



Hello all,

Thank you for your interest in *Swan & Stone*. “Alternativz” ended with Volume 2, Issue 12: [Omphaloskepsis](#). I hope you enjoyed that series.

This 1st issue of *Swan & Stone*, **fMRI, BOLD, & Breathing**, briefly explores functional Magnetic Resonance Imaging and one of it’s technical challenges:
B R E A T H I N G.



Researcher studying fMRI

Magnetic Resonance Imaging (MRI) employs the phenomenon of Nuclear Magnetic Resonance (NMR) to explore the internal structure of the body. It relies on the magnetic properties of hydrogen nuclei (of water molecules) which, when placed in a strong magnetic field align with the field (as does the needle of a compass in Earth’s magnetic field). When radio frequency energy is applied at the resonant frequency, protons that are aligned with the field absorb the energy and reverse their alignment. When the RF energy is removed, realigned protons flip back to their original state, releasing their absorbed energy. This released energy (a tiny voltage) is detected by the large sensitive coil that surrounds the body, the coil being the reason that the MRI tube is quite narrow and close to the body. The time it takes a proton to relax back to its original state is dependent in a complex way on the type of tissue in which it exists. It is the variation in relaxation times that ultimately yield the rich imagery and information that makes MRI so useful as a medical imaging tool.

Where MRI has been used for a number of decades to visualize structure, e.g. bones, tissues, etc., fMRI is presently used to study brain *activity*, specifically in the quest to understand the areas of the brain and their *functions*, i.e. what parts of the brain are associated with different cognitive activities. fMRI is able to identify functional areas of the brain, not by detecting neural activity but by detecting changes in blood flow that are associated with neural activity, for example visual activities require increased blood flow to and in the visual cortex. Prior to fMRI, researchers were largely confined to assessing brain activity at the surface of the head via electroencephalography (EEG) and hemoencephalography (HEG). Positron Emission Tomography (PET) is another technology that is capable of internal imaging but it requires that a radioactive tracer be introduced into the blood stream.

An fMRI machine takes advantage of the fact that deoxygenated blood (deoxyhemoglobin) and oxygenated blood (oxyhemoglobin) possess different magnetic properties, where one aligns with the magnetic field being applied, the other opposes. This difference constitutes the subtle magnetic signal associated with the blood flow changes that are a function of local brain activity. It is called Blood Oxygen Level Dependent (BOLD) contrast. The discovery was made by Seiji Ogawa, a distinguished biophysics researcher at Bell Labs in Murray Hill, New Jersey, circa 1990. He made the discovery while observing the brain of an anesthetized mouse using Magnetic Resonance Spectroscopy (MRS). During the initial part of the observation he was able to see “fine dark blood lines”, capillaries. A bit later he realized that the mouse was oxygen deprived and turned on the oxygen supply which was being provided to the mouse via a breathing tube. When he did, the image detail promptly disappeared. The visibility of detail in surrounding tissue was also greatly reduced. At that moment Ogawa knew that he had just witnessed a change in MRS detection based on the state of hemoglobin, going from being deoxygenated to being oxygenated.



Regarding this observation, Ogawa and colleagues theorized that with increased local brain activation, metabolism would increase and there would be a consequent increase in oxygen utilization and an increase in deoxyhemoglobin (which would make brain detail visible). But it turned out that blood flow to a local area increases much more than the local metabolic rate (a phenomenon that is puzzling researchers to this day), and with it, given that arterial blood is oxygenated, a relative increase in the ratio of oxyhemoglobin to deoxyhemoglobin, resulting in an increase in magnetic resonance signal. Consequently, the greater the increase in arrival of oxygenated blood, as compared to the initial state, the greater the BOLD signal strength.

But there are problems, these being any and all activities that result in oxygenated blood flow to the brain including the heartbeat, breathing, and general low frequency autonomic activities associated with regulating and maintaining the physical body, e.g. control of temperature, blood pressure, etc. Many of these functions share the same general spectrum with the BOLD signal, less than .1 Hertz. So the challenge that *fMRI* presents is that of picking the change in oxygenated blood associated with a cognitive activity of interest from a sea of background “physiologic noise”. To make matters more challenging, researchers are interested in identifying and characterizing networks, multiple areas of the brain that may be spatially diverse but simultaneously activated by a given cognitive task.

I find this matter intriguing because, while breathing induced blood flow changes in the brain have been a fundamental hurdle to *fMRI* research since the 90s, there are so few modern medical references to the fact that breathing even induces blood flow. Most of the material I’ve unearthed on the subject originated with research that took place in the late 1800s and early 1900s, including that by Andre Cournand who won the Nobel prize in 1956 for his discoveries relating to heart catheterization and circulatory system pathology. Cournand and colleagues used the newly invented catheter to invasively measure circulatory pressures and specifically to explore the relationship between respiration and circulation. But alas, most of their work was forgotten, or their silence purchased. We may never know.

To solve their imaging problem, i.e. to be able to observe blood flow to the brain due to cognitive challenge alone, during *fMRI* observation researchers also record the heartbeat (both time and amplitude), and breathing (time and depth), and then “subtract” those large signals out of the complex *fMRI* signal to leave the subtle magnetic signal associated with cognitive challenge. From papers I’ve reviewed on the subject, because the “physiologic noise” factors constituted by both heart beat and breathing are much larger than that of the BOLD signal, it remains a central challenge.

*I’d like to know more about the magnitude of the blood wave in the brain with varying breathing frequency and depth as measured by *fMRI*, especially after learning that the brain demands much more blood than that required for metabolism. My theory is that the thoracic pump and its breathing induced blood wave evolved with vertebrate life out of necessity, i.e., as the head began to be carried above the chest, “breathing” evolved as a critical auxiliary means of moving the blood upward to the head and brain against the force of gravity, especially when the body is upright and active. Had this evolution not occurred, as large muscles demanded blood to perform work, the brain may have been starved for blood – thoracic pump and heart work together to facilitate a working body and a highly functioning brain. If I’m about right, there isn’t a stronger reason for learning to breathe – well.*

Stephen Elliott, President, COHERENCE

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