Towards a Bacteriorhodopsin-Silicon Neuromorphic Photosensor

C. H. Martin, Z. P. Chen and R. R. Birge
W. M. Keck Center for Molecular Electronics and the Department of Chemistry, Syracuse University, Syracuse NY 13244

Abstract

We describe our efforts towards constructing a hybrid protein-silicon neuromorphic photosensor based on the photo-active protein bacteriohodopsin. This protein displays an differential photosensitivity similar to the response of the receptive field of an X-type retinal ganglion cell. Similar bacteriohodopsin photoelectrode arrays display inherent edge detection and motion enhancement. We discuss challenges associated with constructing and understanding the protein-silicon interface and possible chemical solutions for our experimental device.

1 Introduction:

1.1 Visual Computing With Silicon vs. Advanced Materials

VLSI solid state devices dominate computing technologies in every area, including photodetectors (CCDs and CIDs), amplifiers, and processors. In contrast, nature has evolved very different computing architectures, such as in dense and highly parallel neural structures. Briding the gap are the so-called neuromorphic chips–analog VLSI devices which mimic neurological signal processing such as that in the retina [1]. Although current VLSI technology limits the resolution and signal processing capacities of the present devices, the silicon retinas currently under development may one day serve in prosthetic devices for the blind [1].

Advanced materials technology offers the potential for new and improved neuromorphic chips, such as a conducting polymer and our proposed protein-based artificial retina. For instance, a so-called "plastic retina" utilizes conducting polymer in a photosensor architecture to circumvent the expensive analog VLSI components while providing. The conducting polymer simulates the analog VLSI logic circuits which locally correct for global changes in illimuniation. This materials-based artificial retina offer potentially greater spatial resolution with much lower manufacturing costs.

But natural vision also includes inherent motion detection and edge enhancement, and it is here that biotechnology can provides advanced materials suitable for specifically evolved for computation. Natural biomolecular photodetectors consist of highly efficient photo-active proteins such

as the rhodopsins [2,3]. In the primate visual system, biomolecular amplification occurs with G-coupled protein receptors. And one particular protein, bacteriorhodopsin (BR), inherently responds to light with a differential photosensitivity common in edge detection and motion enhancement architectures.

The protein BR is especially suited for technological development because of its inherent signal processing capacity, its photochemical properties, and the wealth of scientific knowledge about its function. In particular, the bR photocycle includes a number of distinct photointermediates which make it a highly efficient photochromic material suitable for device applications of bR. Current bR research applications exploit it for holographic optical memories, 2-photon volumetric optical memory, and spatial light modulators. [7]. The transmembrane proton pump also provides a photo-electrical current, however, which can be used to create a novel protein-based photosensor. We propose the further advancements in materials-based artificial retinas may be realized with thin films of the protein bacteriorhodopsin. [4,5,6]

1.2 The Protein Bacteriorhodopsin

Many researchers seek proteins from microorganisms which live in harsh environments, hoping to take advantage of robustness and stability of these biomaterials. The protein bacteriorhodopsin (BR) is the premiere example of this [7]. Bacteriorhodopsin is the light transducing protein of the ancient, salt-loving bacteria *Halobacterium Salinarium* . This bacteria thrives in marshes where salt concentration is six times that of salt water. When deprived of oxygen necessary for respiration, *Halobacterium Salinarium* calls upon on an ancient mechanism for energy production, switching from respiration to photosynthesis by expressing an abundance of the membrane-bound BR. BR transforms light energy into an electrochemical proton gradient which drives ATP synthesis. Additionally, BR comes in an exceptionably stable trimeric form called the purple membrane (PM). Thus, under the most extreme operating conditions, *Halobacterium Salinarium* produces an exceptionally stable, biomolecular photochemical transducer in order to activate an evolutionary vestige for survival.

Bacteriorhodopsin is the best understood protein of the class the rhodopsins visual pigments [3,7], being one of only a few membrane bound proteins with a known crystal structure [8]. Amazingly, bacteriorhodopsin resembles both animal and invertebrate photoreceptors both structurally and functionally, and yet all three evolved independently. As with all rhodopsins, BR consists of seven transmembrane alpha-helical segments and a functional retinal chromophore, a vitamin A derivative. The BR photocycle, the transmembrane proton pump, provides a photo-electrical

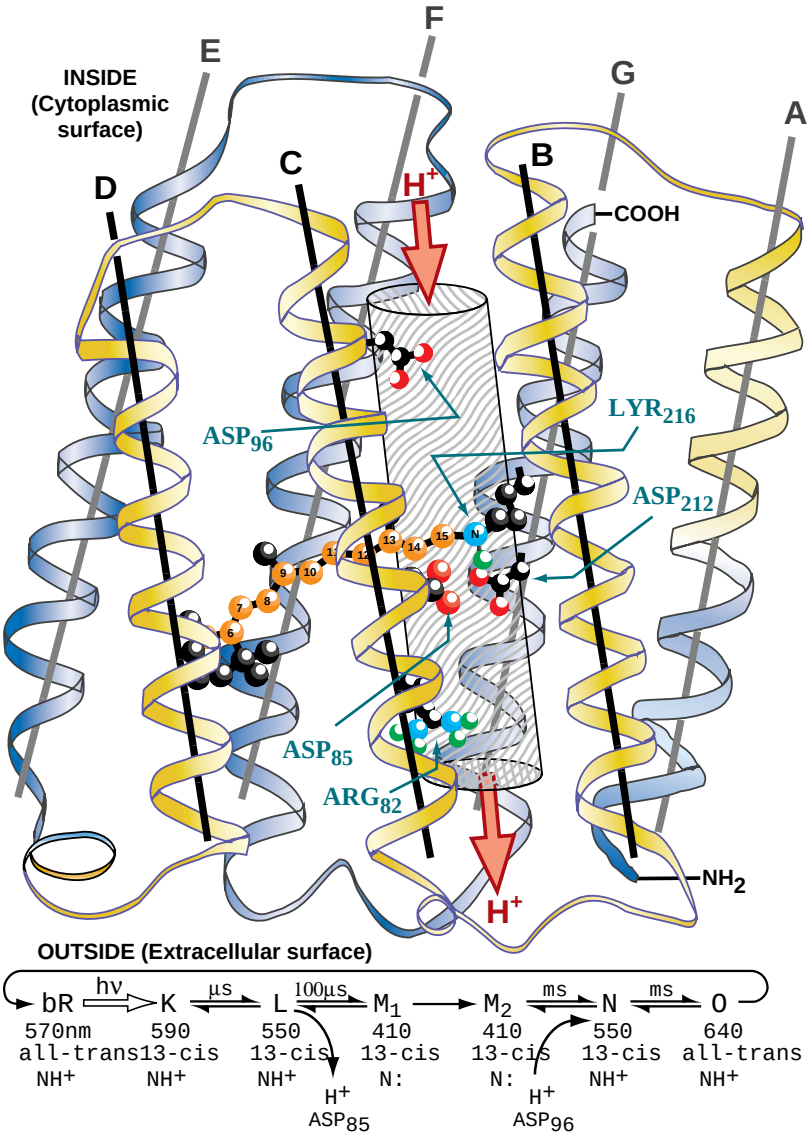

Figure 1: Three dimensional structure and photocycle of the protein bacteriorhopsin. The labels BR_{570} K, L, etc. refer to the spectroscopic intermediates defining the photocyle.

current which can be used to create a protein-based photodetector.

Figure 1 displays the three-dimension structure and the key amino acids involved in the BR photocycle and briefly summarizes the intermediate steps in the photocycle and their lifetimes. Bacteriorhodopsin is the subject of numerous reviews[7,9,10] and current experimental and theoretical research[11,12]. Let us examine the proton motion, key amino acid residues, and protein structural changes through one pass of the photocycle, elucidating the features relevant for device applications. The ground state bR_{570} absorbs green light with an exceptionally high quantum yield (0.65), a desirable property for exploiting this photo-active protein. (Ground state bR_{570} also has an extremely high two-photon absorbtivity and non-linear optical polarizability which distinguishes it as an ideal material in several areas of optical processing[7]) The photo-excited retinal rapidly isomerizes (within 2 ps) to the K form, which can only be trapped at liquid nitrogen temperatures. The fast ($bR_{570} \leftrightarrow K$) interconversion formed the basis of early, cryogenic switches based on BR thin films[7]. The K intermediate thermally relaxes to L, and then, during the $L \rightarrow M_1$ transformation retinal loses its Schiff base proton to Asp85. $M1 \rightarrow M2$ involves an irreversible structural change involving small but significant rearrangements of the alpha-helices. The M forms may be converted back to bR_{570} with blue light – a process important for using BR as holographic recording medium[7] and in a proposed BR-based photosensor (see below)[4]. In the $M_2 \rightarrow N$ interconversion, Asp96 reprotonates retinal. Finally $N \leftrightarrow O \leftrightarrow bR_{570}$ while Asp96 uptakes a new proton from solution. There is also a branched photocycle, $O \leftrightarrow P \leftrightarrow Q$, exploited in BR based volumetric optical memories[7].

The BR photocycle depends on the pH, ionic strength, and detailed amino acid sequence of BR. For example, the mutation D96N dramatically increases the lifetime M state because there is no acidic residue to reprotonate retinal during $M \leftrightarrow N$, thus delaying the second half of the photocycle[7]. Dried BR films yield a smaller photocurrent than wet films because the lower solution proton concentration. The photocycle also may be chemically manipulated by reconsituting BR with a variety of retinal analogs and chemical additives. Below we find that large organic cations can substitute for troublesome BR-bound calcium ions[13].

1.3 Retinal Preprocessing and Neuromorphic Chips

The photocurrent response of BR displays a differential sensitivity common to the X-cell ganglion receptive fields in the primate visual system. Let us first review the X-cell architecture and then compare signal processing features of the primate retina and BR photodetectors.

In contrast to the function of typical solid state photo-detectors, such

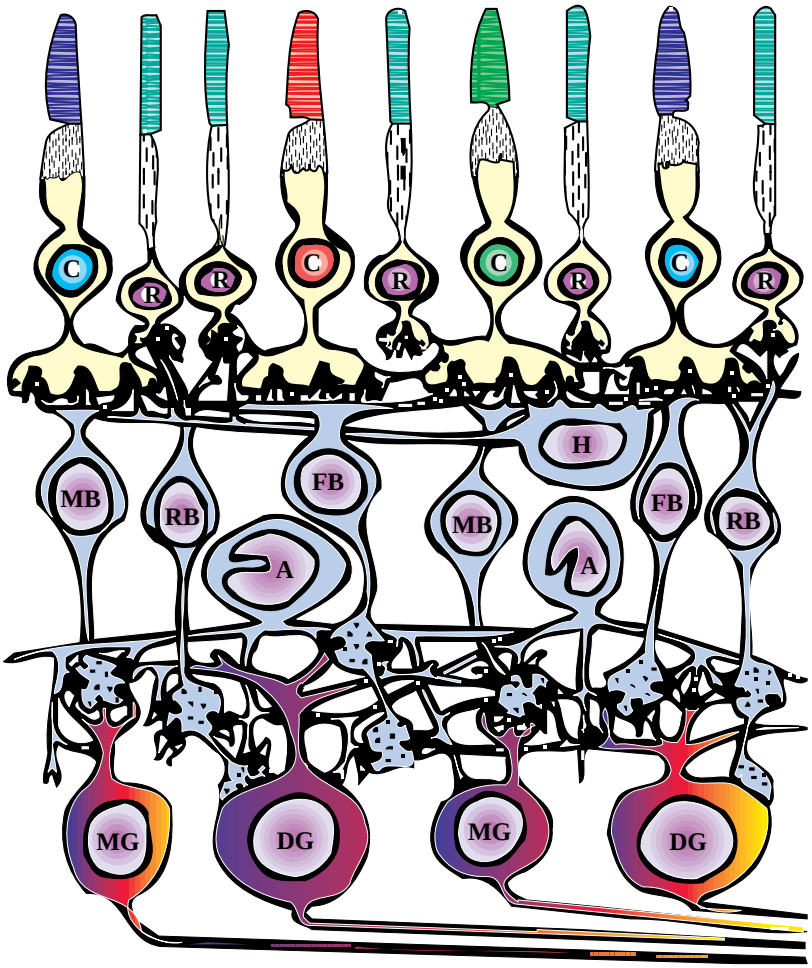

Figure 2: Schematic of the neural components of the primate retina. Depicted are the (R) Rods, (C) Cones, (H) Horizontal, (A) Amacrine, and (MD), (DG) Ganglion cells. Reproduced from Dowling and Boycott.

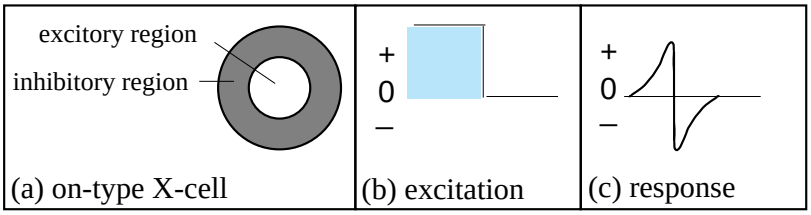

Figure 3: The receptive field and photoresponse of an X-type retinal ganglion cell

as CCD and CID cameras, the vertebrate eye performs edge and motion detection and local contrast control–a result the parallel architecture of retina and the visual processing centers of the brain [14,6]. (In fact, our eyes do not respond to a static image, as evidenced from experiments which project a static image onto the eye, compensating for the continuous and subconscious eye motion.) Here we consider only on the retina, in which a considerable amount of retinal preprocessing takes place. Figure 2 presents the neural components of the primate retina. When light reaches the rod (R) and cone (C) cells, they transmit an electrochemical signal to the overlaying network of Horizontal (H) and Amacrine (A) cells which in turn connect to the neural Ganglion cells (MG, DG) of the optic nerve. This parallel processing network provides initial edge enhancement and motion detection, lumped together as "differential responsivity." The retina also accommodates large scale changes in brightness by with local adjustments to the total contrast (local contrast control) Typical solid state detectors require additional edge and motion enhancement systems and function over a much smaller intensity range [1,15].

The most basic retinal differential responsivity arises in the so-called X-cell receptive field of a single ganglion cell [14]. A receptive field corresponds to the spatial area of the retina which excites that neural cell. [Note that receptive fields overlap extensively, adding an additional layer of parallel processing, however, we consider only one receptive field here] Two types of X-cells exist, on and off, which respond to changes in brightness and darkness, respectively. The receptive field of an on X-cell consists of an circular excitatory region surrounded by a disc-shaped inhibitory region (see Figure 3(a)). When illuminated, the excitatory re-

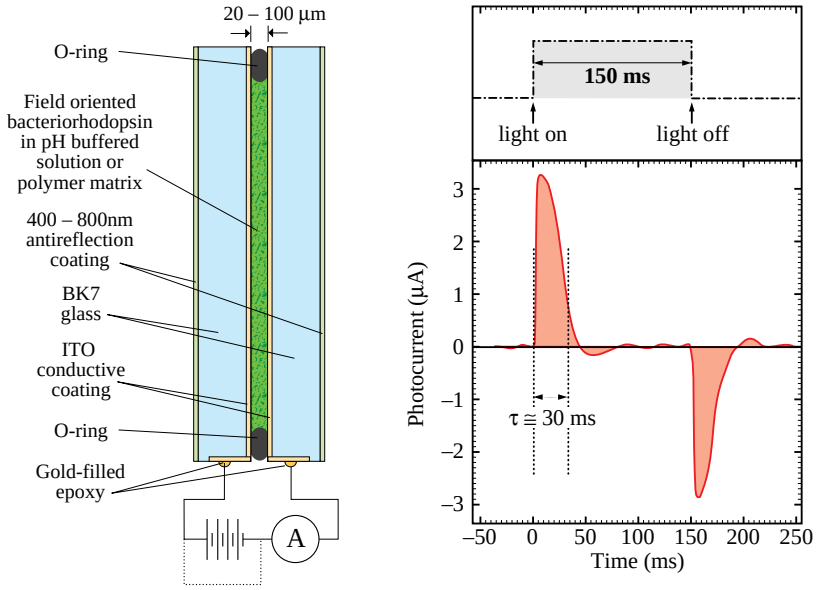

Figure 4: Bacteriorhopdopsin photoelectrode and its photocurrent response

gions produce a positive signal, whereas the inhibitory regions responds negatively. If the entire receptive field is stimulated equally no signal results. When presented with an edge, as in Figure 3(b), the X-cell responds as in Figure 3(c), enhancing the edge through the zero-crossing signal. Hence an X-cell enhances objects passing through its receptive field.

A number of groups have constructed "artificial retinas" which mimic the various image processing features of the retina [1]. By far the most active research occurs in the neuromorphic analog VLSI chips, which utilize traditional semiconductor technologies to implement appropriate parallel signal processing archetectures. Work with organic and biological materials remains comparatively less developed [4,5,15]. The photocycle of BR, however, provides inherent differential responsivity, therefore neuromorphic architectures employing BR films should offer improvements in both resolution and cost over their silicon competitors.

1.4 Earlier Bacteriorhodopsin-based Photosensors

Takei *et. al.* constructed a Bacteriorhodopsin photo-electrode (See Figure 4) with a photo-response that resembles the response of a single X-cell receptive field [4]. They electrodeposited a thin BR-polymer onto a transparent, conducting SnO_2 electrode in order to orient the BR and attach it firmly to the anode. The BR film is dried at high (about 80%) relative humidity to prevent cracking and sandwiched between a second electrodes. Figure 4 depicts this electrode and its photcurrent response . When illuminated with a short laser pulse (150 ms), the BR films yields the differential photocurrent which rises in about 2 ms and with a width of 30 ms. Discontinuing the pulse produces a reverse photocurrent of the similar shape and magnitude. The differential current response apparently arises from proton pump, although the exact details remain unresolved [6]. Never-the-less, the thin BR films respond like the receptive field of a single X-cell, thus motivating the construction of more sophisticated imaging systems based on BR. For example, Lewis *et. al.* propose to recreate the physical architecture of larger receptive fields using BR films oriented to respond in an exhibitory of inhibitory fashion.

A successful BR-based motion sensor has been constructed by Miyaska *et. al.* [5,17]. Instead of creating a dried BR film, as above, they suspended 10 layers of BR Langmuir Blodgett films on top of the 8*X*8 array of ITO pixels printed a glass substrate. (Each pixel connects by wire to a separate, external video amplifier). To close the BR-electrode circuit, a layer of aqueous electrolyte gel (1 M KCL, pH 7 to 8) was added on top of the LB films, and a common Au counter electrode was placed on top. The success of the device depends on the use an electrolyte gel between the BR films and the counter electrode, as the wet electrode responds an order-of-magnitude better than dried BR film electrodes. The sensor does not respond to a static image unless the incident light is modulated at a frequency between 20 and 50 Hz. Additonally, it responds to mobile objects, as expected.

The BR photocurrent in these devices, however, remains puzzling [5,17,16,18]. The sensor above employs randomly oriented LB BR films and yet responds in only one direction (the response is said to be rectified). Koyama *et. al.* explain the rectified photocurrent by assuming that the photocurrent results from the voltage difference across the membrane.

Robertson and Lukashev, however, question this model and instead offers that the BR transient photocurrent results from local pH changes at the BR-ITO interface [18]. They prepared wet BR and mutant D96N BR films of two different thicknesses and either random or specific orientation. First, it is found that the highly oriented wild type BR films produce the same photocurrent response as non-oriented films of D96N BR. Since the D96N mutant lack the proton uptake group (see above),

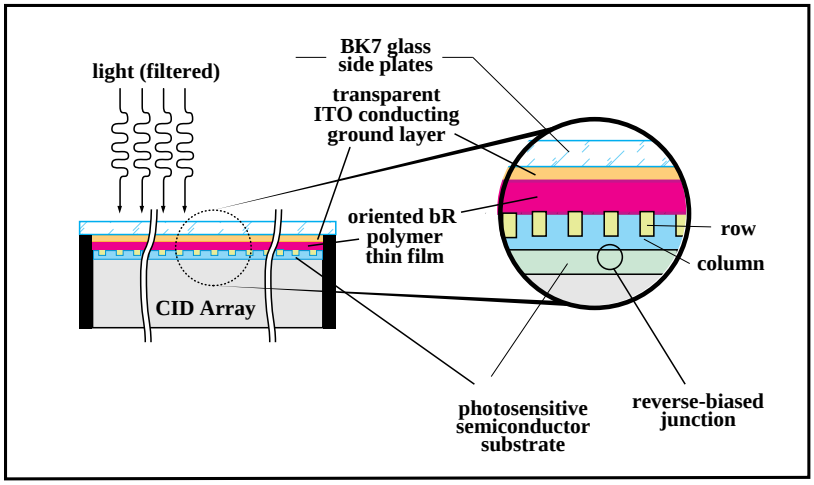

Figure 5: Proposed hybrid protein-semiconductor neuromorphic photosensor

the D96N BR-ITO only experiences the local pH changes associated with proton uptake. Second, the photocurrent D96N BR films shows no volume dependence. Thus, the photocurrent response appears to be solely a surface effect and not associated with the voltage across the membrane. In light of this recent suggestion by Lukashev, we are currently investigating the photocurrent repsonse of a simple BR-silicon interface in an attempt to distinguish between the two possible mechanisms of the BR photoelectric reponse.

1.5 Towards a BR-Silicon Photodetector

Bacteriorhodopsin is the only known material which exhibits differential photoresponsivity. Combined with its high stability, inexpensive and easy production, large quantum yield, etc., it serves as an ideal biocomputing material. The BR-based motion sensor of Miyaska and coworkers is a step in the right direction. In order to compete with the the neuromorphic VLSI devices, however, one requires a higher pixel resolution and integrated silicon architectures (in order to perform additional signal processing).

Our approach to developing a high resolution BR motion sensor is to utilize the on-chip circuitry of a charge injection device (CID) to monitor the photocurrent response of a BR film[6]. The CID provides a high resolution detection silicon grid and the off-the-shelf CID camera provides all of the necessary video amplification circuity– a great simplification

for us. We wish to circumvent the substrate photodetector and instead exploit the signal processing circuitry of the CID array (and camera) to create a high-resolution hybrid BR-silicon photosensor. Figure 5 depicts such a device. Future devices may employ a different semiconductor archectecture as the CID is simply the most convenient device to begin research with.

In order to understand how the CID array can detect the BR photocurrent, lets us review the basic CID operation[19,20]. The CID consists of a low band gap semiconductor substrate, the photodetector, coated with thin, transparent polysilicon columns and rows. Thus, the CID is an array of MOS capcacitors. The CID circuitry monitors the photoinduced charge, or electron-hole pairs, in the semiconductor. Before readout, charge transfers to the columns because the column voltage is maintained below the Fermi level of substrate but twice that of the row voltage. Plus the columns are reversed biased with respect to the substrate so they only collect photoinduced (or thermally induced) charge. Readout occurs in two steps. First, the column voltage is brought to zero, thus transferring all stored charge into the rows. The CID circuitry measures the differential current in each row, which is proportional to the stored, photoinduced charge. Second, the row voltages are made zero, thus injecting all stored charge back into the substrate (hence the name Charge Injection Device)

A thin BR-polymer film lies directly on top of the CID detection grid, blocking all light to the CID substrate but providing an BR-silicon interface on which to monitor the BR transient photocurrent. Upon illumination, the BR photocycle transports protons to the surface of the BR-CID, thus changing the surface potential of the gate and driving the MOS junction further into the accumlation region. Thus, the change in surface potential may draw more carries out of the intrinisic semiconductor region below the MOS junction and thus induce charge flow into the MOS capacitor (without generating electron-hole pairs).

The above device faces several other challenges as well. First, the BR film must have a very high optical density and quality in order to completely completely block out the CID photodetector substrate and yet still yield an appreciable photocurrent response at the surface of the CID-BR interface. Second, the CID chips employed lack the standard passivation layer which protects the silicon from free floating ions. Unfortuneately BR-bound Calcium ions seem to poison the CID. To alleviate this problem, our group has synthesized large organic bolaform cations in order replace the detremental Calcium ions[13]. Work is in progress testing the bolaform regenerated BR films in the CID-BR detector. Third, while monolayer wet BR films produce the greatest photocurrent response, a thick wet gel will exhibit more crosstalk between pixels–another consequence of free floating ions. Finally, if the BR photocurrent arises from

surface pH changes, the H+ ions may electrochemically degrade the CID detection grid, as in some pH sensitive CHEMFETs[21]. Research continues in our lab towards solving all of these problems.

2 Conclusions

The unique photoelectric properties of the protein bacteriorhodopsin (BR) may be exploited to perform real-time visual processing with a protein-silicon hybrid photodetector. In comparisons to standard analog VLSI neuromorphic chips, a BR-based architecture offers a less expensive, simpler design with higher resolution. Research in this area remains in the initial stages, with many challenges to overcome. Most notably, the protein-silicon interface suffers from crosstalk, ion poisoning and requires extremely high sensitivity using the proposed BR-CID design. The ability to manipulate BR both chemically and genetically, however, opens the door to research a wide range of solutions.

Acknowledgments

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