Neuromorphic computers, brains and development:
unifying principles and distinctive differences

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Numerous applications of artificial neural networks (ANNs), and especially Deep Learning, speak to the algorithmic advantages of neuromorphic computing. However, implementing ANNs on digital computers is computationally intensive and this severely limits the use of ANNs on small low power devices. Brains are orders of magnitude more efficient, so engineers are developing biologically inspired neuromorphic computers (Tang *et al*., 2019). These solid state devices are more efficient because they incorporate designs and follow design principles observed in brains but, as we will see, their efficiency is limited because their technology lacks the flexibility and efficiency of protein molecules, and the developmental and regulatory mechanisms that enable neurons to self-assemble, repair and reprogram with molecular precision.

The latest neuromorphic computers (e.g. Davies *et al*., 2018) dramatically increase efficiency by replacing highly simplified ANNs with spiking neural networks (SNNs) that use more realistic integrate and fire neurons. These new devices also follow design principles that improve the efficiency of brains (Sterling & Laughlin, 2015) and biometic, lower power electronic devices (Sarpeshkar, 2012). This three-way convergence demonstrates that these design principles are universal because they depend on the basic physics and chemistry of information processing devices, and the mathematics of information. Some of these principles extend to synaptic development (Ju, Colbert & Levy, 2017), suggesting that trade-offs between speed, accuracy and resources invested (e.g. the numbers, volumes and metabolic rates of cells) also influence the design of developmental processes.

Unlike brains, neuromorphic computers still depend on digital processing to address signals efficiently, to integrate and fire, to allocate resources dynamically and to update synapses according to plasticity rules. Engineers are attempting to replace these costly digital operations with analogue solid state devices: most notably junctions that implement short term synaptic plasticity (Tang *el al*., 2019). How close will such “all analogue” solid state devices come to being truly neuromorphic?

Whereas solid state devices compute directly by manipulating physics and chemistry, a brain manipulates biophysics and biochemistry using its “winning technology”, Molecular Cell Biology. By definition MCB supports living systems that self-assemble, self-repair, actively restructure according to operating conditions and ultimately replicate, all of which depend on the processing of information. Nonetheless, animal, vegetable and mineral computers operate in a similar way: they all process information by directing signals through circuits in which each component transforms specific inputs into specific outputs. The brain’s winning

technology, MCB, largely depends on circuits formed by protein molecules: electrical circuits formed by ion channels and chemical circuits formed by receptors, enzymes, messengers and transmitters. Protein circuits, like solid state electronic circuits, support a powerful repertoire of mathematical operations, have memory and are Turing complete.

MCB has distinct advantages. Its protein circuits exploit protein physical chemistry and diversity to be more versatile, adaptable and efficient than solid state. Using allostery, a single protein molecule transmits and processes information on time scales from microseconds to minutes, is up- and down-regulated according to demand, and retuned to adapt transfer functions to operating conditions. The genome, plus sub-unit combinations and post-translational modifications, provide a "parts list" of >70,000 distinct forms of signaling proteins from which to construct circuits that are precisely adapted to meet specific needs. In neuromorphic computers this flexibility is achieved by programming digital processors whereas MCB uses compact protein molecules whose energy consumption is within factor of 50 of the thermodynamic minimum.

Above all, MCB provides opportunities for analogue computation and dynamic resource allocation that are currently inconceivable in solid state. A cell is a fully integrated system that self-assembles, self-repairs and self-regulates. To achieve this a cell's local control circuits are connected to form a global network that coordinates the cell's activities. This wetware computer performs tasks familiar to developmental biologists and commonly attributed to brains: pattern recognition, pattern generation, output coordination, searching, decision making, and memory (Bray, 2009). Given that Natural Selection is opportunistic, it is no surprise that this internal network also participates directly in the ongoing control of behaviour by augmenting the mechanisms that have evolved to support rapid computation in neural circuits - axons, dendrites, excitable membranes, and synapses.

There are relatively few examples of this internal network in action, but as techniques improve and neuroscientists increasingly recognise the network's potential, more will be discovered. In many nervous systems neuromodulators act on neurons' internal networks to bring about concerted changes in synaptic efficacy and membrane excitability that change behaviour by reconfiguring circuits (Harris-Warrick and Marder, 1991). In cortical neurons, short and long term synaptic plasticity, and hence learning and memory, depend on the coordination of molecular and morphological changes (Nishiyama and Yasuda, 2015). Moreover local circuits operating within dendrites link synapses so that synaptic plasticity is driven by both spatial and temporal patterns of synaptic activation (Mago et al., 2020). In cortical pyramidal neurons and retinal horizontal cells (Raynauld, Laviolette and Wagner, 1979) synaptic contacts are made and broken by directing the growth and retraction of post-synaptic contacts. These well-regulated morphological changes come as no surprise to retinal physiologists. Many photoreceptors change shape from night to day to trade sensitivity for

acuity, and cone outer segments actively align to the direction of incoming light. Indeed, the potential of the computer in every living cell to reprogram and adapt processing dynamically, and to use growth and supply processes to compute on longer timescales, is considerable because it is maintaining a neuron that is in a state of constant flux. The average half-life of a neuron's many thousands of species of protein is approximately 10 days, and when a neuron adjusts its sensitivity homeostatically, it changes the abundance of over 300 synaptic proteins (Dörrbaum et al., 2020).

To close, a message of solidarity. As we all know the computer in every living cell controls the cell's development by acting on inputs and developmental programs are not instruction manuals, they are self-correcting algorithms. Thus the processing of information unites research on neuronal development, homeostasis, plasticity, and the generation of behaviour by neural circuits, as does an important processor, the computer in every living cell.

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