Biomedical Optics—The Next 100 Years

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The previous century of biomedical optics strongly suggests that our technology and capability will be much improved in the next 100 years. Today we have artificial light sources emitting thousands to billions of watts that are routinely used to treat children; photodynamic therapy drugs designed to hit specific molecular targets; reading an individual person's genetic code using molecular-optical probes; changing brain functions by inserting light-activated genes into mammals; and reading human brain activity with light, to name just a few current capabilities.

But what comes next, next, and next? Some doctors, including this author, have been accused of being "often wrong, but never in doubt." With that caveat, what follows is certainly what will happen during the next 100 years.

Optical diagnostics will improve, miniaturize, proliferate, become mainstream, replace conventional biopsies, guide medical and surgical therapy in real time, and then be fully integrated via the extension of what we now call robotics. Optical systems already provide an unprecedented combination of high-speed imaging, resolution, point-of-care molecular assays, and minimally invasive access deep inside the body. By 2040, optical diagnostics will be comparably as different as today's smart phones are from the telephones of 1985—an equal time gap. What will drive this? At the least, cancer detection, surgical guidance, instant diagnosis of infections including their antibiotic sensitivity, and the need for common lab tests done quickly on a single drop of blood, probably as a smart phone app. By 2050, user-friendly optical diagnostics will be nearly everywhere in medicine, surgery, school, public, and home. Data and decision analysis will be rapid, highly automated, almost free, and simultaneously personal and widely shared.

Most of our optical treatments using lasers and light-activated drugs aim to destroy some undesirable "target." But light also stimulates, modulates, heals, controls, or creates. By 2065, the tables will have turned—most of the therapeutic realm of biomedical optics will be non-destructive. An early example now is optogenetics. Rhodopsin genes linked to specific promoter sequences are used to express light-activated action potentials in neuronal systems. The technique started as a way to study brain function. By 2025, it will provide a cure for blindness from the genetic disease retinitis pigmentosa. This is just the first example of a "designer optical interface" with our central nervous system. Other examples will hail from the natural and somewhat enigmatic phenomenon of "photobiostimulation," in which light activates mitochondria, the cellular power plant that produces ATP. Apparently every cell in our bodies has at least one photoreceptor system, and probably several. During this century, light will be used to activate much more than transfected neurons, mitochondria, or naturally occurring photosystems. There will be a steady trend to use light for controlling biological systems. Microscale implanted optical machines will be developed, powered, and controlled by light. Think, "designer tattoos."

Optical technology itself will benefit directly and greatly from biology! The first live-cell laser was demonstrated only a few years ago. Useful optical components occur in natural organisms, including waveguides, gain media, energy storage and transfer, charge separation, quantum-level light detectors at body temperature, and narrow-band emitters. We use a lot of optical devices to study biology, but the flow of capability between optics and biology is ultimately a two-way street. Can you imagine using optical components that respond to their environment, self-align, replicate, and/or repair themselves (because they are alive)? This revolution has already started, by making optical components from natural biomaterials. Some useful optical cyborgs will be around well before 2115.

The past 100 years has seen a steady trend in optics and electronics, toward smaller and smaller devices. Enzymes, RNA, and other macromolecules are incredibly agile nanomachines that specifically manipulate other molecules. Combining three current trends of (a) ever-smaller-devices, (b) designer molecular biology, and (c) near-field optics, one comes up with diagnostic and therapeutic, nanoscale, inside-you, optical robots that work in concert with our natural nanomachinery. This will lead to the design of circulating, biocompatible, harmless, controllable, self-reporting, intervention-capable cyborgic devices that are the size of your cells or smaller. At the end of this century, such things will be in clinical trials. It will be impossible—and irrelevant—to decide if they are devices, drugs, or diagnostics. Eventually, even the FDA will stop caring about that.

Energy, global warming, and environmental change are all, at heart, biomedical optics problems. Evolution came up with photosynthetic algae and forests that are barely 1% energy efficient, yet they are the only power source for life on the planet (except for a few, very weird organisms). Can we do better than photosynthesis? A delocalized, efficient, solar-driven, self-repairing, replicating, energy-generating, non-polluting equivalent of photosynthesis is sorely needed. Like it or not, we have become shepherds of this world. A century ago, Mark Twain famously quoted a friend… "everybody complains about the weather, but nobody does anything about it!" A century from now, global warming may be viewed as an uncontrolled but positive feasibility experiment—yes, we *can* change the weather! Other global challenges will be faced and attacked using biomedical optical technologies. By 2115, people themselves may have the option of being photosynthetic. What if food were plentiful and free? What if people were healthy for a very long time? Traditionally, species populations are controlled by disease, famine, and unfortunately for us, war. Population control is probably going to be an even bigger issue in 2115. Maybe biomedical optics will help that, somehow.

Finally, there is optical exobiology. Bioscience has been fundamentally limited by looking at life, well, *here*. Optical telescopes are the tool that recently allowed us to detect many other planets, orbiting many other stars. Exobiology is likely to be a robust science by 2115, and surely it will depend on much better optics. Someone or some team will use optical spectroscopy to probe what's on those planets. Telescopes now look at a small patch of sky for a small patch of time, with limited spatial and spectral resolution. Why not look at all of it, all the time, with detecting life in mind? If life is found, bioscience will take a giant leap forward thanks to optics.