

Illustration by Sam Loman

# The body as a smart city

# Jerome Lowenstein, MD

Dr. Lowenstein (A $\Omega$ A, New York University, 1957) is Professor of Medicine at New York University School of Medicine. He is a member of *The Pharos* Editorial Board.

laude Bernard is best known for his assertion that when life evolved beyond single-celled organisms and left the aqueous environment in which they were in equilibrium, the tissues of the body were sustained by a "*milieu interieur*" (internal environment). He wrote, "It is as though the organism had enclosed itself in a kind of hothouse where the perpetual changes in external conditions cannot reach it." <sup>1</sup>

That has been seen as the rationale for the evolution of a variety of physiologic systems (predominantly renal and pulmonary) devoted to the maintenance of the constant composition of the extracellular fluid, the internal milieu, in which cells, tissues, and organs are bathed. Bernard's thesis evolved at a time in the history of science (1865) when the knowledge of human physiology was in its infancy. This view of the *milieu interieur* was very much the same when Walter Cannon (A $\Omega$ A, Harvard Medical School, 1906, Honorary) coined the term "homeostasis" in his *Wisdom of the Body*, published in 1932.<sup>2</sup>

There may be value in considering Bernard's *milieu interieur* as a part of a much larger system exemplified by the evolving concept of the smart city. A smart city is an urban development vision to integrate information and communication technology in a secure fashion to manage a city's assets. These assets include local departments' information systems, schools, libraries, transportation systems, hospitals, power plants, water supply networks, waste management, law enforcement, and other community services.

What makes the analogy between the smart city and the internal milieu of the smart body so instructive is that each of the components of the smart city must be carefully designed and integrated with other systems utilizing the most up-to-date technologies. One might consider cells, tissues, and organs as islands in the smart body, i.e., the whole organism.

# Information systems

Bernard's internal milieu can then be seen as more than a bathing fluid whose electrolyte composition serves to maintain the electrolyte and acid-base composition of cells and tissues. Beyond delivering nutrients and removing waste products, extracellular fluid is a central component of signaling throughout the body. It is the carrier of protein-bound hormones, dissolved signaling molecules, dissolved gases, and products of cellular metabolism, both waste products and precursors for cellular synthetic activities.

In the construction of smart cities, such as the Hudson Yards project on the west side of New York City, extensive networks of signaling cables have been imbedded to connect, in ways that will serve both the present needs and anticipated future needs, the many discrete modules of the smart city. Similarly, the manner in which the extracellular fluid serves these roles requires a deeper consideration of the many modules in the smart body that must be interconnected, and the often unique manner in which the extracellular fluid, the internal milieu of the smart body functions to signal to these modules.

Many different types of cables are employed and interconnected to rapidly meet the great number of needs of the smart city. Many components of the smart body require signals that travel much faster than the bulk flow and diffusion of extracellular fluid. The brain; the retina; peripheral receptors for temperature, touch, pain, joint position, skeletal muscle, cardiac muscle, and the adrenal medulla may be considered rapid response systems requiring a communication system far faster than could be supplied by the delivery of signals carried by extracellular fluid. The nervous system, both peripheral and central, serves this function with signals traveling in milliseconds between receptors and effectors.

Information distributed through specialized cables in the smart city are similar to signals sent through the nervous system in that they may be stored and retrieved as memories or conditioned reflexes.

While electrical signals are transmitted along nerves and mediate their effects at specialized nerve endings in the smart body—like electrical outlets in the smart city the manner in which chemical signals are transmitted to targets utilize many different forms of signaling. The simplest signal from the extracellular fluid is exemplified by the diffusion of uncharged, lipid-soluble signals such as oxygen, carbon dioxide, ether, and nitrous oxide. These substances cross the lipid bilayer of all cell membranes following a simple concentration gradient.

More specific targeted signals follow different routes. Hormones, secreted by endocrine organs, are small molecules that are protected from loss across the glomerular capillary, or hepatic-portal capillary network, by binding to specific hormone binding proteins or to albumin. These signals are targeted to cells bearing surface hormone receptors which, having a greater affinity for the hormone than its carrier protein, allow the hormone to activate cell surface receptors or activate ion channels that facilitate down-stream cellular signaling, usually through a chain of cytoplasmic phosphorylation reactions.<sup>3</sup>

In the smart city, electrical signals originating from members of the community via implanted chips, akin to the chips imbedded in dogs that allow them to open entrances to their homes, might serve to activate street illumination, open garage doors, summon an elevator, or announce arrival. This sort of signaling is already in place in some great museums in which rooms are illuminated or allowed to go dark as visitors pass through.

Protein-bound signaling molecules of other classes are transferred across cell membranes by specific organic anion or cation transporters (OATs or OCTs). These signaling molecules exert their effects only at sites of specific organic ion transporters.<sup>4</sup> Signals transported in this manner, activate cytoplasmic signaling cascades.

The omnipresent maps of cell signaling pathways look remarkably like the map of the London Underground or the NYC transit system. In the smart city the equivalent of this selective delivery system might be the incorporation into the cable system of modules that deliver different newspapers to designated customers, or different meals delivered by Fresh Direct.

# **Power plants**

What about energy? Here again, there are parallels between the smart city and the smart body. Both systems are ultimately dependent on some external source of energy. The major source of energy for cities is hydroelectric. Water is stored in dams and moves turbines to generate electrical power. The energy for the smart body is stored in the form of a small, ubiquitous molecule, ATP (adenosine triphosphate).<sup>5</sup> When work is performed, the energy is supplied by the release of one or more high energy phosphates.

The parallel goes well beyond the production of energy. Smart cities harness the products of energy utilization —heat and steam—to power generators thereby recycling energy. In the smart body, the energy expended in active transport of sodium or hydrogen ions results in transmembrane ion gradients that can account for the passive movement of potassium and chloride—an energy-conserving arrangement.

It is interesting to reflect on the fact that there is growing opposition to the dependence on the burning of fossil fuels for energy, seen as a factor in global warming. For the smart body, there has been a mounting campaign to replace the burning of simple carbohydrates as an energy source. Simple carbohydrates, as found in sweetened drinks and many prepared foods, are believed to contribute to the present epidemic of obesity and diabetes.

#### Waste management

Waste disposal represents a major task in both the smart city and the smart body. Our very distant ancestors—protochordates living in a salty soup 500 million years ago—disposed of all waste products via simple tubules that antedated nephrons as we now know them.<sup>6</sup> Waste was simply excreted back into the environment.

The earliest cities similarly disposed of all waste through the sewers—tubes—that ran into nearby rivers, lakes, or larger bodies of water. This is the means of waste disposal still employed in some parts of the world, e.g. the *favelas* of Brazil. Smart cities have worked to refine waste disposal, to allow selective removal of toxic or noxious waste, and reclaim clean water, for which there is a dangerous shortage across the planet.

The smart body, with 500 million years head start, has evolved an elegant system for waste removal. The entire extracellular fluid volume is filtered at the glomerulus roughly 10 times a day. Transporters in the renal tubule actively reabsorb roughly 99 percent of the filtered water, glucose, and dissolved salts, while allowing for the removal of a host of small filtered wastes. Several organic anion transporters secrete protein-bound metabolic waste products<sup>7</sup> into the draining tubule.

# Law enforcement

Safety is a major concern in smart cities. Ultimately, cities will have systems to recognize homeowners, personnel, workers, delivery services, and others who enter the community. These systems will center on finger prints, iris patterns, voice recognition, and ultimately recognition of HLA types—many of which are already in use in house-holds and businesses.

The immune system, from the earliest, most primitive

single cell organism, has evolved recognition systems termed "innate immunity" and "acquired immunity." These defense systems rely on signals not much different from those that guard the entrances, stores, factories, schools, and private and public spaces in smart cities. Pattern recognition, whether it is the pattern of a finger print or the shape of an antigen, is the common feature.

# **Parallel evolutionary paths**

The parallels between the smart city and the smart body are impressive. It may simply be that the two systems have evolved independently, yet for some reason, possibly because they are effective, have evolved along parallel lines. Or, possibly in some way, not always obvious, the lessons learned during the long evolution of modern smart bodies is imprinted on the modern architects, builders, and city planners who have invented the smart city.

# References

1. Bernard C. Leçons sur les propriétés physiologiques et les altérations pathologiques des liquides de l'organisme. Paris: Bailliére; 1859. Quoted in Smith HW. From Fish to Philosopher. Natural History Library edition: 1961: 227.

2. Cannon WB. The Wisdom of the Body. New York: WW Norton & CO; 1932. Quoted in Smith HW. From Fish to Philosopher. Natural History Library edition: 1961: 229.

3. Lodish H, Berk A, Matsudaira P, et al. Molecular Cell Biology, 5th edition: Signaling at the cell surface. New York: W. H. Freeman; 2003: 533–40.

4. Wu W, Dnyanmote AV, Nigam SK. Remote Communication through Solute Carriers and ATP Binding Cassette Drug Transporter Pathways: An Update on the Remote Sensing and Signaling Hypothesis. Mol Pharmacol. 2011;79: 795–805.

5. Harold FM. The Vital Force: A Study of Bioenergetics. New York: WH Freeman & Co; 1986.

6. Lowenstein J. The anglerfish and uremic toxins. FASEB J. 2011;25(6):1781–5.

7. Masereeuw R, Henricus AM, Mutsaers M, et al. The Kidney and UremicToxin Removal: Glomerulus or Tubule? Semin Nephrol. 2014;34:191–208.

The author's address is:

New York University School of Medicine 560 First Avenue New York, NY 10016 E-mail: lowenstein@nyumc.org