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Cell Intelligence and the Future of Medicine

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1. Future stages

What is the next quantum leap in medicine?

Notwithstanding the great advances in modern medicine, we should ask whether we have reached the end of the development of medicine, or whether there is another quantum leap of the understanding the disease process and biology still ahead of us.

Cells, not doctors heal patients

Our guess of the next stage may begin with the recognition that no physician in the history of humanity has ever healed a patient. Only the cells of the patient can heal the patient. Only cells know how to close wounds, understand what to do with insulin and how to destroy pathogens. The best a physician can do, is to move obstacles out of the way of cells (e.g., by surgery), supply materials and weapons to the cells (e.g., drugs and building blocks of life) and leave the fight against disease to the cells.

Can we learn to 'talk' to cells?

So far, we have to leave the hand-to-hand combat against disease to the judgement of the cells. If they decide to heal the stump of an arm rather than to regenerate it, we have to accept their decision. If they decide to encapsulate tuberculosis bacteria rather than to kill them, we have to support their 'mistake' to leave a ticking time bomb. If they are misguided or overreact in the form of anaphylactic shock, or even attack their own body in the form of allergies and autoimmune diseases, we are quite helpless to change their mind. Likewise, we are quite helpless whenever they tolerate cancer cells and even support them by building new capillaries in order to satisfy the high demands of nutrients and oxygen of these 'suicide terrorist' cells. Would it not be a true quantum leap in the development of medicine if we could order metastatic cancer cells to stop invading and growing, persuade immune cells to refrain from making selfdestructive antibodies, and cajole cells to rebuild an arm or an eye? They built them once before when we were embryos, they may be able to do it again. Speaking in military terms, we are in the absurd situation of a commander who has to send supplies and weapons to his front-line troops without being able to communicate with them. We must learn to communicate with the combat troops, i.e., the cells. Once able to do this, we can leave the rest to them, because they are well equipped

and trained to heal anything that we ask of them, provided that it can be healed at all.

2. The case for cell intelligence

Before we can try to communicate with cells, we must first ascertain that they are 'intelligent'. Without their ability to integrate and process signals and data, no meaningful communication would be possible. Therefore, my experimental work for the past 30 years has been devoted to the question whether cells are intelligent.

An operational definition of the intelligent cell.

First a disclaimer. My work did not intend to join the ongoing efforts of philosophers, logicians, and computer scientists to find a universal definition of intelligence. On the contrary, it did not question the common assumption that everybody can tell a mindless, mechanical gadget from an intelligent machine, and proceeded to ask which of the two categories apply to a living cell. Clearly, there are many different levels of intelligence, but I believe that most people consider a machine mechanical and mindless if its actions either do not seem to respond to signals or else always show an immutable set of reactions. On the other hand, we expect an intelligent machine to respond to signals in a large variety of ways, especially if the signals are unforeseeable, and if its responses offer solutions to problems, which were transmitted by the signals. Usually, this means that the intelligent machine contains at least 2 different machines, one which it mindless and carries out some mechanical labor while the other collects and processes signals and controls the action of the first. Therefore, we may use the following operational definition of an intelligent cell.

An intelligent cell contains a compartment, which is capable of collecting and integrating a variety of

physically different and unforeseeable signals as the basis of problem-solving decisions.

Are there reasons to think that cells are intelligent?

The prevailing wisdom of modern biology has it that cells are immensely complex, but rigidly operating chemical machines that derive their operating instructions internally from their genes and externally from chemicals and electrical signals emitted rigidly by other cells. Unable to believe that any machine can be designed that contains an instruction library which anticipates all the mishaps and glitches of a billion years of evolution without crashing over and over again, I began almost three decades ago to search for signs that the cell was actually a 'smart' machine. In other words, I looked for experimental evidence that cells contained a signal integration system that allowed them to sense, weigh and process huge numbers of signals from outside and inside their bodies and to make decisions on their own.

Under what circumstances would a cell reveal that it is 'intelligent'?

I thought that the best place to start searching was the field of cell movement. A moving cell has to operate its own body in sophisticated ways and, in addition, may have to navigate in space and time while dealing with numerous unforeseeable events, such as encounters with other cells and other objects that its genome could not possibly have anticipated. I think that cell motility, indeed, revealed cell intelligence. This website highlights some of the experiments and offers the images and the arguments that support the claim of cell intelligence.

Medicine, and other reasons that it matters if cells are intelligent.

If cells were, indeed, intelligent it would have major medical and conceptual implications.

a) Language of cells

As pointed out above, if cells were intelligent, medical treatment may involve 'talking' to cells rather than to flood the organism with pharmaceuticals as we do today. If cells were intelligent, they would be capable of integrating physically different signals (mechanical, electrical, chemical, temperature, pH, etc.) before they generate a response. Integration of physically different signals is only possible if each is first transduced into a common, unifying type of signal. The unifying signals are then integrated and subsequently re-transduced into the response action. For example, all the different kinds of signals that we integrate in our brain are first transduced into unifying electrical pulses, called action potentials, before we integrate them. Finally, we return the same kind of signal, namely electrical response pulses from our brain to the e.g., muscles which retransduce them into mechanical actions. If cells have an integrative system, it must also use unifying signals which it links and gates by genetically inherited, cellspecific logical rules before it responds. (Of course, the unknown cellular unifying signals will not be electrical signals like action potentials. Cells are far too small for that.) In other words, the cells must use some kind of language which we can learn to imitate.

b) Inversion of paradigms

If cells were intelligent, molecules and their genes would be the 'collaborators' or even 'slaves', but not the 'masters' of the life functions of cells. We have all accepted this in the case of organisms. For example, consider the voice of an organism like me. Everybody takes it for granted that there is no gene that programmed the actin and myosin molecules of the muscle cells of my throat to interact in the rhythm of the words that I speak. Instead, we know that there is an information processing speech center in my brain, much

larger than molecules, which makes the molecules in my throat act and interact upon its command. Yet, when it comes to cells we tend to believe the opposite: Daily, biologists claim to have found new genes and molecules that act and interact to produce this or the other cell function. If cells were intelligent we would have to rethink all the cause—and—effect chains from genes to molecules to cell function that we believe today to be true.

c) Body as socio-biological system

If cells were intelligent, an organism would be the ecology of a huge population of intelligent individuals. We tend to believe today that our bodies are highly organized buildings composed of cells, which we consider to be dumb miniature machines. Even neurons are treated as complex, yet rather dumb signal switching gadgets. However, if each cell has a certain intelligence to make decisions on its own we would have to reconsider this concept, too. In this case, we would have to look at the structures and functions of our bodies as the result of the interaction of a huge population of intelligent individuals. Possibly, we would have to learn to look at our bodies much the way we consider the complex structures and actions of cities and nations as the result of the actions and interactions of huge numbers of individual people. And 'huge' hardly does justice to the number of cells that make up an organism. For example, one human body has more cells than there would be people on 1000 planets Earth. Also, of course, every cell is a much less intelligent part of a body than a human is part of a city or nation. Still, many of our rather mechanical explanations of body functions would have to be reexamined.

3. Do cells 'speak' using light signals?

Among the many amazing actions and reactions of mammalian cells that support the notion of cell intelligence (presented in this website) perhaps the most astonishing quality is their ability to 'see' (see "3. Infrared 'vision' of cells"). They are able to locate and differentiate between multiple microscopic light sources that emit pulsating near-infrared signals around 800 nm wavelength. The natural emitters of these signals are not yet known, the light scattering by the peri-nuclear granules plays a major role. (see " 4. The role of nearinfrared vision in the social behavior (cell sorting, tissue formation) of cells ". Vision of an organism is a sure sign of intelligence, as the detection of objects requires sophisticated signal processing as to its intensity, color, location, and dynamics. I have also shown, that the pulsation frequency of the signals affects the behavior of fibroblasts and epithelial cells. (ref 17). In other words, it appears that continued research along these lines may demonstrate that mammalian cells exchange near infrared signals that influence their behavior. Therefore, the ability of mammalian cells to emit and detect signals may belong not so much to the realm of optics but to the realm of long-distance communication.

4. Cell-cell communication over distances may determine a cell's development and function.

Let us remember that cell differentiation requires that the cells know where inside the embryo they are before they change their phenotype. As shown by numerous grafting experiments with early embryos, this knowledge of location will determine their future differentiation as kidney, lung, skin or brain cells. Of course, 'location' must not be understood in a purely spatial sense, but' means the position and functional dependence of any cell relative to the other cells in the embryo. In

contrast to plants, the determination of cell location in animals is greatly complicated by the fact that huge numbers of animal cells migrate around during development. What clues can tell a moving cell where it is, especially, if the 'where' is still under development? There is no outside power shaping the forming embryo, and the only preformed inside information of cells, namely their genome, is the same for all of them. It does not get us off the hook to claim that extracellular matrices and morphogenetic gradients are the 'traffic signs and billboards', that tell cells where they are. After all, they were put up in the right places by earlier cells, which had to know where they were. It seems that the only way for cells to find their location, is to form some kind of 'consensus' which of them is going to be what kind of cell. Such consensus among large numbers of cells requires communication over large distances because the number of cells in immediate contact with any given cell can be no more than six. And six is far too small a number to achieve a meaningful consensus among trillions of cells of an early embryo. There is some evidence already to suggest that cells have along-range interaction via near-infrared light scattering (see "4. The role of near-infrared vision in the social behavior (cell sorting, tissue formation) of cells.").

5. Cellular 'vision' and the future of medicine.

In summary, the study of cellular 'vision' may be the door to our next quantum leap in the development of medicine. As mentioned above, all diseases are ultimately healed by cells. Doctors 'merely' aid the cells of their patients to do their job. Just imagine, the powerful medicine doctors might practice in the future if they can literally 'tell' cells in their own language what they want them to do! For example, cancer cells might be 'told' to stop growing or at least may be 'summoned' to a

certain place on the skin where surgeons can easily scoop them out. Cells at the wound of a lost limb or eye may be 'told' to grow it again. They did it once. If we learn the right 'commands' maybe, we can persuade them to do it again. Obviously, we need to learn to speak the language of cells if we want to carry medicine to this advanced level. Initially, we would record the light signals of cells in different parts and stages of an embryo. Subsequently, we could reproduce them using microchips and laser diodes, and 'play' them back to the cells of an adult patient, which we want to perform one of the embryonic functions Later, we may learn to compose our own messages in the language of cells, in order to compel cells to carry out specialized tasks, which they have never performed, even in the embryo.

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