The Nobel Prize in Physiology or Medicine 1974
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Albert Claude - Nobel Lecture

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The Coming Age of the Cell

Inventory of living mechanisms by cell fractionation, biochemistry and electron microscopy, and a view of the impact of the findings on our status and thinking.

Fifty years of cell research can hardly be summarized in the twenty to thirty minutes of a lecture; to expose only part of it might be unrepresentative, unfair, and altogether unnecessary, since by now you have already been informed of the essential facts and discoveries that have accumulated in the course of these years.

What I would like to do instead, is to discuss with you the impact of these discoveries on our daily life, and their significance for the present and the future. At the same time I will try to recall, first hand, what has been my own experience in this century's endeavor to uncover what were, not so long ago, the mysteries of life itself.

Until 1930 or thereabout biologists, in the situation of Astronomers and Astrophysicists, were permitted to see the objects of their interest, but not to touch them; the cell was as distant from us, as the stars and galaxies were from them. More dramatic and frustrating was that we knew that the instrument at our disposal, the microscope - so efficient in the 19th century - had ceased to be of any use, having reached, irremediably, the theoretical limits of its resolving power.

I remember vividly my student days, spending hours at the light microscope, turning endlessly the micrometric screw, and gazing at the blurred boundary which concealed the mysterious ground substance where the secret mechanisms of cell life might be found. Until I remembered an old saying, inherited from the Greeks - that the same causes, always produce the same effects. And I realized that I should stop that futile game, and should try something else. In the meantime, I had fallen in love with the shape and the color of the eosinophilic granules of leucocytes and attempted to isolate them. I failed - and consoled myself later on in thinking that this attempt was technically premature, especially for a premedical student, and that the eosinophilic granules were not pink, anyway. It was only postponed. That Friday, the 13th of September 1929, when I sailed from Antwerp on the fast liner "Arabic" for an eleven-day voyage to the United States, I knew exactly what I was going to do. I had mailed beforehand to Dr. Simon Flexner, Director of the Rockefeller Institute, my own research program, hand-written, in poor English, and it had been accepted. My proposition had been to isolate, and determine by chemical and biochemical means the constitution of the Rous, chicken Tumor I "Agent", at that time still controversial in its nature and not yet recognized as a bonafide Virus. This task occupied me for about five years. Two short years later the microsomes, basophilic components of the cell ground substance, had settled in one of my test tubes, still a structureless jelly, but now captive in our hands.

In the following ten years, the general method of cell fractionation by differential centrifugation was tested and improved, and the basic principles codified in two papers in 1946. This attempt to isolate cell constituents might have been a failure if they had been destroyed by the relative brutality of the technique employed. But this did not happen.

The subcellular fragments obtained by rubbing cells in a mortar, and further subjected to the multiple cycles of sedimentations, washings and resuspensions in an appropriate fluid medium: continued to function in our test tubes, as they would in their original, cellular environment. The strict application of the balance sheet-quantitative analysis method permitted to trace their respective distribution among the various cellular compartments and thus, determine the specific role they performed in the life of the Cell.

Small bodies, about half a micron in diameter, and later referred to under the name of "mitochondria" were detected under the light microscope as early as 1894. Although they continued to be extensively investigated by microscopy in the course of the following 50 years, leaving behind an enormous and controversial literature, no progress was achieved, and the chemical constitution and biochemical functions of mitochondria remained unknown, to the end of that period.

In the early 1940's, I began to make plans for an investigation on the distribution of respiratory pigments in cells. Considering the complexity of the problem, I realized that it should be a collaborative undertaking. A year or so before, I had collaborated with Dean Burk and Winsler in providing them a material of interest to them, Chicken Tumor No 10, which they used in their studies of the respiratory function in tumor cells. We started experimenting, although they were but mildly impressed by the scientific value of my project, as they told me years later. Their laboratory was conveniently located at the corner of York and 68th, at street level with the Cornell University Department of Vincent du Vignaud. I remember turning across the street, handing them, through the window, each fraction as it was isolated, my share being the determination of the chemical constitution of the fractions, and their respective distribution within the Cell. One day, Rollin D. Hotchkiss appeared, returning from a one-year fellowship spent in Cambridge, England, who was delighted to find on arrival, quote, "the golden fruits on my doorstep". We were soon rejoined by Hogeboom, and later by W. C. Schneider as regards the distribution of cytochrome c in the Cell, and its participation in respiratory processes. Together, the observations provided conclusive evidence to support the view that most, if not all, of cytochrome oxidase, succinoxidase and cytochrome c, three important members of the respiratory system responsible for most of the oxygen uptake, were segregated in mitochondria. In parallel with these biochemical studies, evidence was also obtained, by tests carried out with characteristic dyes, both under the microscope and in vitro, showing that the respiratory organelles and the mitochondria seen under the microscope were one and the same, a morphological information which would have remained meaningless, however, if we had not secured beforehand, the knowledge of their biochemical functions.

Altogether, these observations demonstrated that the power of respiration exists in a discrete state in the cytoplasm, a fact which led me to suggest, in my Harvey Lecture, that the mitochondria may be considered "as the real power plants of the Cell". At about the same time, with the help of electron microscopy, the microsomes became the endoplasmic reticulum.

Looking back 25 years later, what I may say is that the facts have been far better than the dreams. In the long course of cell life on this earth it remained, for our age for our generation, to receive the full ownership of our inheritance. We have entered the cell, the Mansion of our birth, and started the inventory of our acquired wealth.

For over two billion years, through the apparent fancy of her endless differentiations and metamorphosis the Cell, as regards its basic physiological mechanisms, has remained one and the same. It is life itself, and our true and distant ancestor.

It is hardly more than a century since we first learned of the existence of the cell: this autonomous and all-contained unit of living matter, which has acquired the knowledge and the power to reproduce; the capacity to store, transform and utilize energy, and the capacity to accomplish physical works and to manufacture practically unlimited kinds of products. We know that the cell has possessed these attributes and biological devices and has continued to use them for billions of cell generations and years.

In the course of the past 30 or 40 years, we have learned to appreciate the complexity and perfection of the cellular mechanisms, miniaturized to the utmost at the molecular level, which reveal within the cell an unparalleled knowledge of the laws of physics and chemistry. If we examine the accomplishments of man in his most advanced endeavors, in

theory and in practice, we find that the cell has done all this long before him, with greater resourcefulness and much greater efficiency.

In addition, we also know that the cell has a memory of its past, certainly in the case of the egg cell, and foresight of the future, together with precise and detailed patterns for differentiations and growth, a knowledge which is materialized in the process of reproduction and the development of all beings from bacteria to plants, beasts, or men. It is this cell which plans and composes all organisms, and which transmits to them its defects and potentialities. Man, like other organisms, is so perfectly coordinated that he may easily forget, whether awake or asleep, that he is a colony of cells in action, and that it is the cells which achieve, through him, what he has the illusion of accomplishing himself. It is the cells which create and maintain in us, during the span of our lives, our will to live and survive, to search and experiment, and to struggle.

The cell, over the billions of years of her life, has covered the earth many times with her substance, found ways to control herself and her environment, and insure her survival. Man has now become an adjunct to perfect and carry forward these conquests. Is it absurd to imagine that our social behavior, from amoeba to man, is also planned and dictated, from stored information, by the cells? And that the time has come for men to be entrusted with the task, through heroic efforts, of bringing life to other worlds?

I am afraid that in this description of the cell, based on experimental facts, I may be accused of reintroducing a vitalistic and teleological concept which the rationalism and the scientific materialism of the 19th and early 20th centuries had banished from our literature and from our scientific thinking.

Of course, we know the laws of trial and error, of large numbers and probabilities. We know that these laws are part of the mathematical and mechanical fabric of the universe, and that they are also at play in biological processes. But, in the name of the experimental method and out of our poor knowledge, are we really entitled to claim that everything happens by chance, to the exclusion of all other possibilities?

About a year ago, I was invited to an official party by the Governor of a State. As the guests were beginning to leave, the Governor took me aside in a room nearby. He looked concerned and somewhat embarrassed. "Dr. Claude," he asked, "you seem to know much about life. Please tell me: what do you think about the existence of God." The question was unexpected, but I was not unprepared. I told him that for a modern scientist, practicing experimental research, the least that could be said, is that we do not know. But I felt that such a negative answer was only part of the truth. I told him that in this universe in which we live, unbounded in space, infinite in stored energy and, who knows, unlimited in time, the adequate and positive answer, according to my belief, is that this universe may, also, possess infinite potentialities. The wife of the Governor had joined us in the meantime. Hearing this, she seized her husband by the arm and said, "You see, I always told you so."

Life, this anti-entropy, ceaselessly reloaded with energy, is a climbing force, toward order amidst chaos, toward light, among the darkness of the indefinite, toward the mystic dream of Love, between the fire which devours itself and the silence of the Cold. Such a Nature does not accept abdication, nor skepticism.

No doubt, man will continue to weigh and to measure, watch himself grow, and his Universe around him and with him, according to the ever growing powers of his tools. For the resolving powers of our scientific instruments decide, at a given moment, of the size and the vision of our Universe, and of the image we then make of ourselves. Once Ptolemy and Plato, yesterday Newton, today Einstein, and tomorrow new faiths, new beliefs, and new dimensions.

As a result of the scientific revolution of the present century we are finding ourselves living in a magic world, unbelievable less than hundred years ago-magic our telephone, radio, television by multichannel satellites, magic our conversations with the moon, with Mars and Venus, with Jupiter-magic these means which transform our former solitude into a permanent simultaneity of presence, among the members of the Solar System.

And here, at home, thanks to these new media, and the ever increasing speed of transports, we are witnessing a vast mutation taking place, no longer local, but at the dimensions of the Globe: the birth of a new biological organism, in which all Continents, and all the human races participate.

For this equilibrium now in sight, let us trust that mankind, as it has occurred in the greatest periods of its past, will find for itself a new code of ethics, common to all, made of tolerance, of courage, and of faith in the Spirit of men.

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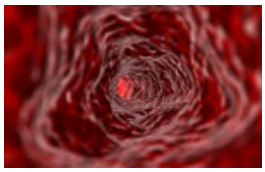

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