THE MAGNETIC FIELD COMPONENT OF THE NEURAL IMPULSE

Final Report

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Summary:

The existence of electric and magnetic field components possibly associated with the transmission of neuronal impulses was studied in isolated bullfrog sciatic nerves. The existence of the electric component was easily confirmed. Using detectors sensitive only to magnetic fields, a magnetic component could not be detected at a level equivalent to 0.9 microampere of 5 KHz current. Theoretical analyses of the sodium ion flows associated with the transmission of impulses in these nerves are presented. The absence of a signal at this detectability limit suggests that at least 99.8% of the sodium ion flux conforms to the local circuit theory. It is, however, not possible to conclude that a magnetic impulse, albeit small, does not exist since the confidence level of these experiments is a factor of 1000 greater than the signal predicted from the local circuit theory. These experiments also do not rule out the possibility that other appreciable biologically generated magnetic fields exist and can be used to study or influence the activity of neuronal tissue, particularly if resonant frequencies exist. Recommendations for future studies are presented.

Background and Rationale:

Burr and Mauro,[1] Seipel and Morrow,[2] and Gengerelli, Holter, and Glasscock[3,4] have reported the existence of electric and magnetic fields arising from neuron impulses. These fields are reported to be of sufficient strength that they are fairly readily detectable through air at an appreciable distance from the stimulated preparation. Additionally, Baule and McFee[5] and Stratbucker, Hyde, and Wixson[6] have reported magnetic components of the cardiac impulse.

Further studies of biologically generated electromagnetic fields are necessary in view of their great potential importance. First, the demonstration that neuronal electrostatic and magnetic fields exist indicates that neurons can interact otherwise than via the classical synaptic contacts and volume conductor effects. Such fields may have facilitatory or inhibitory influences over considerable distances and must be considered in interpretation of CNS organization and function. Second, considered as electromagnetic radiation, such fields may become the basis for new methods of monitoring or stimulating the intact neurons system without implanted or other destructive transcutaneous instrumentation. New information may be obtained which may be difficult or impossible to obtain by present methods. New methods of direct information transfer or signalling which avoid the usual sensory channels may be possible. Third, such fields may interact with ambient fields, such as those arising naturally from the earth and sun or artificially from sources such as television, radar, and electric power transmission. Such interactions may have profound positive or negative influences on human neurologic or psychiatric function, perhaps far outweighing the apparent biophysical forces involved; this will be particularly true if resonant frequencies exist. Fourth, and most immediately important, detectable magnetic fields are not predicted by classical membrane theory. The previously reported presence of such fields reveals a serious flaw in the present understanding of mechanisms basic to the entire nervous system, especially in the principles of neuronal impulse propagation.

Research Plan:

The research plan for this project entailed, as its initial step, the careful repetition of the previously reported studies [1,2] to confirm the existence of and to quantitatively measure biologically generated electric and magnetic fields in at least one case prior to extensions probing the generality of the phenomenon, areas for further investigation, and possible immediate and future applications. Further, since their detectors were not electrostatically shielded, the reports[2-4] of the neuronal magnetic component may be erroneous; the investigators actually may have observed the electric component. Confirmation of these studies is thus additionally necessary prior to broader investigations.

Theoretical analyses of the neuron impulse, based on well established measurements, were simultaneously undertaken in an attempt to determine the maximum magnetic signal detectable for two cases, first, where there is no appreciable internal longitudinal current, and second, where the internal longitudinal current balances the external longitudinal current as postulated by the presently accepted theory of impulse propagation.

Investigations:

I. Theoretical Analysis of the Neuron Impulse:

The theoretical analyses will be presented first as they offer an excellent basis for discussion of the experimental planning and results.

During the past thirty years, much work has elucidated the mechanisms involved in the conduction of impulses by excitable tissues. Nerve cell axons in general consist of a semipermeable membrane separating the interior of the axon from the surrounding tissue fluid. The interior material, axoplasm, contains a relatively high concentration of potassium ions, a relatively low concentration of sodium ions, and shifts of other ions which will not be considered here. The surrounding extracellular fluid contains a relatively low concentration of potassium ions and a relatively high concentration of sodium ions. It is postulated that a metabolically supported sodium "pumping" mechanism actively removes sodium ions from the axon interior to the external fluid and that the potassium ions diffuse or are pumped in the opposite direction. In the resting condition there is a net negative potential across the membrane, with the interior approximately -70 millivolts to the outside, due in large part to the above concentration differences. During activity, the membrane suddenly becomes permeable and permits the sodium ions to flow rapidly into the axon interior. This influx is followed by a slower outward shift of potassium ions and redistribution of other ions towards concentration equilibrium. Following this activity, the membrane rapidly returns to its former state as the metabolic mechanism restores the resting concentration imbalances.

The propagation of this altered permeability wave along the membrane is generally accepted to be effected by the forward shift of potassium, sodium, and other positive ions inside the membrane as the sodium ions cross the membrane, enter the axoplasm, raise the local positive charge density, and

repel the cations already present longitudinally along the fiber. Those ions moving rearward are redistributed according to the processes of recovery and need not concern us here. Those moving forward tend to depolarize the negative potential across the adjacent resting membrane and cross it to the exterior; when this depolarization reaches a sufficient value, the semi-permeable membrane becomes unstable, "breaks down," and permits the ionic flows of the actual impulse. The impulse thus moves along an axon as a continuous disturbance. The longitudinal internal flow of ions is termed the internal longitudinal current and is considered to be equal to and opposite in direction to the external longitudinal current arising from the streaming of ions outside of the fiber towards the permeable area. From this postulated activity arise the familiar drawings of circularly moving ion currents, the "local circuit" theory of impulse propagation. By this theory, the net amount of charge moving across the membrane is zero although spatially distributed over a short length of axon; equally, the net amount of charge moving along the axon is zero as the internal and external longitudinal currents are equal but opposite in direction. This activity is cylindrically symmetrical about the axon; the current paths form two toroids centered on the membrane, one leading and depolarizing, one following and repolarizing.

Using representative values, theoretical currents and their magnetically induced signals can be calculated for two limiting cases: first, the case for the maximum possible unbalanced current and maximum induced signal where the internal longitudinal current is absent; and second, the case for the minimum unbalanced current and minimum induced signal where the internal longitudinal current is present as postulated by the presently accepted membrane theory.

The following symbols and values[7,8] will be used:

x = distance from a fixed point on the axon; positive toward the active region
t = time in seconds
N = number of sodium ions moving inwards across the membrane per impulse = 3×10^{-12} M/cm^2
D = average diameter of axon = 10×10^{-4} cm
C = circumference of fiber
n = number of fibers in frog sciatic nerve = 500
Vc = conduction velocity of impulse = 20 meters/sec.
I = external longitudinal current in amperes
Q = quantity of charge moving across the membrane per impulse
H = magnetic field in oersteds
Φ = flux in maxwells
l = length of detector coils measured along the nerve = 1.0 cm.
NA = area turn factor for the detector coils = 600 cm^2 turns*
$/E/$ = signal induced in coil

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* as determined by the United States Bureau of Standards.

For a single frog sciatic axon, where the impulse is moving at a velocity of Vc toward x = 0, a point well beyond the inductive probe, in dx of the active region measured from its leading edge:

$$dQ = 1.6 \times 10^{-19} \text{ CN dx coulombs/molecule}$$

The time for dx to occur is:

$$dx = Vc\ dt$$

If the duration of the sodium ion flow during the total impulse = dt = 1 msec, the amount of sodium charge passing per impulse is:

$$dQ = 1.6 \times 10^{-19} \text{ CN Vc dt}$$

$$= 1.6 \times 10^{-19} \pi \text{ DN Vc dt}$$

And, substituting the assumed values:

$$dQ = 1.8 \times 10^{-9} \text{ coulombs}$$

Thus, 1.8×10^{-9} coulombs of sodium ions cross the membrane per impulse. This quantity of charge crosses the membrane in 1 msec; in terms of current:

$$I = \frac{dQ}{dt} = 1.8 \times 10^{-6} \text{ amperes of sodium ion per impulse}$$

For a nerve of 500 fibers firing simultaneously:

$$I = 9.0 \times 10^{-4} \text{ ampere}$$

1. Case I: Maximum Detectable Signal:

Assuming an external longitudinal current equal to the transverse membrane current, not balanced by an internal longitudinal current and composed of two currents, i_f flowing toward the active region from the resting region and i_r flowing toward the active region from the region along which the impulse has traveled:

$$I = i_f + i_r$$

Assume $i_f = i_r$:

$$i_f = 4.5 \times 10^{-4} \text{ ampere}$$

The magnetic field at 1.0 mm is:

$$H = \frac{2i_f}{10R} = 9.0 \times 10^{-4} \text{ oersted in a clockwise direction about the fiber}$$

Assume the change of direction from i_f to i_r follows the simplest case, that of linearity; then Δt, the time for the impulse to pass the probe face having a length, l, is:

$$\Delta t = \frac{1}{Vc} = 5 \times 10^{-4} \text{ sec for current reversal}$$

For the detector probe oriented for maximum flux through the coils:

$$\Phi = AAH = 600 \times 9.0 \times 10^{-4} = .54 \text{ maxwells}$$

Since this flux completely changes direction as the current reverses the induced EMF in the coil will be:

$$/E/ = \frac{d\Phi}{dt} = \frac{2 \times .54}{5 \times 10^{-4}} \times 10^{-8}$$

= 22 microvolts peak signal induced across the coil leads.

Note, however, that if the detector probe is calibrated in terms of current, the maximum detectable current would be i_f, or .45 mampere.

2. Case II: Signal Compatible with the Local Circuit Theory:

The local circuit theory external magnetic field and its induced signal (and apparent unbalanced current) can be calculated from the above relations. If the distance from the probe to a fiber is 1.0 mm., the fiber diameter is 10 microns, and the membrane is approximately 100 Å thick, its external longitudinal current will lie at distances of R_1 = 1.0 mm. and R_4 = 1.0 mm + 10 microns. The internal longitudinal current will lie at distances of R_2 = 1.0 mm + 100 Å and R_3 = 1.0 mm + 10 microns -100 Å. The resultant field will be the sum of the fields from each of these currents:

$$H_{LC} = H_1 + H_2 + H_3 + H_4$$

If the internal and external currents are identical but in opposite directions:

$$H_{LC} = \frac{2\,i_f}{10\,R_1} - \frac{2\,i_f}{10\,R_2} - \frac{2\,i_f}{10\,R_3} + \frac{2\,i_f}{10\,R_4}$$

$$= \frac{2\,i_f}{10}\left(\frac{1}{R_1} - \frac{1}{R_2} - \frac{1}{R_3} + \frac{1}{R_4}\right)$$

Substituting the values of the various radii:

$$H_{LC} = \frac{2\,i_f}{10}\left(2 \times 10^{-6}\right)$$

Here, the magnetic field that might be expected from consideration of the local circuit theory would be a factor of 2×10^{-6} smaller than the field resulting from an unidirectional flow of the same current if, indeed, such a field exists at all. This 2×10^{-6} factor would carry through the Case I calculations giving an induced signal of approximately 44 picovolts, a signal not readily detectable under any circumstances.

In terms of apparent unbalanced current which should be detectable in the local-circuit theory case:

$$i_{f_{II}} = 2 \times 10^{-6}\ i_{f_I} = 9.0 \times 10^{-10} \text{ ampere.}$$

Thus, the current which is to be detected magnetically lies between 450 microamperes and 900 picoamperes.

II. Experimentation and Results:

The Fourier analysis of a typical neuron voltage impulse contains frequency components to 50 KHz.[9] Considering the rise time, the major components center at 5 KHz; this frequency was chosen for testing and calibration of the various detectors.

1. Electric field studies:

The neuron electric field reported by Burr and Mauro[1] was easily confirmed. Since the eventual intention was to quantitatively measure both the electric and magnetic components simultaneously at the same point on the nerve, a number of commercial high impedance probes and electrometer amplifiers were tested and found unsatisfactory. A completely shielded, miniaturized, electrometer probe with a cathode-follower circuit having an input impedance of 10^{14} ohm was designed. This unit is linear to 40 KHz, sensitive, and relatively free of self-generated noise.

2. Magnetic field studies:

a. Coil detectors:

The detectors originally used[2] consisted of two small coils of #44 wire, semishielded with steel and potted. Similar coils were prepared following a design suggested by Dr. Otto Schmitt.[9] These coils were epoxy potted with mu-metal cores in place and shielded with two epoxy coated, mutually insulated, grounded layers of staggered-gap conductive silver paint giving an electrically continuous but magnetically discontinuous conductive shield.

Testing with a 40 KV Van de Graf generator proved the complete effectiveness of the electrostatic shielding.

Calibration at various frequencies was disappointing. The minimum detectable signal at 1.0 mm. was 3.0 ma at 5 KHz due primarily to high background and amplifier noise. This approach was temporarily discontinued.

b. Other magnetometer studies:

A survey of magnetic field detection methodology was disappointing. Virtually nothing had been done in the frequency and sensitivity range required

for this project. One commercially available instrument, the Electro-Mechanics Company's Variable-Mu magnetometer, had sufficient claimed sensitivity and frequency response to be potentially useful. An instrument was purchased after redesign for use in this project. Tests with this unit gave a minimum detectable signal of 10 ma at 5 KH_z and confirmed the previous coil detector findings of significant ambient fields limiting detector sensitivity in the laboratory work area.

3. Ambient Magnetic Field Reduction:

The detector studies indicated that further ambient magnetic field reduction was necessary. Two approaches were pursued.

a. Magnetically shielded room:

This room was specially designed and built as an area for biomagnetic research in 1962 when no commercially built enclosures were available. Following its completion, scans by the Bureau of Standards indicated that the power mains for the building were located in the basement room directly beneath the shielded room. The floor and the lower portion of the walls were then sheathed with a layer of high permeability magnetic shielding material resulting in further ambient field attenuation to 4 milligaus at 60 Hz with appreciable higher harmonics. Further detector studies were little changed from those reported above and indicated that relocation of the room and redesign of the enclosure were indicated. As this was not feasible, a second approach was necessary.

b. Preparation shielding:

Since the ambient fields in the working area could not be reduced further, the possibility of shielding the nerve preparation and detector was investigated. Several enclosures were designed and constructed but proved inadequate. A large, Navy-surplus, triply-shielded mu-metal container was obtained[10] and modified to improve its shielding capabilities. Tests of the Variable-Mu magnetometer performed in this shielded enclosure gave a minimum detectable 5 KH_z signal of 20 microampere, a considerable improvement over the previous results.

4. Nerve Studies:

a. Nerve Chamber:

Nerve chambers prepared for the earlier studies could not be used in the shielded enclosure; an improved chamber was designed and constructed. Details are given in the previous research report and need not be repeated here. Nerves kept in this chamber remained viable for periods as long as one week under refrigeration despite several six hour periods of study at room temperature.

b. Nerve magnetic field studies:

(A). Magnetometer studies:

Despite a minimum detectable signal of 20 microampere for the Variable-Mu magnetometer, no detectable nerve signal was observed from four preparations which gave excellent nerve voltage impulses. As described in previous reports, this magnetometer cannot be upgraded without considerable expense. The previously prepared coil detectors were then restudied.

(B). Coil detector studies:

The smallest and most recently designed and prepared coil detector was selected for further study; this unit gave a minimum detectable signal of 16 microamperes. Studies of two nerve preparations again yielded no recognizable nerve magnetic signals.

(C). Averaging computer studies:

The above negative results indicated that further refinement of the experimental procedures was necessary. The possibilities included further ambient field reduction, redesign of the detector for increased sensitivity, and purchase of instrumentation having greater sensitivity and less self-generated noise (or modification of the present instrumentation to the same end). Budgetary and personnel limitations precluded these direct approaches. Since noise reduction can also be effected by signal averaging and an averaging computer was available, this approach was investigated. A typical experiment will be described.

Instrumentation:

Grass III B stimulator & SIU 4 isolation unit
Grass P 511 preamplifiers & power supply
Tektronix Type 122 preamplifier
Tektronix Type 502 dual channel oscilloscope
Mnemotron Model 400 B CAT averaging computer
Moseley Autograf X-Y recorder

The isolated frog sciatic nerve was suspended on the following sequence of platinum wire electrodes in the nerve chamber: 2 stimulus electrodes, 1 ground electrode, 1 voltage electrode, and a final second reference grounded electrode. The neuron voltage impulse was oscilloscope-monitored across the final pair of electrodes with the magnetic pickup placed between but close to the voltage electrode. Signals from the magnetic detector were amplified differentially to sufficient magnitude for CAT processing by either two Grass preamplifiers in series or by the Tektronixs preamplifier followed by a Grass preamplifier. The CAT input was monitored by oscilloscope. CAT sweeps were triggered by the Grass stimulator; average waveforms were plotted by the X-Y recorder. All leads were shielded by carefully grounded electrostatic shielding.

Typical experimental run:

Using Grass stimulator settings of 5.0 v. amplitude, 1 msec. duration, 5 msec. delay, and a stimulus repetition rate of 55/sec to avoid spurious signal components associated with 60 Hz noise, the resulting monophasic square-wave stimuli elicited an almost maximal nerve voltage impulse of 20 mv. peak-peak amplitude.

Run A: The neuron voltage impulse was amplified 50 X to 1.0 v. and averaged by the CAT on its shortest online analysis time of 31.25 msec. for the complete

400 addresses. Averaging was continued for sufficient time to give a clean signal for comparison with later runs.

Run B: With the magnetic detector axis perpendicular to the nerve (position of maximum sensitivity for wire-conducted electrical currents), its signal was amplified 2 x 10^5 and similarly averaged for 10,000 pairs of stimuli. The average waveform shows only stimulus artifact.

Run C: Run B was repeated using 2 Grass preamplifiers cascaded to obtain an amplification of 1 x 10^6. The average waveform shows only stimulus artifact and is identical to that found in Run B.

Run D: The magnetic detector was next placed near a thicker portion of the nerve immediately before the impulse voltage electrode, perpendicular to the nerve, and similarly averaged for 10^4 stimulus pairs at an amplification of 4 x 10^5. The average waveform differs from those of the previous run in that the trace follows a smooth curve in returning to baseline after the stimulus artifact.

Run E: Similar to Run D with the magnetic detector rotated 90° (axis parallel to the nerve). The average waveform is identical to that in Run D.

Run F: Similar to Run A.

Run G: Following killing of the nerve with NaCN solution, Run D was repeated. The average waveform is identical to that in Run D.

Run H: Run E was repeated on the dead nerve. The average waveform is identical to that in Run D.

The above results are typical of the findings on 16 nerves. No evidence of a magnetic component of the neuron impulse was recognizable in any run.

(D). Computer averaging of the magnetometer output:

Studies similar to the above substituting the magnetometer for the coil detector and amplifier gave similar results.

III. Discussion:

In theory, averaging of a repetitive signal results in a reduction in the random noise which is proportional to $n^{-1/2}$, where n is the number of signals averaged. Thus, if 10^4 signals are averaged the background noise would be reduced by a factor of 100. In the experiments herein reported, the minimum detectable signal is equivalent to 16 x 10^{-6} ampere of noise; averaging should result in a background noise reduction rendering a 16 x 10^{-8} ampere signal detectable. However, experiments with known currents indicated that the minimum signal detectable with prolonged averaging and the present equipment was 0.8-0.9 x 10^{-6} ampere, an actual enhancement factor of 20. Thus, the nerve experiments suggest that, if a magnetic field accompanies the nerve impulse, the apparent unbalanced current must be smaller than 0.9 x 10^{-6} since the results are identical for the same nerve living or dead.

To the degree that the previous theoretical model and calculations validly

represent the actual case for the frog sciatic nerve, these experiments present additional support to the well established local circuit theory of neuron impulse propagation. The calculated maximum possible neuronal signal is 4500×10^{-7} ampere, while no signal could be detected at a 9×10^{-7} ampere level. As a first approximation, these findings suggest that less than 0.2% (9/4500) of the Na^+ external longitudinal and transverse membrane currents is not balanced by charge shifts within the axon.

Considering these results, it is apparent that the previous reports of a neuronal magnetic component[2-4] are probably erroneous. The reported signals most likely arose from the electrostatic component of the impulse due to inadequate detector shielding.

A few words of caution are appropriate. The present results, while indicating that an appreciable magnetic field component external to the axon probably is not associated with the neuronal impulse, the detectability confidence level of these experiments is a factor of 1000 greater than the level of the predicted maximum local circuit theory signal. Thus, the present results cannot be construed as conclusive evidence that a magnetic field is not associated with the neuron impulse and that such a field, albeit small, does not indeed exist.

Further, these results cannot be construed as indicating that other biologically generated magnetic fields do not exist. It is entirely possible that appreciable fields may be associated with the volume conductor currents arising from the intrinsic activity of larger neuronal structures such as the brain.[5] Such fields would be entirely analogous to those detected for the heart.[5,6] Equally, it is quite likely that an appreciable magnetic field is generated within the toroidal ionic currents associated with the impulse. This field would have its greatest strength within the membrane in the region immediately adjacent to the active region. Calculations for a single axon having a 100 Å thick membrane suggest that the field can reach a value of 2 oersteds at this site, would be contained entirely within the membrane, and would be directed parallel to the axon circumference. Such an appreciable directed field could exert strong orienting effects on ionic structures within the membrane, realign lattice resting interionic attractions and could conceivably cause the change in membrane permeability underlying the neuron impulse.

Finally, these results cannot be construed as ruling out the various possibilities mentioned in the Background and Rationale section of this report. Transcutaneous monitoring and stimulation, signaling, ambient field interactions,[11] and subtle effects remain possible, particularly if resonant frequencies exist. However, if such frequencies do not exist, the results suggest that the level of sensitivity required for such detectors and the field strengths which must be generated by such effectors may be difficult to achieve. It should be noted, however, that nerve stimulation by magnetic fields has been accomplished.[12]

Recommendations for Future Studies:

As previously indicated, no neuronal magnetic component was detected at the 16 microampere level with direct monitoring. The averaging computer was then used as the only available means of increasing detector sensitivity beyond this level but was not particularly satisfactory for this purpose. It is recommended that further studies aimed at approaching the theoretical local circuit signal

detectability using better shielding, preamplifiers having lower intrinsic noise, and coils having higher ~~Hr~~ factors and impedances matched to the pre-amplifiers. It is also recommended that other means of detecting low level neuronal magnetic fields be studied, such as the stimulation of an isolated nerve in a strong magnetic field to detect movement

Biologically generated magnetic fields associated with neuronal activity may exist and may be more easily detectable for other nerve preparations and larger nervous tissue structures, such as the brain. It is recommended that an adequate search be conducted for such phenomena. A particularly interesting case for study would be that of a primate brain stimulated to massive synchronous discharge, i.e., a seizure.

Finally, it is still possible that nervous tissue structures and their activity can be influenced by magnetic signals and fields, particularly if resonant frequencies exist. It is recommended that these possibilities be investigated. A particularly feasible approach is the use of multiple sources focused or arranged in such a manner that a high field strength is developed in a small geometric volume within, for example, a brain.

References:

1. Burr, H.S., and Mauro, A., "Electrostatic Fields of the Sciatic Nerve of the Frog," Yale J. Biol. Med., 21, 457-462, (1949).

2. Seipel, J.H., and Morrow, R.D., "The Magnetic Field Accompanying Neuronal Activity, A New Method for the Study of the Nervous System," J. Wash. Acad. Sci., 50, #6, 1-4 (1960).

3. Gengerelli, J.A., Holter, N.J., and Glasscock, W.R., "Magnetic Fields Accompanying Transmission of Nerve Impulses in the Frog's Sciatic," J. Psych., 52, 317-326 (1961).

4. Gengerelli, J. A., Holter, N.J., and Glasscock, W.R., "Further Observations on Magnetic Fields Accompanying Nerve Transmission and Tetanus," ibid, 57, 201-212 (1964).

5. Baule, G., and McFee, R., "Detection of the Magnetic Field of the Heart," Am. Heart J., 66, 95-96 (1963).

6. Stratbucker, R.A., Hyde, C.M., and Wixson, S.B., "The Magnetocardiogram - A New Approach to the Fields Surrounding the Heart," IEE Tr. BioMed. Eng., BME-10, 145-149 (1963).

7. Handbook of Physiology Section 1: Neurophysiology, Volume I, J. Field, Editor. American Physiological Society, Washington, D.C., 1959.

8. Gasser, H.S., and Erlanger, J., Am. J. Physiol., 80, 522-547 (1927)

9. Dr. Otto Schmitt, personal communication.

10. Courtesy of Dr. Dietrich Beischer.

11. Gernsbach, H., Editorial in Radio-Electronics Magazine, 31 #9, August, 1960.

12. Dr. R.G. Black, O.H. Best Institute, University of Toronto, Toronto, Canada, Personal communication.