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# Bioelectricity: From Endogenous Mechanisms to Opportunities in Synthetic Bioengineering

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**D**EVELOPMENTAL BIOELECTRICITY BEGAN with the study of ionic phenomena in living forms.<sup>1</sup> In the early days, the focus was less on discrete model systems and more on a broad investigation across the web of life. Especially prescient were workers such as H.S. Burr and E.J. Lund, who performed electrophysiological measurements in a very wide range of organisms undergoing processes such as morphogenesis, regeneration, and cancer.<sup>2</sup>

Since then, workers in bioelectricity have sought to combine the wealth of data and biological diversity with the insights that can be gained by a focused application of “high” technologies for tracking and manipulating bioelectric states, such as genetically encoded voltage reporters<sup>3,4</sup> and optogenetic actuators<sup>5</sup> in a few flagship organisms. As always in such novel conceptual studies, and in the spirit of Hodgkin, Huxley, and the squid giant axon, use of model systems is paying dividends.<sup>6</sup>

In recent years, our field has seen many important advances,<sup>6</sup> as new tools and mechanistic investigations continue to form a synthesis between bioelectrical signaling and the biochemical and biomechanical pathways. Notable examples include the regulation of Hedgehog signaling through membrane potential,<sup>7</sup> the control of membrane potential of cells by substratum stiffness<sup>8</sup> and geometry,<sup>9</sup> and transdifferentiation of endothelial cell progenitors.<sup>10</sup> New endogenous roles have been characterized, including the role of proton fluxes in neural induction in the frog *Xenopus laevis*<sup>11</sup> and orientation of feathers in chicken embryo skin.<sup>12</sup>

An important opportunity for the future of the field concerns its application in synthetic biology.<sup>13</sup> Although most toolkits for cell engineering today focus on metabolic and transcriptional circuits, there is a huge opportunity of taking what has been learned about bioelectrics in endogenous roles<sup>14</sup> and exploiting it in constructing novel multicellular creations.<sup>15</sup> This ranges from optogenetic control of living organisms as a kind of biorobotics<sup>16</sup> to the study of bio-

electric signaling in organoids, assembloids, and organs-on-a-chip<sup>17</sup> to the future use of bioelectric circuits to control morphogenesis and physiological signaling in networks of prokaryotic<sup>18,19</sup> and eukaryotic<sup>20</sup> cells. The unique features of bioelectric signaling as a medium for computation and coordination across tissues promise many applications in synthetic and biomedical contexts.

We invite workers in all of these fields to use our journal as inspiration and a source of ideas and expert contacts for novel collaborative projects in the expanding space of bioelectricity—science, engineering, including synthetic bioengineering, and medicine.

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