass through the membrane (towards the beaker) as the final osmotic flow makes pass towards the internal vase.
A well known case of osmosis in practice is the rise of water in trees. The cells of roots 'pump' ground water by osmotic pressure. The sap (a nourishing aqueous solution) moves up the roots and towards the branches by osmotic pressure too.

Indeed, by placing the strands of a mould mixed with water in a watch glass, he had observed, under the microscope, the water entering the 'capsules' that constituted them, and the corresponding expulsion of globules without contraction of capsules. Some time later the animal kingdom supplied him with a similar example, when he noticed that the spermatophore of the sperm sacs of slugs were expelled if these bags were placed in the water. He explained this expulsion by the influx of water through the sac walls. In another experiment, he placed in water a chicken caecum filled with milk. After 36 hours, the caecum had become turgid[2] and increased by 50 % in weight. On the other hand, when filled with water and placed in a solution of gum arabic, it lost weight. He named the action by virtue of which the small hollow organs fill with liquid which seems to be forcibly pushed into and accumulated in their cavity, *endosmosis*. When the most dense fluid is outside the cavity, the less dense fluid, which is inside, is pushed outside by inverse action[3] which Dutrochet called *exosmosis* (a word derived from *ωσmoς* [osmos], impulse). Thirty years later, Thomas Graham (1805-1869) used the term 'osmosis' interchangeably for both endosmosis and exosmosis, and this is the term that will be used from hereon.

SEARCH FOR CAUSES: CAPILLARITY, ELECTRICITY OR OTHER?

Dutrochet describes the experimental device that he uses. It is the osmometer, which, in its simplicity, will be used, hardly modified, by generations of high school students:

2. 'Turgidity' means swelling in physiology.
3. *L'Agent immédiat du mouvement vital dévoilé dans sa nature et dans son mode d'action chez les végétaux et chez les animaux,* Baillière, 1826, p. 115.

A tube of glass furnished with a wide mouth, which was closed with a plated of baked pipe clay [...] was filled with a solution of gum arabic, and then plunged in water, above which the empty part of the tube rose vertically. The endosmose *took place, and the gummy fluid rose gradually in the tube.*

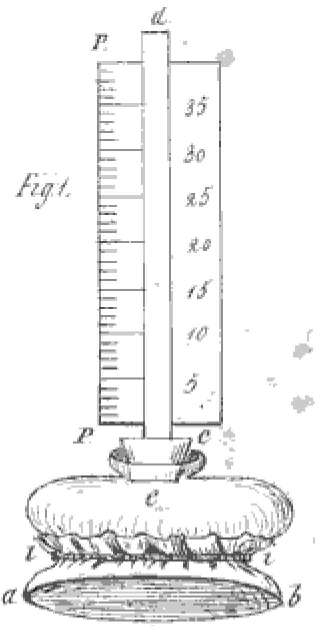

***Figure 3:* Dutrochet's Osmometer.** *Where ab is a semi-permeable membrane, and cd is the gauge used to measure the water height.*

The reading of the following lines reveals a conflict between Dutrochet and Poisson. Indeed, with this device, Dutrochet is going to demolish Poisson's theory of the mechanism of osmosis. The latter, in an article published a few months earlier,[4] envisioned a container in which two different liquids were separated by a vertical partition pierced with little, horizontally placed capillary canals. He proposed, logically, that the liquid with greater 'capillary strength' (that is the strongest ascent in a capillary tube) would push out the other liquid through the canal, and would pour in and occupy the other compartment. Dutrochet tested this proposal on various liquids and obtained variable results. Sometimes, there was an accumulation of fluid at the side of the liquid with the greatest capillary strength, while at others it was the opposite. Dutrochet concludes from this: 'Capillary action is not the cause of the phenomenon of accumulation'.

4. Poisson, S-D.. 'Note sur des effets qui peuvent être produits par la capillarité et l'affinité des substances hétérogènes', *Annales de Chimie et de Physique,* 1827, **35**, 98-102.

Later studies on the effect of temperature will consolidate his opinion. Poisson, who was informed of Dutrochet's only when they were published, does not pretend to give a full explanation:

> *I have not claimed, however, to assign to these phenomena a cause exclusive from all others, and neither did I give it a sufficient explanation.* [...] *They could be produced by capillary action without an appeal to electricity, in rest or in movement.*

Dutrochet maintains that :

> [...] *it is caused by electricity, allowing, however, that this electricity does not manifest itself in the galvanometer* [...]. *It appears to me probable that this electricity is caused by the contact of the fluids with the separating membrane.*

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Two similar experiments will later consolidate his opinion. He makes the electric current of a battery pass through two compartments separated either with a membrane of chicken caecum or a plate of clay. He notices that, in both cases, water passes to the compartment connected with the pole of the pile; he proposes at first that an electric phenomenon lies at the origin of endosmosis.[5] Let us note that the first experiment had already been carried out by R. Porret[6] in 1816, and that this had been acknowledged by Dutrochet. But in 1832 – a turnabout: Dutrochet claimed that electricity played a role because it 'only produced the heterogeneity between the two liquids of which one was subject to the positive pole and the other the negative pole'[7]. To prove this, he presented an experiment where he simply added violet dye to both compartments. After the passage of current, the liquid inside the caecum became green, while that outside was red. In contemporary terms, the transfer of water is explained by saying that the electrolysis of the water releases two molecules of hydrogen at the cathode, and a single molecule of oxygen at the anode, which creates a difference of osmolarity between both compartments, resulting in the flow of water towards the cathode. Yet, in the case of the experiment with a plate of clay, Dutrochet was partially wrong in his negation of the role of the electric field: it did indeed have a direct effect, by disrupting the double ionic layer

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5. *Nouvelles recherches sur l'endosmose et l'exosmose suivies de l'application expérimentale de ces actions.* Baillière éditeur, 1828, page 36.
6. Porret, R. Jr. 'Expériences galvaniques curieuses', *Annales de Chimie et de Physique,* 1816, 2, 137-140. Actually, the author is Robert Porrett (1783-1868), a British amateur chemist.
7. *Annales de Chimie et de Physique*, 1832, 49, 411-437.

covering the surface of the capillaries. Dutrochet had just copied (supposedly unwittingly) the experiment of Ferdinand-Friedrich von Reuss[8] (1778-1852), who is credited with the invention of the electro-osmosis in 1808, a purely electric phenomenon, and which was going to prove invaluable in fighting rising damp.

***Figure 4 :* Treatment of damp walls with electro-osmosis;** *(left) Water ascends in the capillaries of the positive pole (the ground) towards the negative pole (the wall), thus inflicting damage; (right) inserting electrodes into the wall (copper, positive pole) and in the ground (iron, negative pole) inverts the natural wall / ground polarity, and the passage of water changes direction. Some mortar is then injected by electrophoresis to block the capillaries (photo credits Sté Sofrelop).*

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For the 20 years that Dutrochet was interested in osmosis, he invariably displayed great scientific integrity, and did not hesitate to acknowledge mistakes such as that of osmosis relying on electricity. Modesty also manifested itself when he admitted that he could not explain osmosis by a difference in the viscosity of liquids, as he had envisaged it. He revised his assertion according to which some liquids, such as sulphuric acid, were 'inactive' in terms of osmosis. In other words, he realised that acid simply destroyed the membrane. In his last article, of 1837, he observed - using oxalic, citric and tartaric acids of low concentration - an effect irreconcilable with what he had learned to that point, and admitted he could not explain it.

He also regretted that the terms he had coined, endosmosis and exosmosis, had permeated into common terminology in relation to the understanding that the impulse in a cell leading to turgescence could very well be inverted and lead

8. Reuss, F.F. 'Sur un nouvel effet de l'électricité galvanique', *Mémoires de la Société Impériale des Naturalistes de Moscou* 1809, 2, 332

to plasmolyse if the cell were plunged into an environment more concentrated than its internal one.

Finally, some 11 years after his first article, he openly admitted in 1837 that he could not explain osmosis. He wrote there about 'the penetrating force of water' being proportional to the relative excess density of liquids. He envisaged two 'intercapillary' forces, essentially different, one of which remains unknown.[9]

THE MECHANISTIC CONCEPT IN PHYSIOLOGY, OPPOSED TO VITALISTIC CONCEPTION CURRENT AT THAT TIME

In the experimental device presented in the analysed article, Dutrochet used clay to close the glass tube, while previously he had used only animal membranes, such as pig bladders or chicken caecums. He remarked:

> *My experiments have shown me that this phenomenon is not exclusively produced by organic membranes. Porous inorganic plates very thin produce them also.*

The approach is truly innovative: 'Contrary to the usual process, which consists in calculating physiological phenomena on the physical model, he overthrows the data and makes a physiological phenomenon a model for the physical phenomenon, which, in return, reveals laws common for both categories of phenomena'.[10]

This is the point determining not only Dutrochet's evolution towards the experimental approach, but also that of his contemporaries, and the reflections that arise from this. Let us note that Poisson sees confirmation of his theory in that:

> *A living body no longer being necessary for the production of these phenomena, the opinion which attributes them to a general cause, such as capillary action, acquires more probability.*

The conclusions drawn by Dutrochet changed the course of the development of life sciences in the 19th century:

> *Thus the double phenomenon of endosmose and exosmose is by the fact and not by its nature a phenomenon entirely physical. It is the point at which the physiology of living bodies is confounded with the physiology of inorganic bodies. The more we advance in the knowledge*

9. 'Mémoire sur l'endosmose des acides', *Mémoires de l'Académie des sciences*, 1838, 15, page 311.
10. Schiller, J. et Schiller T., *Henri Dutrochet. Le matérialisme mécaniste et la physiologie générale*. Albert Blanchard, 1975, page 31.

of physiology, the more reason we have for ceasing to believe that the phenomena of life are essentially different from physical phenomena; this opinion, which the authority of Bichat has above all others contributed to establish, is indubitably erroneous.

Here is the clear and precise comment which frontally attacks the vitalism advocated by Bichat 25 years before. Bichat considered life as 'all the functions which oppose death' and claimed that the vital principle, underlying all operations of life, is a resistance to death, understood as a change of physical objects. He thus imagined a battle between the dynamics of matter (which proceed towards degradation) and those of life (which are about preservation).

Mechanism *vs.* vitalism

Vitalism is a philosophic approach, and was for a long time considered scientific, according to which life is not reducible to physical-chemical phenomena (the mechanistic concept). It envisages life as matter enlivened by a principle or a vital force, which is ascribed to all living creatures as something additional in relation to the laws of matter.

***Figure 5 :* François Marie Xavier Bichat (1771-1801), French doctor of medicine and physiologist.**

The scientific vitalism was especially advocated by Bichat, who considered life as all the functions which oppose death, understood as the change of physical objects. Thus there was a conflict between the dynamics of matter (towards degradation) and those of life (aiming at preservation). Such theoretical coherence provided vitalism with a certain success in scientific opinion until the 19th century.

Dutrochet's mechanistic concept was reinforced in 1828 by Wöhler's synthesis of urea, namely the artificial creation of an organic compound, the process of which consolidated Dutrochet's vision by abolishing the barrier between inorganic and organic chemistry. Furthermore, for Dutrochet, there is a similarity between vital phenomena in animals and plants. He wrote in 1837:

> *Life is one. The differences shown by its various phenomena, in all things that are alive, are not fundamental differences. If these phenomena are tracked down to their origins, the differences are seen to disappear, and an admirable uniformity of plan is revealed.*[11]

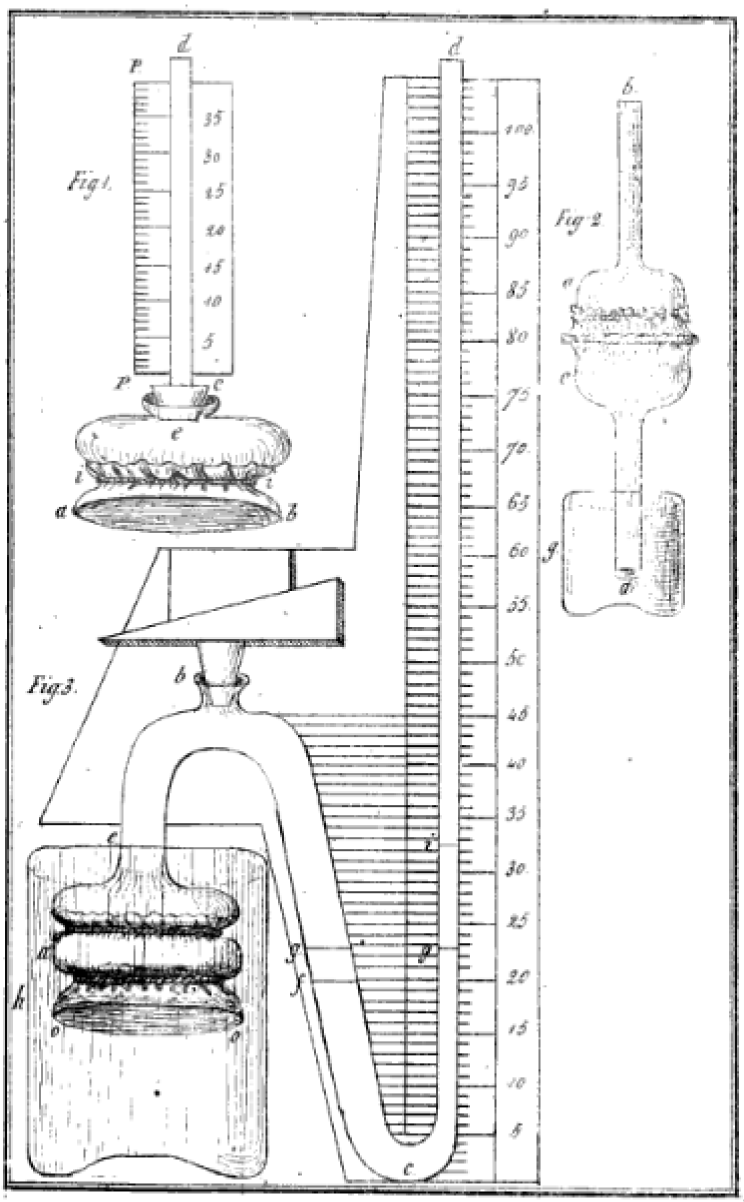


***Figure 6 :* Board of figures (p. 111) from the 1828 work by Dutrochet** *(cf. footnote 5). The osmometer is the same as the one under figure 3.*

11. *Mémoires pour servir à l'histoire anatomique et physiologique des végétaux et des animaux*, vol. 1, Baillière 1837, p. 326.

DUTROCHET'S VISION OF A CELL.

To see how Dutrochet came to understand the importance of membranes, it is necessary to note that he developed at first the concept of general physiology based on the cell. For him, utricles (cells) of various tissues were the fundamental part of their structure. The variations of structure have no importance. Cells differ only by the nature of liquids that they contain; yet this difference of liquids contains evidence of difference in the intimate structure of the membrane that forms an elementary utricle. This functional conception of cell is the most scientific that the first half of the 19th century knew.

The difference of secretory action proves difference of the nature of the secretory filter (the membrane). The active element is the cell wall. Thus the notion of cellular membrane is omnipresent in Dutrochet's memoirs; he constantly hints at it, but does not elaborate upon it. This is not surprising when we consider that the very existence of these membranes was questioned for a long time; at the end of the 19th century, the cell was considered by some as a colloidal mass without any clear border. It was not until 1958 when the first photo using electronic microscopy definitively convinced all scientists of its existence.

About plant cells, Dutrochet writes that 'fluids, to pass from one hollow organ to another, need to pass two walls akin to these organs: because observation shows that all these organs have a proper membrane each'.[12] This assertion is original compared with that of previous authors, who thought, on the contrary, that there was a direct communication between 'organs' (plant cells). As for animal cells, Dutrochet described the cells of the salivary glands of a snail, and specified that they 'faint as soap bubbles in the presence of potassium hydroxide'. He observed well that endosmosis obtained by the suspension of cells in water led to the lysis[13] of cells, and said about this in the red blood cell (haemolysis) that 'it is surrounded by a membrane of an extreme delicacy.' It is amusing to note the mistaken proposition that the membrane is the 'only depositary of the red matter which colours these corpuscles', whereas haemoglobin does not reside in the membrane.

12. *Recherches anatomiques et physiologiques sur la structure intime des animaux et des végétaux, et sur leur motilité*, Baillère 1824, p. 49.
13. 'Lysis' means bursting of a cellular membrane.

He essentially worked on pig bladders and chicken caecums, that is, he used epithelial tissues.[14] The structure of these tissues is complex and contains, in particular, an epithelium made of closely connected cells bound by tight junctions of proteins, which block the circulation of fluids between cells and provide for impermeability between tissular compartments. Naturally, the passage through an urothelium (the epithelium of the bladder) raises additional problems with regard to the entry of a molecule into cells put in suspension and isolated in an aqueous environment for the needs of the experiment. Dutrochet, limited by the knowledge of his time, was not able, obviously, to properly investigate these small structures and to analyse the details of their osmotic function. For him, cellular membranes, as well as epithelia represented 'black boxes'. He never envisaged the concept of semi-permeability, that is, the permeability of the membrane only in the solvent (water), and its impermeability in other constituents of the solution, which in fact supplied the explanation of the phenomenon, as we shall see below. For Dutrochet, there were always two opposing currents across membranes; that of exosmosis was less important, as his experiments with the indigo dye allowed him to claim. He was not totally wrong, for the ideal semi-permeable membrane does not exist, and the real membrane with a whole network of channels and pumps is far from it.

THE PRECURSORS AND THE SUCCESSORS - VAN'T HOFF'S NOBEL PRIZE

What was the historical environment of Dutrochet's research on osmosis, before the 1820s and after? How did it influence the notion of semi-permeability? As has been said, the discovery of osmosis is often attributed to Dutrochet. But this is not taking into account the study by Abbot Jean-Antoine Nollet[15] who, in 1748, immersed in a water container a cylindrical phial filled with ethanol ('spirit of wine') and closed by a bladder. He noticed, after five hours, that the bladder was much inflated.

14. An epithelium is a tissue of closely connected cells. An epithelium is often found at the border of two environments: epidermis and cirumference of organs are epitheliums.
15. Nollet, H.L. 'Recherches sur les causes du bouillonnement des liquides', 1748, 101-104. *Mémoires de Mathématiques et de Physique* 1748 in *Histoire de l'Académie Royale des Sciences* 1748, Imprimerie Royale, Paris, 1752.

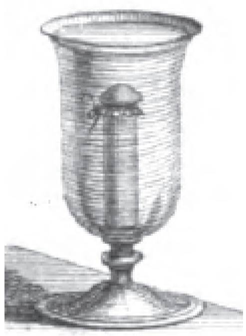


***Figure 7 :* One of the first experiments on osmosis, by Abbot Nollet (1700-1770)**

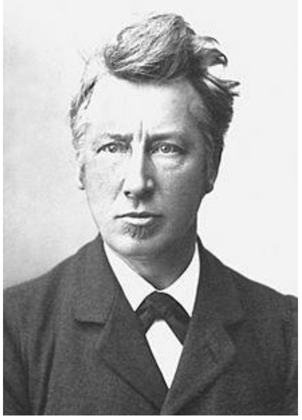
Resuming the experiment with a half-filled bottle, he observed that some water went into the bottle if the ethanol was in contact with the bladder. Pursuing his work, he demonstrated well that the membrane was permeable in water but not in alcohol. In other words, it was semi-permeable – a hypothesis that Dutrochet did not explore. We have already reported the work of Porret, which Dutrochet used to demonstrate the role of electricity, thus recognising the former's anteriority. Dutrochet stands out from these experimenters, as he recognised the generality of the phenomenon and looked for its mechanism and meaning.

As for the ensuing works, they are well-known, and it suffices to summarise them. In 1864, Moritz Traube (1826-1894) created the first artificial membrane that demonstrated osmosis with precipitates of copper ferrocyanide. In 1871, Hugo de Vries studied fragments of beet immersed in water; neither the sugar nor the intracellular pigment passed into the bath, and cells seemed unchanged inside their stiff cellulosic walls.

If pure water is replaced with a concentrated solution of NaCl, or with sugar, the cell contracts, separating from the cellulosic wall. De Vries concluded that the cellular membrane is semi-permeable, allowing water to pass but opposing the transfer of dissolved substances. Wilhelm F. Pfeffer (1845-1920) postulated in 1877 that all living cells are surrounded with a semi-permeable membrane, which has strong permeability in water but weak permeability in alcohol and sugars.

Finally, in 1886, Jacobus van't Hoff established the analogy between the aqueous solutions and the perfect gases, and applied thermodynamics to osmosis. He established a law similar to that of Gay-Lussac. For these results and those on chemical kinetics, he was awarded the first Nobel Prize, in 1901.

Figure 8 : Some scholars on the path to the understanding of osmosis in the 19th century. *After Porret[16] and Dutrochet, here at the top is an Englishman, Thomas Graham (1805-1869) and a German, Moritz Traube (1826-1894); below are a German, Wilhelm Pfeffer (1845-1920), and Dutchmen Hugo De Vries (1848-1925) and Jacobus van't Hoff (1852-1911).*



The desalination of sea water by reverse osmosis

The use of the osmotic phenomena is well-known in three fields. These are the electro-osmosis required to tackle humidity in walls (cf. figure 4), dialysis in medicine, in particular in treating renal insufficiency, and reverse osmosis for the purification of water and the desalination of sea water. The principle of this last application is to invert the direction of osmosis by applying pressure to the most concentrated liquid. It is then the solvent of the most concentrated environment that crosses the membrane towards the less concentrated environment (reverse osmosis). Here, the molecules of sea water (without salt solutes), pass into the compartment of pure water.

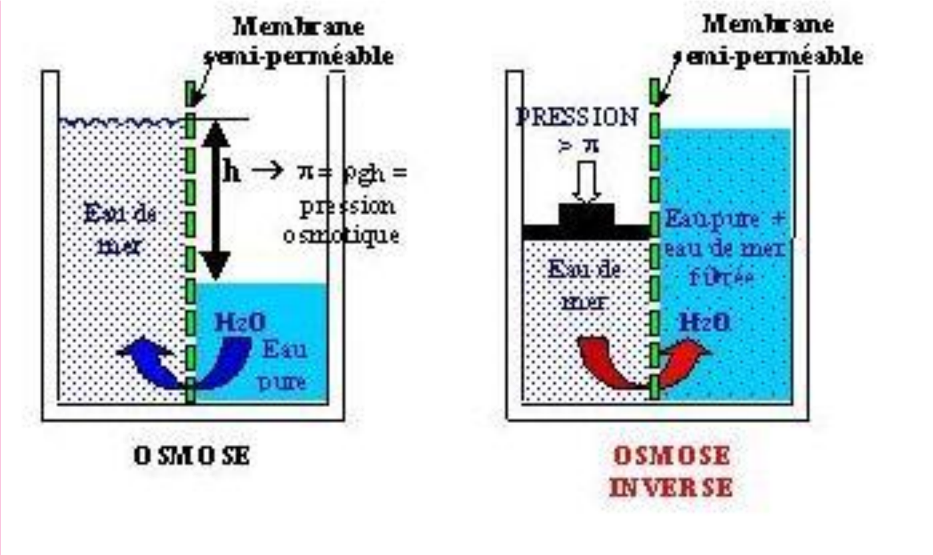


***Figure 9* : Desalination of sea water by reverse osmosis** *(image Culture Sciences Chimie, Eduscol, MEN) ; Below, desalination plant in Hadera, Israel (photo : Ide-tech)*

A SYMBOLIC DEMONSTRATION OF OSMOSIS, WITH HEMOLYSE FINALLY INCLUDED – AND A NOBEL PRIZE FOR AGRE

By what molecular mechanism does water penetrate into red blood cells placed in water and make them burst? In the 1990s, molecular mechanisms allowing the passage of water through animal membranes were still unclear. Indeed, it was difficult to explain the easy passage of water through membranes within the framework of the fluid mosaic model proposed in 1972 by Singer and Nicholson, and widely accepted by the scientific community. The passive transport of the water through such a membrane, along the gradient of concentration, is realised either by diffusion directly through the lipid bilayer, or by diffusion facilitated by a transport protein.

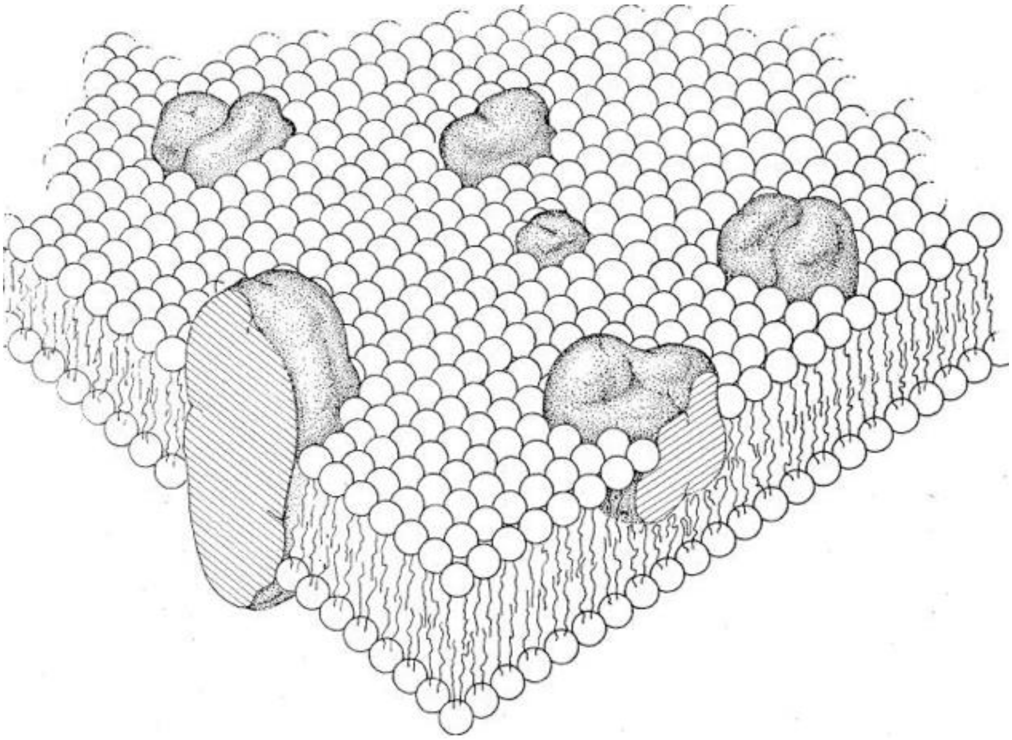


***Figure 10* :** *Singer and Nicholson's fluid mosaic model,* Science*, 1972, 175, pp. 720-731. In this model, the membrane matrix is made of a bilayer of phospholipids and cholesterol. Every lipid has the hydrophilic polar head directed to the outside of the membrane, and its hydrophobic tail (a chain of saturated or unsaturated fatty acid) directed inward the bilayer. Some proteins are buried in this bilayer. The group is heterogeneous and unconstant in space and time, hence its name: fluid mosaic.*

The use of experimental models of purely lipid bilayers allowed their water permeability to be determined, and it was found to be approximately 50 times weaker than that observed in red blood cells. Thus it was suspected that a membrane protein had to facilitate the entry of water. But what protein? In 1986, Gheorge Benga, a Romanian researcher (born in 1946), proved that a protein or a group of proteins could indeed facilitate the passage of water through the membranes of red blood cells.

In 1992, Peter Agre, an American researcher, reconstructed a protein of the red blood cell membrane (CHIP 28) in a xenopus egg, and observed that it induced water permeability. This protein, renamed 'aquaporin', was part of the group proposed by Benga and justified the high permeability of this membrane in water. A puzzle that had been insoluble for almost two centuries had finally been solved, and for this Agre received the Nobel Prize for Chemistry in 2003.

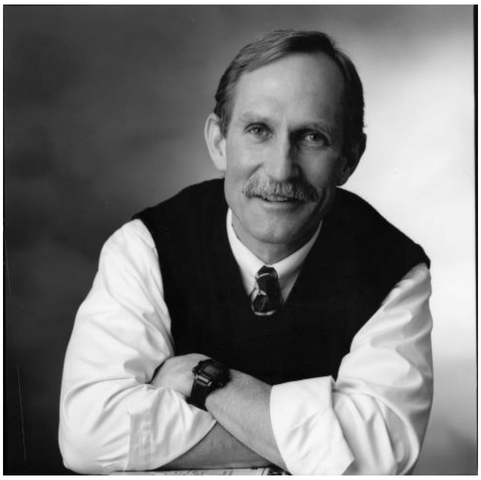


Figure 11 **: Peter Agre (born in 1949), Nobel Prize in Chemistry 2003** *(photo John Hopkins School of Medicine, Baltimore, Md).*

Since then, more than 500 aquaporins have been discovered. But it should not be assumed that the molecular mechanisms of the flow of water through the pig bladder or chicken caecum have been totally explained. In view of the complexity of these epithelia, controversies remain rife. The osmotic phenomena analysed by Dutrochet are still not totally understood.

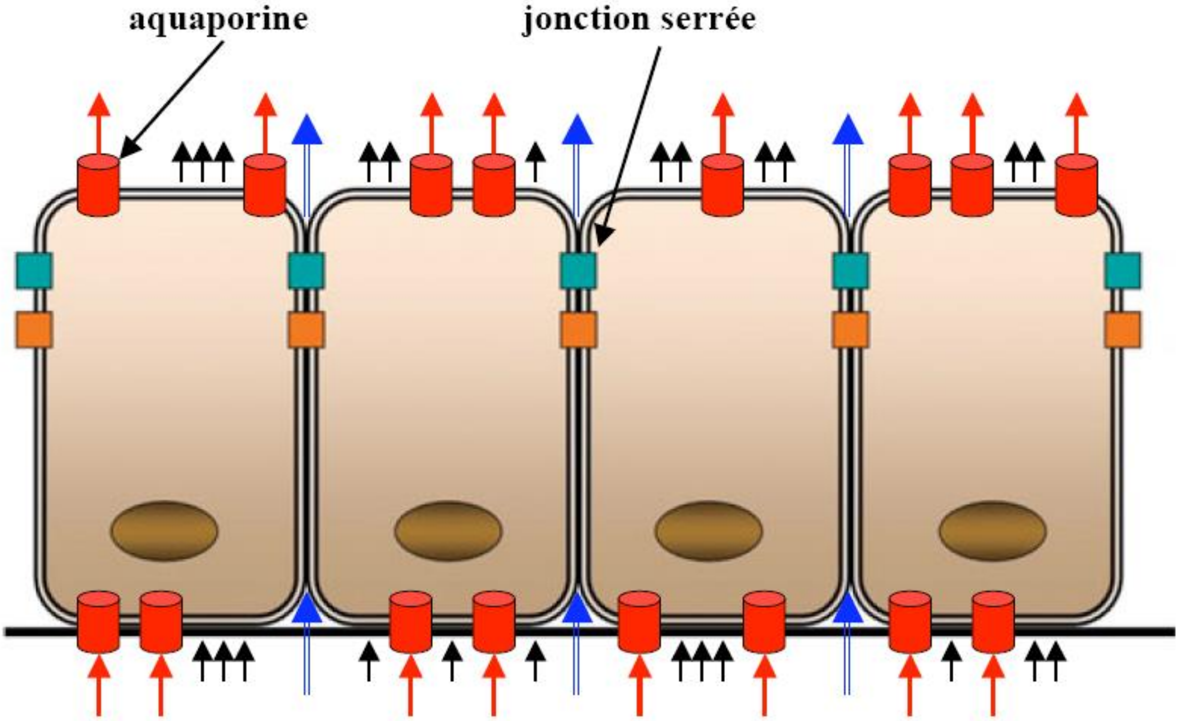


Figure 12 : ***Three possible ways that water could travel through an epithelium.*** *An epithelium (for example, a pig bladder or chicken caecum) includes a unicellular layer*

of cells in contact with one another, connected by tight junctions. If aquaporins are present, water will cross preferentially through them (red arrows). Water can also pass by passive diffusion through the lipid bilayers (blue arrows), or through the tight junctions (black arrows)[17].

Conclusions

In 1827, the osmotic phenomenon had been known for about 50 years, and Dutrochet was not the discoverer. But it is Dutrochet who, for the first time, focused on the analysis of its mechanism - by which he distanced himself from the approach of other botanists and physiologists of his time. It was also he who, for the first time, recognised the generality and significance of the process. He wrote in 1828 that 'endosmosis is indeed the fundamental action of life'.

He was original in considering cells as physiological entities, as the fundamental units of metabolic exchange - their nutrition being governed by the selective entry of nutrients through cellular membrane, waste being eliminated by their selective exit. He introduced a materialistic, mechanistic, physical process into the life sciences, allowing a biological phenomenon to be understood outside the vitalistic framework, which he considered as 'mysticism', and of which he was one of the most determined opponents in the years 1820-1830. He opened the doors of science to an exact and rational general physiology.

■

(May 2012)

(English translation published December 2015)

17. For details see Fischbarg, J., 'Fluid Transport Across Leaky Epithelia: Central Role of the Tight Junction and Supporting Role of Aquaporins'. *Physiological Reviews* 2010, 90, 1271-1290