EXPLAINING LIFE…

SYNTHETIC BIOLOGY THROUGH INORGANIC CHEMISTRY IN THE EARLY 20TH CENTURY

Abstract

Among the many great mysteries which science attempted to tackle in the 20th century, the ability to explain the origin of life has thrilled generations of researchers from all fields. When he invented ‘synthetic biology’, Stéphane Leduc (1853-1939), a professor at the Medical School of Nantes in 1933, really believed that he had found the answer. A century after his discovery, with the kind help and skills of our photographer, we have recreated his breakthrough experiments and tried to shed new light on all the magnificent forms and colours which his theory allowed him to create.

Keywords

Synthetic biology, Stéphane Leduc, history of chemistry, mechanisms of life, osmosis, chemical gardens.

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Abstract

Among the many great mysteries which science attempted to tackle in the 20th century, the ability to explain the origin life has thrilled generations of researchers from all fields. When he invented 'synthetic biology', Stéphane Leduc (1853-1939), a professor at the Medical School of Nantes in 1933, really believed that he had found the answer. A century after his discovery, with the kind help and skills of our photographer, we have recreated his breakthrough experiments and tried to shed new light on all the magnificent forms and colours which his theory allowed him to create.

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The very nature of experimental science is to observe the world around us, question it, intervene in it in order to broaden the range of possible observations, and, then, to model it in order to explain it. For physicists, chemists and biologists, explaining the universe, matter and life itself, means, above all, trying to understand them in order to use them, control them, copy them and even recreate them.

Wednesday, June 21st, 2006, 6.54 am. The night train from Geneva (CH) enters Pau (FR) railway station.

It is dawn in this small Pyrenean city and we chemists, who have always been fascinated by the almost godlike power of our field of research, are about to embark on a similar mission. Arriving in the summertime peace of a deserted lab, after several weeks of research and preparation, the next few days will be devoted to reproducing one of the most extraordinary feats in which our predecessors invested their hearts and souls: recreating life.

The breakthrough experiments of Stéphane Leduc[1] which we are about to rediscover are not very well known. At best, from time to time, chemists attempting to explain their art to the general public will show astonished audiences the amazing shapes and colours of these osmotic growths commonly known as 'chemical gardens' (figure 1)[2]. They are relatively easy to realise, at least in their most elementary form, as can be seen in the chapter *Chemical Recreations* in Oliver Sacks' book *Uncle Tungsten: Memories of a Chemical Boyhood* [3]:

"*I commandeered the kitchen table to make a 'chemical garden', sowing a syrupy solution of sodium silicate, or water-glass, with differently coloured salts of iron and copper and chromium and manganese. This produced not crystals but twisted, plantlike growths in the water-glass, distending, budding, bursting, continually reshaping themselves before my eyes*".

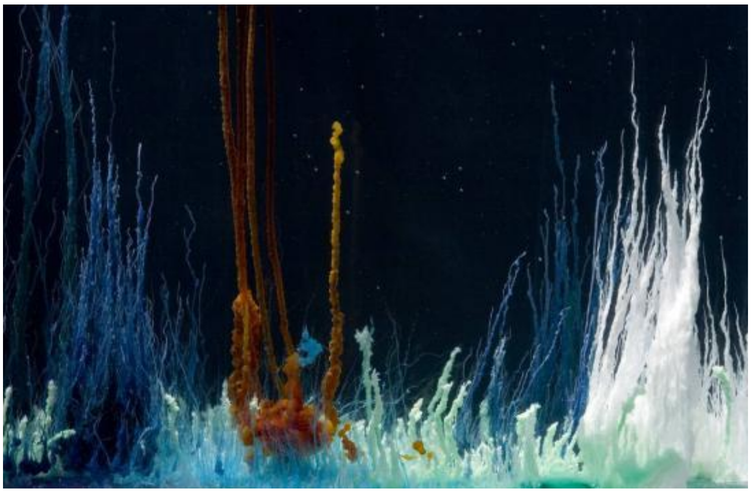

Figure 1: An example of a 'chemical garden'.
30 minutes is all it takes for this mixture of crystals to blossom into tangled filaments.

We gather our equipment, check the cleanliness of our beakers, Erlenmeyer flasks and other volumetric containers and neatly lay out the small bottles which, later, will produce the metallic salts we have carefully selected (figure 2). Our photographer examines the layout of the room and the light sources and sets up his spotlights, screens and other state-of-the-art equipment. Above all, we prepare the essential component of all our experiments, the 'vital liquid' for osmotic growth: the concentrated sodium silicate[4] solution, also known as 'water-glass'[5], which we will use as the 'stock solution'.

Figure 2: Some of the metal salts used to create chemical gardens.

Inspired by Leduc's main book published in 1910, *Théorie physico-chimique de la vie et générations spontanées* (figure 3)[6], and purposely avoiding the first part which focuses mainly on the diffusion shapes obtained when pouring India ink into salty water, and crystallisation fields in colloidal environments, we concentrate on his work which refers to 'osmotic cells' and 'morphogenesis'[7]. For this, he used 'melted' calcium chloride, which we obtain by heating the hydrated commercial version of the product: we observe an initial ebullition which corresponds to the evaporation of crystallisation water followed by actual fusion at a temperature of about 770° C. The calcium chloride has taken on a paste-like texture and we use a spatula to remove it from the crucible in order to shape it into amorphous fragments. The objective of this fusion is to eliminate trapped air bubbles, which hinder growth in an isotropic cell.

Figure 3: Three typical pages from the English and French versions of Leduc's books

As an alternative to the sodium silicate stock solution, Leduc recommends preparing saturated solutions of various types. Again, the notion of 'saturation' was fairly vague for him, and we obtain the best results using saturated solutions which have been diluted five times. Indeed, saturated solutions are much too slimy; however, as we will notice later, in a solution which has been diluted ten times, the cells sink disappointingly. We are going to struggle with this phenomenon on many occasions because the descriptions of Leduc's recipes lack the precision to which a modern-day chemist is accustomed and the units of measurement employed a century ago are far from clear…

During our experiments, we start to understand that, during two decades of relentless and repetitive work, Stéphane Leduc gained remarkable understanding and exceptional intuition with regard to the substances and phenomena on which he focused all his experimental energy. We must accept that we are not going to achieve such awareness in only a few days of work, in the same way that it would be impossible for a novice painter to replicate the delicacy of Ingres's or the accuracy of Leonardo Da Vinci's paintings simply by copying them…

Figure 4: Osmotic cell created by the insertion of a fragment of calcium chloride into a greatly diluted solution. The spikes are microscopic crystallisations, invisible to the naked eye.

Nevertheless, after some attempts, we are able to achieve some quite rewarding results (figure 4) but our creations are short-lived: the finest cells crack and produce odd tree structures (figure 5). The appearance of these primal cells is not going to be the most conclusive result of our series of experiments, however, it does allow us to understand and gain an initial idea about the phenomenon of 'osmotic growth', which, in the following days, we will return to with the help of a large range of different metal salts.

When introduced into the stock solution, the metal salts (firstly calcium chloride, and then iron, nickel, copper, manganese, cobalt salts, etc.) dissolve. When they come into contact with the silicate ions, the freed metal ions immediately form a strong membrane around the initial crystal[8]. The 'cell' is born.

This membrane is semi-permeable: no substance other than water can pass through it. After this, it delimits two areas: an internal solution containing nothing but the dissolved metal salt, and an external solution containing only the sodium silicate (also dissolved). For reasons which only chemical thermodynamics is able to explain, this difference in composition results in an inflow of water through the membrane. This phenomenon is called 'osmosis' and led Leduc to give the cell its 'osmotic' property.

However, the growth of the cell still remains to be explained. The inflow of water leads to an increase in the internal pressure, and then the rupture of the membrane which is reformed immediately… but slightly further away. The phenomenon is repeated continually over the entire circumference of the cell and, as a result, it grows.

However, in most cases, the density of the internal solution is lower than that of the external environment: the rupture tends to be upwards. This means that growth is ascendant, filamentary and arborescent[9].

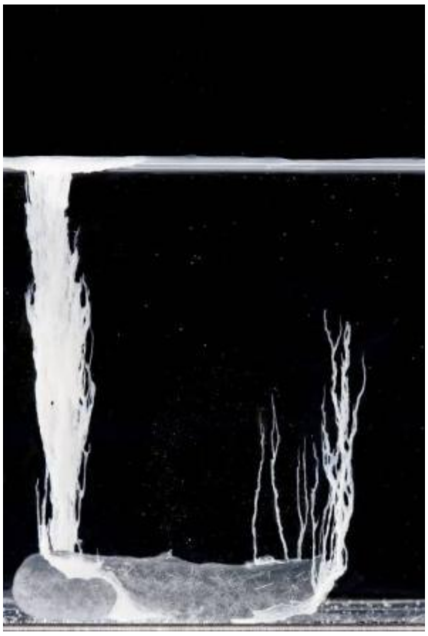

Figure 5: Tree structures resulting from the puncture of an osmotic cell of melted calcium chloride.

Late 1910. A laboratory at Nantes Medical school (FR).

With fervour and precision, once again, Stéphane Leduc reads the English translation of his *Théorie physico-chimique de la vie*, which is to be published in a few months time under the title *The mechanism of life* (figure 3)[10].
Above all, the foreword, written by W. Deane Butcher, lifts his spirits:

"*There is, I think, no more wonderful and illuminating spectacle than that of osmotic growth, - a crude lump of brut inanimate matter germinating before our very eyes, putting forth bud and stem and root and branch and leaf and fruit, with no stimulus from germ or seed, without even the presence of organic matter. For these mineral growths are not mere crystallizations as many suppose […]. They imitate the forms, the colour, the texture, and even the microscopic structure of organic growth so closely as to deceive the very elect*."

But, who is Stéphane Leduc (figure 6), this figure who was completely forgotten and who has only recently been reconsidered by Evelyn Fox Keller[11]? Born in Nantes, a Bachelor of Science and Doctor of Medicine, he was a Professor at Nantes School of Medicine. In the same way as the work by Jöns Jacob Berzélius (1779-1848)[12], which we will refer to later, Leduc's work, conducted one century later, concentrated mainly on the use of electricity as a therapeutic support. A promoter of electrotherapy[13], he discovered that certain forms of epilepsy could be treated with electric shocks and that a general anaesthetic effect could be obtained by applying an electrical charge. He also worked on exploring the role of ions in organisms. However, he is best known for his work on synthetic biology which is referred to in the present article.
In the Dictionnaire de Biographies Françaises (*Dictionary of French Biographies*), *Stéphane Tirard wrote[14]: "*Believing that beings were constituted by their form and structure, Leduc affirmed that the study of forces responsible for the acquisition of the characteristic forms of living organisms was an initial step in obtaining a true understanding of living organisms. The study of the modes of reproduction should follow on from the methods for this same 'synthetic biology'. Therefore, beyond simple analogies in form, Leduc explained the formation of these structures by basing his theories on a concept of life, which according to him is '*a specific form of movement of matter, a harmonious series of movements of liquids and a manifestation of the same molecular forces which give life to non-living matter*'.

Stéphane Leduc denied the existence of an impenetrable frontier between inert and living matter. For him, '*all matter contains life within it, whether in its present state or its potential state*'. On the strength of this principle, he actively defended the method which, through experiments, consisted of producing mineral structures resembling living structures, believing himself to be on the experimental path to the synthesis of living beings".

It should be noted that Leduc was not the first person to create these types of semi-lunar landscapes, half-living but chemical. In the 17th and 18th centuries, Erasme Bartholin (1625-1698), Louis Lémery (1677-1743, the son of Nicolas Lémery) and other experimenters were already creating 'chemical plants' using electrolytic growth. These gave rise to the first Diana's trees or Mars trees[15].

Figure 6: Stéphane Leduc[16].

Here, Leduc's work on synthetic biology[1] should be placed within the context of the history of biology and chemistry. Since ancient times, with the great philosophers such as Aristotle or Lucretius, the Middle Ages with Albertus Magnus (circa 1200-1280) and the Renaissance period with Van Helmont (1580-1644), up until the end of the 19th century two dogmas persisted: the origin of life lay in spontaneous generation, the result of the existence of a vital force. It is true that his chemist predecessors succeeded in making the scientific community acknowledge that it was possible to synthesise artificially substances which, to date, had been produced exclusively by living beings (see inset). But, by filling the theoretical void which, until then, separated the living from the non-living, by offering a new version of the 'missing link' between inorganic and organic, thus reviving the frustrated hopes of the anti-vitalists after the demise of the *Bathybius Haeckelii*[17], his experiments cast a decisive light on the nature and the origin of life. In effect, as Evelyn Fox Keller explains: "*Leduc's models responded to a much felt need at the time, although it is not the case nowadays: they demonstrated that complex forms (similar in complexity to those to be found in the living world) could be engendered by properly identified physical and chemical processes*"[18], and by doing so, he played a part in revealing the remains of vitalism[19].

In a famous letter dating from 22 February 1828, the German chemist Friedrich Wöhler (1800 – 1882) informed his mentor Jöns Jacob Berzélius (1779-1848) that he had succeeded in synthesising a natural organic product, urea, by processing lead isocyanate with ammonium chloride, two products of inorganic origin. "I must inform you that I know how to make urea without the help of a man or a dog's kidney. Ammonium cyanate is urea".

Although this discovery did not really surprise the chemists of the time (urea is a substance which is excreted rather than one which participates in the living world), the reception reserved for this discovery was modest and biologists did not pursue it. Nevertheless, from the 1850s onwards, a significant number of natural molecules were going to be (re)produced from inorganic compounds.

One person who made his mark through his work was the much criticised Marcellin Berthelot (1827 - 1907)[20]*, a chemist noted for his anti-atomism who became the advocate of organic synthesis. The many synthesis experiments which he carried out were of outstanding importance. Let us refer in particular to the electric egg experiment (1866), during which Berthelot produced acetylene from carbon and dihydrogen, the synthesis of benzene through the pyrolysis of acetylene (1863) and the 53,000 agitations (*sic*) required to obtain ethanol by putting ethylene in contact with sulphuric acid after hydrolysis (1855). Although largely inspired by the work of his time, Berthelot actively participated in the development of organic chemistry by creating the first total synthesis projects, a precursor to what, one century later, talented chemists such as Robert Burns Woodward (1917 - 1979) elevated to a state of the art.*
In this second half of the 19th century, copying nature was an activity which occupied many chemists; copying it in order to understand it better. For this reason, let us recall the famous extract from the lecture entitled 'In the Year 2000' *which Berthelot gave at the* Banquet de la Chambre syndicale des produits chimiques *on 5 April 1894:* "The synthesis of fats and oils has been carried out for the past forty years, that of sugar and carbon hydrates is being accomplished today, and the synthesis of nitrogenous bodies is not far away. Thus, let us not forget that the problem of food is a chemical problem. The day that energy is obtained economically, we will not waste time manufacturing foodstuffs from scratch, with carbon taken from carbonic acid, hydrogen taken from water, nitrogen and oxygen taken from the atmosphere. We are already doing what plants have done up until now, […] and we will do it even better, in a wider and more perfect way than nature does: because that is the power of chemical synthesis. The day will come when, in order to feed himself, each person will carry a small nitrogenous tablet, a small mound of fatty matter, a small amount of starch or sugar and a small flask of aromatic spices suited to his personal tastes: all of this will be manufactured economically and in inexhaustible quantities by our factories and will be independent from the irregularity of our seasons, rainfall, drought, the heat which dries out plants or the frost which destroys the hope of fertilisation; all this will be free from the pathogenic microbes which are behind epidemics and which are the enemies of human life. […]. Man will become gentler and more ethical because he will no longer be living from the carnage and destruction of living creatures"[21].
Thus, from the examination of gases in the second half of the 17th century and after a laborious 19th century of building its concepts, theories and vocubulary, chemistry gradually constructed itself to become, at the dawn of the 20th century, a discipline in full expansion, based on the riches of artificial colourings and the first medicines produced by the flourishing chemical industry.

However, in Great Britain and in the United States, as opposed to France, where, since 1907, he had found himself up against the Academy of Science because of his experiments which gave value to spontaneous generation[22], the recent works of Louis Pasteur (1822-1895) on this subject were not yet sufficiently well known to the public to obstruct Leduc's claims that life may have originated from chance encounters between chemical substances. Consequently, his efforts were widely publicised in the English-speaking scientific press from 1905 to 1913.

But very quickly, Leduc's ideas were swept aside by the convergence of new knowledge emerging in the fields of chemistry, astronomy and, of course, genetics. This explains why philosophers and science historians tend to do greater justice to these hypotheses which, today, appear to us to be wild theories. He faced a fast growing challenge when he published his works, and as early as 1907, Henri Bergson (1859-1947) contradicted his ideas in *Creative Evolution*.

Although he does not quote Leduc directly, he writes with criticism[23]: "*Chemists have pointed out that even in the organic - not to go so far as the organised - science has reconstructed hitherto nothing but waste products of vital activity; the peculiarly active plastic substances obstinately defy synthesis*" and (page 35) "*As for the artificial imitation of the outward appearance of protoplasm, should a real theoretic importance be attached to this when the question of the physical framework* *of protoplasm is not yet settled? We are still further from compounding protoplasm chemically. […] But instructive above all is the fact that the tendency to explain everything by physics and chemistry is discouraged rather than strengthened by deep study of histological phenomena".* And, finally (page 36): "*To sum up, those who are concerned only with the functional activity of the living being are inclined to believe that physics and chemistry will give us the key to biological processes. They have chiefly to do, as a fact, with phenomena that* are *repeated continually in the living being, as in a chemical retort. This explains, in some measure, the mechanistic tendencies of physiology. On the contrary, those whose attention is concentrated on the minute structure of living tissues, on their genesis and evolution, histologists and embryogenists on the one hand, naturalists on the other, are interested in the retort itself, not merely in its contents*".

In more brutal terms, some twenty years later, Edouard Leroy (1870-1954), Professor at the *Collège de France*, wrote about Leduc's 'alleged biogenesis': "*Life has not been imitated, not even slightly […]. Let me just say that they are mere effects of osmosis with no more relevance to the problem at hand than flowers or tree structures drawn by ice on a window pane on a winter's day*". Later, when Alexandre Oparine (1894-1980) refers to him in his book *Origins of Life* in 1936, it is merely to point out that the similarity between his productions and living cells is "*no greater than a superficial resemblance between a living person and a marble statue*"[24]. In Leduc's defence, it has to be said that it must have difficult not to have believed in it (figure 7). It even appears to us to be possible to find extenuating circumstances for him: in effect, what could be more fascinating than seeing the formation of structures which are so close to natural elements and life forms? The ease with which these tubular structures develop is certainly surprising… and, in the absence of the knowledge we have today about the nature of biological phenomenon, it is not surprising that Leduc was able to find a natural appearance in this spontaneity.

Figure 7: You might think that this is a snail… It is the result of an osmotic growth of iron chloride (III).

In fact, by discovering that matter is able to spontaneously produce extraordinarily complex forms, without a doubt, Leduc played a role in helping to understand life. In 1938, Reinhard Beutner, did not fail to notice this and wrote: "*there is a lot to learn from these perishable artificial structures. They brilliantly reveal the prevalent action of nature's formative forces. […] Thus, a little of the mystery of life is unveiled*"[25]. It seems fairer to judge Leduc in the light of these specific contributions and bear in mind his astonishing experimental skills rather than focusing on the *theoretical amateurism* of which Pierre Thuillier (1927-1998) accused him in 1978. Despite his mistakes and his over-excited naivety, we even believe that he deserves to be rehabilitated.

There are similarities to be found in Thomas Mann's *Doctor Faustus*, where the author refers to chemical gardens and their deeply 'melancholic nature': "*Leverkuhn's father asked us what we thought about it, we replied shyly that they could not be plants, to which he declared: "It is true, they are nothing of the sort, they are pretending; but, this does not diminish their merit. It is precisely the fact that they simulate and try their hardest which is worthy of our respect*."[26]

Another aspect worthy of our esteem is Leduc's perseverance; it is true that he made mistakes, but these do not necessarily diminish his merit. E. Fox Keller, in particular, wrote about this[11]: "*The ambitions which these efforts reflect, as well as the interest which they generated at the time, represent an episode in the history of biological explanation and are instructive precisely to the same degree as what, today, may appear to us to be their absurdity".*

Thursday, June 22nd, 2006, 9 am. University of Pau (FR).

After our first day of experimental explorations and blind searching, we decide to be more methodical and to test all the possible combinations by introducing the different metal salts at our disposal into the various solutions we have prepared. We obtain a wide range of results from the most promising to the most disappointing. We also notice that, out of all the preparations, the simple sodium silicate solution gives the best results and that all the other ones - mixtures of various solutions of various concentrations - must have only been devised by Leduc within very specific frameworks designed to give strength to his theory: the intentional creation of forms resembling living beings, such as mushrooms, sea shells, leaves, madreporaria and other annelida.

Figure 8: The starry background resulting from the air bubbles
which adhere to the wall gives a sidereal atmosphere to the movement of the manganese sulphate.

Indeed, for him, it is an undeniable conviction: "*Is it possible to doubt that the simple conditions which produce an osmotic growth have frequently been realised during the past ages of the earth?*" And he deduces that: "*Millions of ephemeral forms must have succeeded one another in the natural* *evolution of that age, when the living world was represented by matter thus organised by osmosis*"[27]. Therefore, he renews the almost metaphysical dimension which, in 1827, René Joachim Henri Dutrochet (1776-1847) had already imputed to the phenomenon of osmosis: "[osmosis] *is the point at which the physics of living bodies and the physics of inorganic bodies merge*"[28].

The phenomenon of osmosis was studied for the first time in 1748 by Abbot Jean-Antoine Nollet (1700 - 1770)[29]. It was then René Joachim Henri Dutrochet (1776-1847), the French physician, botanist and physiologist who continued the work on osmosis in 1827 - 1832, at the same time defining the terms endosmosis and exosmosis. After this, in particular, came the work of Thomas Graham (1805 - 1869) around 1854, Moritz Traube (1826 - 1894) around 1864 and Wilhelm Friedrich Philipp Pfeffer (1845 - 1920) in 1877. In 1886 Jacobus Henricus van 't Hoff (1852 - 1911, the recipient of the first Nobel Prize in Chemistry in 1901) studied osmosis from the point of view of thermodynamics[30]. Therefore, osmosis was a phenomenon which was understood perfectly by scientists when Leduc created his first osmotic sculptures.

Yet, all these attempts are far from being fruitless; each of the experiments we conducted was an opportunity to make new observations, which we listed meticulously in our laboratory notebook. One of them was even going to allow us, later on, to refute one of Leduc's arguments concerning the mechanism of the kind of growth which we explored the most: that of vermiform and filiform growth (figures 8, 9 and 10):

"…*the slightest consideration will show the inadequacy of the usual explanation that the growth is due to mere differences of density, or to amorphous precipitation around bubbles of gas. These may indeed affect the phenomenon, but can in no way be regarded as its cause*"[31].

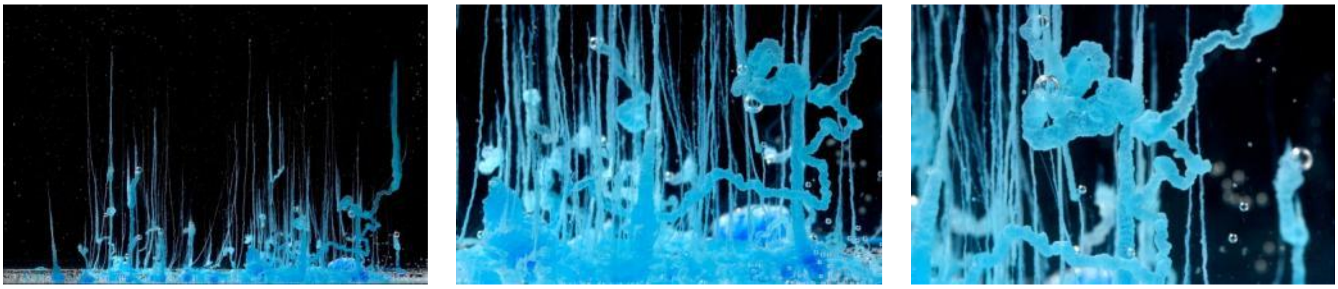

Figure 9: Various stages of the filiform growth of thin copper sulphate crystals which show particularly well the influence of gas bubbles. Wide-angle shot and close-up.

However, on the contrary, a century later, with the help of modern techniques of macrophotography, the most basic observations have permitted the highlighting of the fundamental influence of gas bubbles, the production of which is stimulated by the degassing of the stock solution under the influence of the heat from the floodlights. In effect, whenever they accompany the birth of arborescent stems, these bubbles hugely accelerate their growth, before separating from them, sometimes suddenly, thus interrupting the process[32].

The buoyancy's origin is clearly osmotic, but the gas bubbles can, in some cases, play a major role, adding their influence to the differences of density which alter growths in a vertical direction. Still, Leduc would have done anything, even betray his own observations, to defend an idea which, to him, appeared to be almost as dear as that of the mineral origin of life: "*Of all the ordinary physical forces, osmotic pressure and osmosis alone appear to possess this remarkable power of organisation and morphogenesis*"[33].

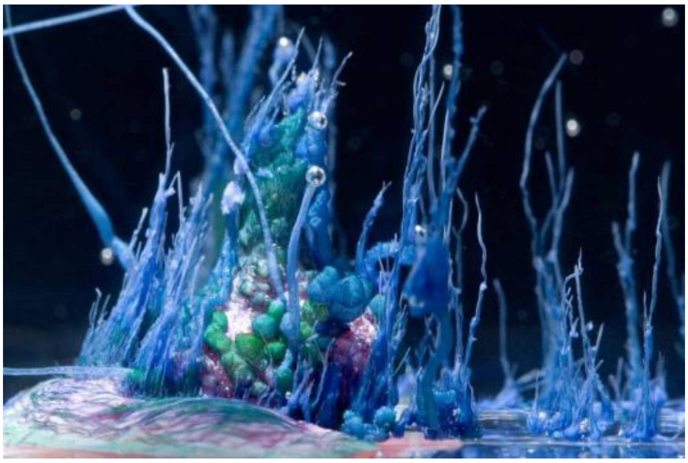

Figure 10: All variations of colours and shapes seem possible with cobalt chloride, for which degrees of oxidation and the hydration rate control the shades.

Friday, June 23rd, 2006, 7:30 am. University of Pau.

It is the third and last day of work. The main work has been done, but there are still variants to be tested: adding foreign substances during a growth, superimposing layers of stock solutions of different concentrations (figure 11), using clusters formed by mixing different metal salts with each other, or with caster sugar, as Leduc himself recommends doing, etc. A thousand photographs are not enough to duplicate the infinite range of shapes and colours which Leduc's original work is capable of offering us (figure 12). However, at least we compensate for this frustration by the belief that we now possess a small piece of his know-how and experimental intuition.

Figure 11: Two solutions of sodium silicate, one concentrated, the other diluted twice, have been laid out one on top of the other. The tree structure of cobalt chloride changes its configuration as it passes through them.

In the light of today's knowledge, it is easy to see the disconcerting complexity of the mechanisms of life. We know the composition of cells, made up of phospholipid bilayers, transmembrane proteins, enzymes, receptors, DNA, messenger, transfer, ribosomal and interferential RNA. We know that cells communicate using hormones, steroids or others, and diverse and varied neurotransmitters, all of which are orchestrated magnificently by regulation mechanisms, feedback loops and other signalling tools which inhibit or activate one type of process or another and which maintain the autocoherence of living beings. In view of this, what is the legacy of Leduc's work from the point of view of contemporary research?

Unfortunately, despite the renaissance of a modern form of 'synthetic biology'[34], today's science does not draw much inspiration from it and, apart from D'Arcy Wentworth Thompson's (1860-1948) use of it[35], very little of it remains in scientific life. This is often the case: when 'die- hard' science considers questions which have been relegated to fields qualified as 'parascientific', thus wiping the slate clean of all existing interpretations evoked over the centuries[36]. Given this, our work to rehabilitate his name is slowly making progress and it is now possible to find his name in the transcription of a lecture given by Professor Jacques Livage at the *Collège de France* at the end of 2006, on the subject of chemical morphogenesis[37].

Figure 12: Out of all the salts used, iron chloride is the one with the fastest and liveliest growth.
It may be downwards, taking the form of folds, or upwards, in bunches, producing some of the most evocative forms.

We can also find his name in some recent biomimetic studies of inorganic bodies[38], or in research on fossils[39], as well as extraterrestrial life[40], but, from angles of which, undoubtedly, he would have disapproved. For example, with the help of his work, researchers recently showed how some concretions, which palaeontologists had considered to be fossils, were mere remains of osmotic mineral formations, therefore, completely… lifeless.

How to make a 'chemical garden'

Obtain a commercial solution of water-glass and dilute it twice with distilled and preferably, degassed water. Filter on sintered glass if it is troubled with hanging particles. Use within the next few hours.

Pour into a Plexiglas container[41], 10 to 15 cm deep. Leave it to rest for a few minutes.

Insert small crystals of carefully selected metal salts: $CuSO_4$, $Ni(NO_3)_2$, $FeCl_3$, $CoCl_2$, $MnSO_4$... Those for 'chemical garden' kits sold by chemical product suppliers are perfectly suitable. The nature of the counter-ions is not vital, but variations are obtained when they are replaced.

Avoid amassing the crystals and laying them too close to one other, and above all, avoid shaking the recipient. Observe[42].

Complementary bibliography

A brief biography of Stéphane Leduc by Suzanne Ballereau-Dallongeville can be found in *La santé en Bretagne* (available at the *French Académie Nationale de Médecine*). She refers to his thesis at the University of Nantes (1865), but it would appear that this document is very difficult to find. An interesting review of Leduc's work can also be found in '*Stéphane Leduc a-t-il créé des êtres vivants ?*' (*Has Stéphane Leduc created living things?)* by M. D'Halluin, *Revue des Questions Scientifiques*, XII, 20 juillet 1907, p.5-56.

At the François Mitterrand library, in Paris, France, there is a written transcript of one of his lectures, given under the patronage of the *Presse Médicale*, December 7th, 1906: '*Les bases physiques de la vie et la biogenèse*' (*The physical bases of life and biogenesis*). One of his first records can also be found there: '*Cytogenèse expérimentale*' (*Experimental cytogenesis*), a lecture given at the congress of the *French Association for the advancement of sciences* (Ajaccio, September 8th to 14th, 1901), during which he refers to the review of the *Académie des Sciences* session dated June 17th, 1901.

More recently, in several scientific magazines, we can also find experiments complementary to the ones we have carried out, although Stéphane Leduc is never referred to: injection of metallic ion solutions into silicate solutions[43], as well as other alternatives[44], formation of chemical gardens in weightlessness[45], or in the presence of powerful magnetic fields[46], etc.

It should also be noted that the understanding of all these phenomena has led to their practical implementation in a variety of fields, such as the formation of green earths used by Vermeer[47], the hydration of Portland cement[48], as well as the understanding of the reaction produced at the bottom of the ocean by the 'black smoker'[49] as well as research into the origins of life[50].

Acknowledgments and credits

All images used in the present article were taken by *Stéphane Querbes (www.stephanequerbes.com) for* Les Atomes Crochus *and* Anima-Science. *They were published for the first time in a portfolio article in the September 2006 issue of* La Recherche[51].

Our thanks to Bernadette Bensaude-Vincent, Michel Morange, Juli Pereto, Francine Pellaud, Luc Allemand and Stéphane Tirard for their thorough proofreading and their sound advice, as well as to Professor Jacques Livage for his invitation to set up a seminar at the Collège de France *and for publicising the physico-chemical mechanisms at play in osmotic growths.*

[1] These experiments, a breakthrough in the broad field of 'artificial life', were conducted between 1905 and 1928. Especially focusing on 'synthetic biology', Leduc replicated the concept of biogenesis in various manners, according to the degree of life quality which he focused on reproducing: cyto-, plasmo-, histo-, morpho- and physiogenesis. Leduc, S. *Les bases physiques de la vie et la biogenèse*, Masson, Paris, 1906 (*Physical bases of life and biogenesis*), and Leduc, S.:1912, *La biologie synthétique, étude de biophysique*, A. Poinat, Paris, (*Synthetical biology, study of biophysics*). This second work is available in French online at the following address: www.peiresc.org/bstitre.htm Last connection on 03/11/2007.

[2] See, for instance, Cartwright, J. H. E. Garcia-Ruiz, J. M. Novella, M. L. Otalora, F.: 2002, 'Formation of Chemical Gardens', *Journal of Colloid and Interface Science*, **256**, 351–359.

[3] Sacks, O.: 2001 *Uncle Tungsten: memories of a chemical boyhood*, Knopf, 2001 (p. 90 in the French version). Oliver Sacks is a neurologist and a novelist. Allow us to mention *The Man who Mistook his Wife for a Hat*, Touchstone, 1998.

[4] Comprising more than 27% of the earth's crust, silicon is a chemical element omnipresent in geology and is the second most important element after oxygen. Isolated for the first time by Jöns Jacob Berzélius (1779-1848) in 1824 in an unpure amorphous form through the redcution of silica, it was Henri Sainte-Claire Deville (1818-1881) in 1854 who succeeded in obtaining it in its pure crystalline form. A superior homologue of carbon – the atom of life if ever there was one – silicon occupies a special place in the periodic table of elements. As for silicates, they have been used since ancient times to treat venereal diseases and offer their virtues in spa waters and clayish mud which contain high quantities of it.

[5] This liquid could be described as concentrated sodium hydroxide in which glass would have been melted. It is a highly corrosive solution which leaves mark when kept in a glass container and, if left in the open, gradually absorbs carbon dioxide and loses its properties. It constrains the user to prepare it immediately before using it, as well as using distilled water to make it, as any residue of foreign substances may trouble photographs.

[6] Published by A. Poinat in Paris. From now on, this work will be referred to by the initials TPCV. Translated as *The Mechanism of Life*, London, William Heinemann, 1911. This book was extensively reviewed by Pierre Thuillier (1927-1998) some thirty years ago: Thuillier P.:1978, *Stéphane Leduc a-t-il créé la vie ?* La Recherche, janvier, 85-88, janvier (*Did Stéphane Leduc recreate life?*).

[7] Chapter XI. Leduc uses a technique taken from the chemist Moritz Traube (1826-1894) who, in 1867, had synthesized the first 'artificial cells' thanks to the osmotic properties of chemical precipitates.

[8] The formation of the membrane actually follows a double process of olation and oxolation. Indeed, when the metal salt melts, the cations freed in the solution connect firmly with water molecules, which, in presence of basic silicates, lose protons. The result is a first precipitation of metal hydroxide, which forms the interior of the membrane; this is olation. Furthermore, with the environment having been acidified by the freed protons, the silicate ions are no longer water-soluble and precipitate, thus forming the external face of the membrane; this is oxolation. Between the internal and the external faces of the membrane, chemists actually have been able to observe a gradient of composition, ranging gradually from metal hydroxide to almost pure silicon dioxide. In the middle, the metal silicates predominate. See, for instance, Pagano, J. J. Thouvenel-Romans, S. Steinbock, O.:2007, 'Compositional analysis of copper-silica precipitation tubes', *Phys. Chem. Chem. Phys*. **9**, 110-116 or Collins, C. Zhou, W. Klinowski, J.:1999, 'A unique structure of $Cu_2(OH)_3.NH_3$ crystals in the 'silica garden' and their degradation under electron beam irradiation', *Chemical Physics Letters*, **306**, 145-148.

[9] With regard to observing hollow tubes, consult for example: Balköse, D.,Özkan, F. Köktürk, U. Ulutan, S. Ülkü, S. 1 Nili, G.:2002, 'Characterization of hollow chemical garden fibers from metal salts and water glass', *Journal of Sol-Gel Science and Technology*, **23**, 253-263.

[10] Published in New York by Rebman and in London by Heinemann.

[11] Fox Keller, E.: 2004, *Expliquer la vie : Modèles, métaphores et machines en biologie du développement*, (*Explaining life: models, metaphors and machines in development biology*), Bibliothèque des sciences humaines, Gallimard, Paris.

[12] Famous Swedish chemist the criticisms of whom were greatly feared; he studied medicine before becoming interested in chemistry. His thesis, published in 1802, concerned the physiological action of electricity and was entitled *De electricitatis galvanicæ apparatu cel. Volta excitæ in corpora organica effectu*.

[13] His experiments on the injection of strychnine and cyanide into rabbits 'connected in series' into an electrical circuit showed that, depending on the sense of polarisation, the rabbits may either be killed or spared.

[14] Tirard, S. in Prevost, M. d'Amat, R. Tribout de Morembert, H. et Lobies J.-P.: 2006, *Dictionnaire de biographies françaises*, Librairie Letouzey et Ané, Paris.

[15] Fleury, V.: 1998, *Arbres de Pierre*, Flammarion,

[16] www.mairie-orvault.fr/images/photos/0005/img_1151323407967.jpg Last connection on 03/11/2007.

[17] Grainy set of gelatinous matter, considered in 1872 by Thomas Huxley (1825-1895) as primeval protoplasm after Ernst Haeckel's (1834-1919) researches on the composition of sea bottoms. According to their hypothesis, this simplest possible structure, formed

spontaneously at the bottom of the ocean, constituted the much sought-after missing link between the non-living and the living. See Thuillier P.: 1975, '*Requiem pour un Bathybius'*, (Requiem for a Bathybius) *in* Le petit savant illustré n°3, La Recherche n°62, déc.

[18] See footnote 11.

[19] And at almost the same time (1917), along with him, D'Arcy Wentworth Thompson (1860-1948) in the influential work *On Growth and Form*. Jean-Baptiste de Lamarck (1744-1829) himself stood up against vitalism and, in 1809, wrote in *Philosophie zoologique (Zoological philosophy):* "Nature does not need particular laws; those which govern all bodies are perfect enough for this object*"*. Thompson, D'A.W.: 1961, '*On growth and Form'*, abridged edition, Cambridge University Press, Cambridge.

[20] Jacques, J.: 1987, *Berthelot, autopsie d'un mythe*, Belin, Paris.

[21] Berthelot, M.:1896, *Science et morale*, Calmann-Lévy, Paris, pp. 512-513.

[22] The committee of the Académie des Sciences even decided to exclude his research from its reviews, thus sanctioning his unpardonable assertions.

[23] Bergson, H.: 1911, *Creative Evolution*, Henry Holt and Company, p. 34.

[24] Oparine, A. I.:1938, *The Origin of Life*, Macmillan, New York, p. 57.

[25] Beutner, R.: 1938, *Life's Beginning on the Earth*, Williams&Wilkins, Baltimore.

[26] Mann, T.: 1948, *Doctor Faustus*, Alfred A. Knopf.

[27] TPCV, p. 202.

[28] René Joachim Henri Dutrochet (1776-1847) quoted by Pierre Thuillier (1927-1998), *Annales de chimie et de physique*, **35**, 1827, p. 400.

[29] Abbot Nollet is known for his work on electricity and, in particular, for his controversies with Benjamin Franklin (1706-1790). He studied the effect of osmosis between mixtures of water and ethanol through the bladders of animals. A rather curious connection should be highlighted here, because Abbot Nollet is also the author, in the same way as Jöns Jacob Berzelius (1779-1848) and Stéphane Leduc, of works on electrotherapy.

[30] For further information, see the famous work by Wilhelm Ostwald: 1916, *L'évolution d'une science, la chimie*, Flammarion, Paris pp. 97-109.

[31] TPCV, p. 149.

[32] This impression is confirmed in the following publication: Thouvenel-Romans, S. Pagano, J. J. Steinbock, O.: 2005, 'Bubble guidance of tubular growth in reaction precipitation systems', *Phys. Chem. Chem. Phys*. **7**, p. 2610.

[33] TPCV, p. 152.

[34] Pereto, J.Catala, J.: 2007, 'The Renaissance of Synthetic Biology', *Biological Theory*, **2**(2), 128–130.

[35] See footnote 19 on D'Arcy Wentworth Thompson

[36] Such has been the case for the appropriation by science of the 'clouds stones', transformed into meteorites by Jean-Baptiste Biot (1774-1862) during a lecture at the Académie des Sciences in 1803.

[37] The slideshow of this lecture is available at the following website: www.labos.upmc.fr/lcmcp/livage/cours_college.html Last connection on 03/11/2007.

[38] Garcia-Ruiz, J. M. Hyde, S. T. Carnerup, A. M. Christy, A. G. Van Kranendonk, M. J. Welham, N. J.: 2003, 'Self-Assembled Silica-Carbonate Structures and Detection of Ancient Microfossils', *Science*, **302**, 1194-1197.

[39] Kerr, R. A.: 2003, 'Minerals Cooked Up in the Laboratory Call Ancient Microfossils into Question', *Science*, **302**, p.1134.

[40] Garcia-Ruiz, J. M. Carnerup, A. Christy, A. G. Welham, N. J. Hyde, S. T.: 2002, 'Morphology: An Ambiguous Indicator of Biogenicity', *Astrobiology*, **2**, 335-351.

[41] The hyperbasic solution attacks glass and the osmotic growths adhere to it with extreme force. If photographs are to be taken, to ensure better results, use a recipient with parallel walls, such as an aquarium, to avoid spherical dioptre effects.

[42] The recipient can then be covered and protected from vibrations allowing the tree-structures to remain intact for several weeks.

[43] Thouvenel-Romans, S. van Saarloos, W. Steinbock, O.: 2004, 'Silica tubes in chemical gardens: radius selection and its hydrodynamic origin', *Europhys. Lett*. **67**, 42-48.

[44] Stone, D. A. Lewellyn, B. Baygents, J. C. Goldstein, R. E.: 2005, 'Precipitative Growth template by a fluid jet', *Langmuir*, **21**, 10916-10919.

[45] Jones, D. E. H. Walter, U.: 1998, 'The silicate garden reaction in microgravity: a fluid interfacial instability', *Journal of colloid and interface science*, **203**, 286-293.

[46] Yokoi, H. Araki, Y. Kuroda, N. Usuba, S. Kakudate, Y.: 2006, 'Double helical formation of cobalt silicate tubes under magnetic fields', *Journal of physics*; Conference Series, **51**, 454-457 or Uechi, I. Katsuki, A. Dunin-Barkovskiy, L. Tanimoto, Y.: 2004, '3D-Morphological chirality in zinc membrane tube using a high magnetic field', *J. Phys. Chem. B*, **108**, 2527-2530 and also Duan, W. Kitamura, S. Uechi, I. Katsuki, A. Tanimoto, Y.: 2005, 'Three-dimensional morphological chirality induction using high magnetic fields in membrane tubes prepared by a silicate garden reaction', *J. Phys. Chem. B*, **109**, p. 13445.

[47] Gago-Duport, L. Fernandez-Bastero, S. Pimentel, F. Villar, P. Santos, A. Serra, C. Vilas, F.: 2000, 'Glauconite Nucleation in Silica Tubular Microstructures from Low-Temperature Solution Experiments', *Journal of Conference Abstracts*, **5**, 418-419.
[48] Double, B.D. Hellawell, A.: 1976, 'Portland concrete hydration', *Nature*, **261**, p. 486.
[49] Stone, D. A. Goldstein, R. E.: 2004, 'Tubular precipitation and redox gradients on a bubbling template', *PNAS*, **101**, p. 11537-11543.
[50] Russel, M. J. Hall, A. J.: 1997, 'The emergence of life from iron monosulphide bubbles at a submarine hydrothermal redox and pH front', *Journal of the Geological Society, London*, **154**, p. 377-402.
[51] Eastes, R.-E. Darrigan, C.: 2006, 'Recréer la vie ?' (Recreating life?), *La Recherche*, numéro spécial **400**, septembre, p. 90-97.