**Sensor Optimization by Adjusting Volume Fractions of Superparamagnetic Nanoparticles in Hydrogel**

**2015 Intel Science Talent Search: Research Report**

**Applicant PIN: 82556347673**

**Abstract:**

This project involved the optimization of a new design of chemical sensor, employing superparamagnetic maghemite (Fe2O3) nanoparticles embedded in poly-(acrylamide-co-methacrylic acid) hydrogel capillaries to detect changes in pH. The combination, dubbed a “ferrogel,” changes volume in response to a specific trigger, in this case pH, and alters the ferrogel’s magnetic permeability, which is detected by an external magnetometer. Twelve batches of pH-sensitive hydrogel with varying concentrations of maghemite nanoparticles were synthesized and tested for accuracy to a modified form of the Bruggeman effective medium approximation. After the equation was determined to be accurate to within 0.0346%, it was used to predict the concentration of iron in the ferrogel that would ensure maximum sensitivity. The results showed that the optimal concentration of iron was approximately 1\*10-5; the sensitivity of the ferrogel sensor approached an optimal 8.9465\*10-3 as the concentration approached zero. The most dilute verified test, with a volume fraction of 0.00221 iron, confirmed the theoretical conclusion with a sensitivity of 8.9442\*10-3. The optimization of this non-intrusive, wireless, and purely chemical sensor allows it to be used to accurately measure any phenomena for which there exists a responsive hydrogel.

**Introduction:**

**Background:**

An effective sensor must be able to provide an accurate understanding of the quantity it monitors. When dealing with frequently-changing conditions, sensitivity to change must be maximized to ensure that the information delivered is accurate and appropriate. To measure quantities within the human bloodstream, a broad range of sensors, from simple ones measuring blood pressure to those like cardiac MRI are used by medical professionals to glean information on a patient's health and thus provide appropriate treatment. As the usefulness of treatment depends upon an accurate diagnosis, which in turn depends on correct information, the ability of a sensor to provide that correct information is of the utmost importance. In the bloodstream, the slightest miscalculations in dosages, incisions, or timing can have disastrous consequences.1 Frequently, the quantity of importance within the bloodstream is not the absolute quantity, but the change in said quantity – the body’s homeostasis ensures that internal conditions are kept approximately constant background levels, so the interest is in changes.1 The difference between 0 and 9 parts per billion of methylmercury is minute, but the change between them is of immense significance to the immune system.2 Thus, sensors effective in the bloodstream must accurately detect even miniscule changes in the extant equilibrium.

However, to detect quantities within the human body requires a particular design of sensor. Even the mere possibility of disturbing the homeostatic equilibrium within a human being raises all manner of medical obstacles, not to mention the inevitable ethical and legal objections. While the most practical means of gathering reliable data over long periods of time is through the implantation of a sensor, such permanent measures demand even higher standards in safety than the already-stringent ones for medical devices. Generally speaking, the more simple a sensor’s construction and operation, the easier it is to implant and utilize within the human body.13

**Previous Literature:**

In 2013 Ziaie published a paper proposing a new type of sensor design: a wireless, non-electrical, non-mechanical, and extremely simple sensor reliant solely on basic chemistry and physics for its detection.3 Magnetite (Fe3O4) superparamagnetic nanoparticles (SPMNP) were dispersed in a pH-sensitive poly(methacrylic acid-co-acrylamide) (MAA/AAm) hydrogel to form a “ferrogel” sensor, which was subsequently tested at a various pH levels. A planar inductor was used to measure the change in magnetic inductance as the hydrogel swelled and shrank (thus changing the concentration of ferroparticles) in response to pH changes, which revealed that inductance rose in direct proportion to the degree of swelling. A network analyzer collected the resonant frequency while the sensor was tested and quantified the sensitivity to changes between pH 4 and 6.

Although there has been considerable study regarding both superparamagnetic nanoparticles and hydrogels, this paper is one of the few to combine the two and explore the idea of using hydrogel swelling to alter magnetic fields in order to act as a sensor.4 Hydrogel-nanoparticle compounds were used by Zhai for electrocatalytic activity5, by Riedinger conjunction with quantum dots6, and by Yuan with graphene layers for glucose-sensing purposes.7 Likewise, Satarkar and others employed magnetic hydrogels for the single-use purpose of delivering an included drug. All employ some of the same materials and/or methods, but using magnetic hydrogels as sensors is a largely unexplored concept.8

Unfortunately, this means that the concept, while intriguing, remains largely undeveloped and unrefined. Ziaie has served to raise the prospect of new innovations, but thorough and quantified explorations of a ferrogel’s many implications have yet to be done. Gaps in the specific gel or particle composition, the fabrication methods, and widespread applications have yet to be filled.3 In particular, as a prototype, this ferrogel sensor has only been shown as a potentially promising concept.

**Objectives:**

This gap in knowledge offered many opportunities for further development, but before specific applications could be realized, an optimized version of the overarching concept had to be determined. Given the simplicity of a ferrogel, the only real variable that could be optimized was ferroparticle concentration. My purpose was thus to expand upon Ziaie’s proposal, discover the concentration of ferroparticles that would make an optimal ferrogel sensor, and thus develop a model of maximum sensitivity (derivative of permeability with respect to volume fraction of SPMNP) for all subsequently developed ferrogels. My hypothesis was that:

* An increase in the concentration of magnetic ferroparticles will be mirrored by a rise in ferrogel sensitivity,

and that

* The relationship between ferroparticle volume fraction and ferrogel sensitivity will be mathematically-expressible.

**Materials and Methods**

**Mathematical Modeling:**

My project began with finding a mathematical equation to model the behavior of ferrogel sensors.22 In order to successfully model the differing properties of both the nanoparticles and their hydrogel solvent in such a single equation, I searched for a suitable one among extant effective medium approximations. The Bruggeman effective medium approximation (henceforth referred to as “Bruggeman equation”) provided a relatively simple equation, could easily be converted into appropriate terms, and was created for spherical constituents; I thought it would serve as a reasonably accurate ferrogel model.22

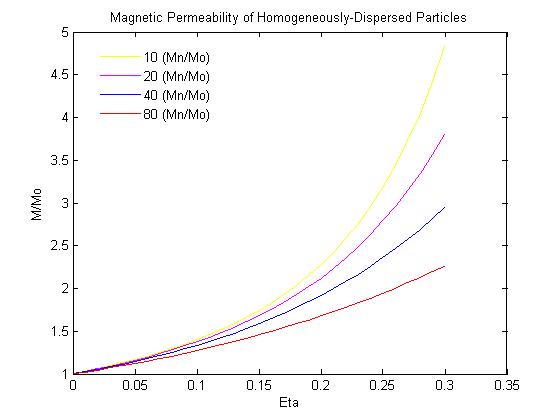
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*Figure 1: Original Form of Bruggeman Equation*

 n  *being a Euclidean spatial dimension that has an arbitrary number of components,* \delta_i *and* \sigma_i *respectively the fraction and the conductivity of each component, and* \sigma_e *is the effective conductivity of the medium.*

The equation was originally in terms of electrical conductivity, so I had to first convert the terms into magnetic equivalents, before rearranging the equation to solve for the relative permeability of the ferrogel as a function of ferroparticle volume fraction and said material's relative permeability. (Appendix A) It is important to note that for this experiment, the relative permeability of the ferroparticle material itself remains constant while the volume fraction is the variable modifying the ferrogel relative permeability (henceforth referred to as “permeability”). Although said constant may be altered by substituting another magnetic nanoparticle, I focused on the effects of ferroparticle concentration changes and thus kept the value of ferroparticle relative permeability (henceforth referred to as “permeability constant”) constant. This constant was experimentally determined by measuring a sample of pure solute. Once completed, the rearranged Bruggeman equation allowed me to model the permeability as a function of volume fraction, for homogeneously dispersed nanoparticles. A further modification was made to the derived equation (Appendix D) for the purposes of modeling non-homogeneous nanoparticle dispersions. (“Conclusions and Future Work”)

After I derived this form (Appendix A), I then used it in conjunction with MATLAB to construct Figure 2 (below), a graph of four sample ferrogel permeabilities, given a range of volume fractions from 0 to 0.3 and an initial ferroparticle permeability constant of 10. I repeated the process with constants of 20, 40, and 80. Combined, these curves gave me a rough idea of ferrogel behavior as a function of volume fraction. As the volume fraction increased, the ferrogel permeability rose quadratically; the higher permeability constants caused a proportionally constant rise in ferrogel permeability.

 *Figure 2: Benchmark Permeabilities*

*being the volume fraction, M/Mo the total permeability, and Mn/Mo the permeability constant*

Before calculating an optimal concentration of ferroparticles, I first decided to verify the Bruggeman equation’s accuracy. Practical considerations with our supply of materials prompted me to use relatively small concentrations of ferroparticles. I calculated volume fractions appropriate for testing purposes, and settled on three samples, at 0.000162, 0.00221, and 0.01. These three fractions would approximate a low, medium, and high concentration, respectively. For materials synthesis, I followed published procedures for both the superparamagnetic nanoparticles9 and hydrogel.3

**Ferrogel Synthesis:**

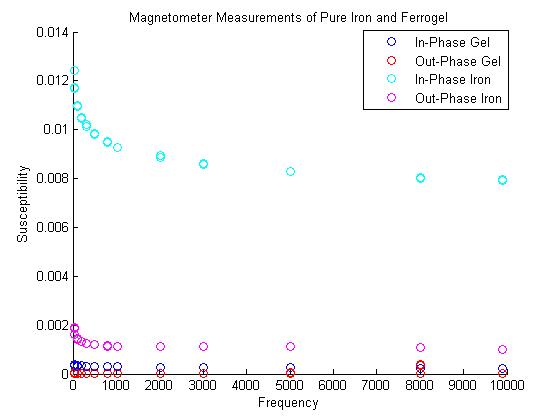
Though ideally, I would duplicate Ziaie and use magnetite (Fe3O4) for my SPNMP material, I elected to employ maghemite (-Fe2O3) instead.9 Though the two have very similar magnetic properties, both being spinel ferrites and ferrimagnetic, the latter is the topotactically oxidized form of the former and can hence be stored and used over several weeks.10 To synthesize my maghemite nanoparticles, I followed the procedure laid down by [Aliahmad & Moghaddam](http://www.bibme.org/journal#), first preparing magnetite nanoparticles through the standard co-precipitation method,23 before using a thermal-decomposition of those nanoparticles to produce maghemite ones.9 0.8273 grams of maghemite were synthesized through this two-stage method, and dispersed in 60 ml of 0.0001 M (pH 10) KOH. The concentration and thus mass were determined by colorimetric assay.24

The materials and procedures available to me gave me three choices of hydrogels: glucose, thermal11, and pH-sensitive3. Given that I was basing my work on Ziaie, who had employed pH-sensitive gels, and that blood pH was a commonly measured medical quantity, it seemed logical to employ pH-sensitive hydrogels for my own project.3 As such, I followed the procedure stipulated by Ziaie, which instructed me on how to prepare poly(methacrylic acid-co-acrylamide) hydrogel.3 Because he stated, “thin cylindrical hydrogel columns are likely to swell and shrink more rapidly,”3 I used 1 mm diameter plastic capillaries with a length of 1.5 cm for the hydrogel molds. I sliced 60 10-mm pipettes (Kimble, 100 l Microcapillary Pipettes) at 15-mm intervals, and wasged the segments in dichloromethylsilane (DCMS) and toluene for ten minutes each. The 360 capillaries were then dried with N2 (g) and baked for 24 hours at 80o C. The next day, I placed them vertically in 10-ml flasks, 30 to a flask, for 12 flasks.

Before the final step in the hydrogel synthesis– adding ammonium persulfate ((NH4)2S2O8, Sigma-Aldrich) to activate polymerization– I dispersed the respective concentrations of maghemite nanoparticles within the 12 pregel solutions, with three batches at each concentration (0.0162%, 0.221%, 1%) and three blanks without any nanoparticles. The solutions were then vortexed to ensure an even dispersion. I then placed the pregel solutions in an ice bath to slow activation, added the ammonium persulfate, vortexed the solutions again, and poured them into the capillary-flasks before placing them in a 15o C refrigerator overnight to polymerize. Once polymerized, I removed the 12 flasks from the refrigerator, broke open the flask mouths with a hammer, and extracted the bundle of capillary-encased ferrogels from each. I then separated these bundles into individual capillaries and washed them in acetone ((CH3)2CO, Sigma-Aldrich) for twenty minutes. After the ferrogels had loosened, I tapped the capillaries on a beaker rim to extract them. I separated the contents of the twelve flasks into four sets of three beakers, each set holding buffers of pH 4, 7.4, and 10. Therefore, each concentration, including the blanks, was divided into three beakers at three different pH levels. The beakers sat untouched for 24 hours to allow their contents to adjust to their respective pH levels.

**Measurement of Ferrogels:**

I used a Magnon Variable Frequency Susceptibility Meter (VSFM II) magnetometer to measure the magnetic susceptibility of my samples, the results of which are shown in Figure 3.25 I also measured a sample of maghemite nanoparticles on their own, to use in calculating the permeability constant. The pure gel was non-magnetic and hence had a permeability equal to the permeability of free space (1.25663706 × 10-6 m kg s-2 A-2), while both the ferrogel and nanoparticles returned significantly larger readings (Figure 3).12 Measurements of all ferrogels were taken in triplicate at thirteen frequency intervals, from 30.518 Hz to 9901.123 Hz. The data was then averaged and converted from susceptibility to permeability, so that the experimental results could be directly compared to the Bruggeman predictions. The measurements were converted by the equation: e / 0 =+1, where X’ was in-phase susceptibility, X’’ the out-phase susceptibility, and e / 0 the relative permeability of ferrogel with respect to pure hydrogel.

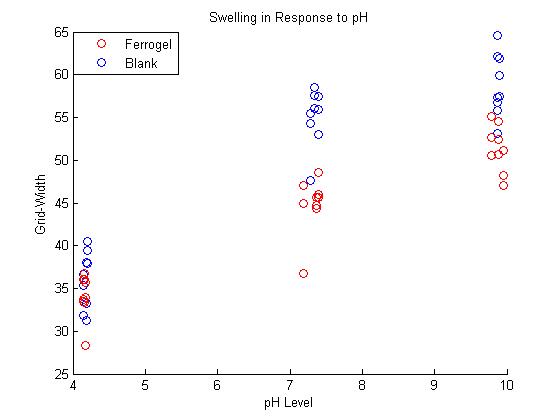


*Figure 3: Magnetic Susceptibility Relative to the Permeability of Free Space*

*Blue being the in-phase ferrogels, red the out-phase ferrogels, cyan the in-phase iron sample, and magenta the out-phase sample.*

*See Appendix B for data*

In order to evaluate the ferrogels’ responses to changes in pH, I measured the widths of identical-concentration ferrogels after they had adjusted to various pH levels; the results are displayed in Figure 4, below.. To do so, I used a simple microscope apparatus available in the lab. A camera projected the enlarged image of the microscope plate onto an adjacent screen. An adjustable measurement grid was superimposed on the screen, which I adjusted to align with the hydrogel edges. The specific width of the grid, in its own measurements, was reported on-screen. I placed a small ruler on the screen to ascertain the conversion from grid-widths to millimeters.



*Figure 4: Gel Widths at Various pH*

*Red being the ferrogels and blue the blank gels*

*One millimeter equals 18.4 grid-widths*

*See Appendix C for data*

Using this apparatus, I took three measurements of the twelve batches, exchanging the buffers after each measurement, so that I could document the volume changes as they adjusted to their specific pH values.

**Model Verification:**

Using my experimental susceptibility measurements, I converted them to permeability with the above formula and compared them with my Bruggeman-calculated values at all 13 frequencies. The readings for maghemite susceptibility enabled me to calculate the permeability constant, while the volume fraction was simply the value(s) specified in my synthesis. However, when the measurements were converted to sensitivity, some major discrepancies between the predicted and actual values became evident. The actual values at different pH levels were significantly lower than expected by my hypothesis. I found the answer in the balance of the two factors that largely dictated ferrogel sensitivity.

The first, and hypothetically-expected one, was the concentration of iron within the ferrogel. (Figure 3) As shown in both predicted and experimental results, the greater the concentration, measured in volume fraction, the greater the permeability. Naturally enough, this applied not only to the permeability itself, but to the derived sensitivity that was my to-be-optimized quantity. Theoretically, an increase in the volume fraction should have the effect of increasing sensitivity. However, rather than raising sensitivity, as I had expected and predicted, my actual data showed that an increased volume fraction or concentration of maghemite nanoparticles actually lowered ferrogel sensitivity. The answer to this paradox lay in the second, newly-discovered factor.

While measuring the ferrogel widths under the microscope (Figure 4), I noticed a trend in the gel diameters. As expected, both the pure and magnetized hydrogels swelled as pH rose and shrank as it fell. However, I also noticed that the presence of the embedded nanoparticles had an inhibitory effect on both the expansion and contraction of the gel to pH changes, and hence its capability to react to said changes. Because the ferrogels could neither swell nor shrink to the same extent that the pure hydrogel was capable of, their sensitivity was correspondingly less than if they could fully expand and contract. The greater the concentration of nanoparticles, the more the swelling or shrinking was inhibited. (Figure 4) After taking this newfound variable into account, I recalculated my predictions, and compared them to my actual values. This time, the two aligned very closely, the largest discrepancy between the predicted and actual results being 0.0346%, at 30 Hz.

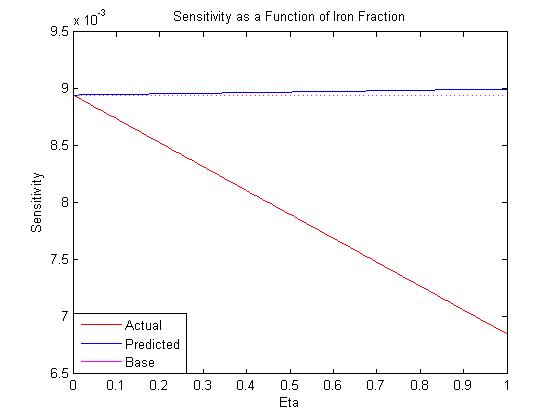
**Designing an Optimal Sensor:**

With the model verified as accurate, I could and did use it to generate my desired outcome: the volume fraction needed for an optimized sensor. Taking the volume-fraction-adjusted Bruggeman equation’s first derivative (with respect to volume fraction) gave me the sensitivity, which had to be maximized to find the optimal sensor. Calculating the extrema for said function, I found that the highest sensitivity was found at its lowest x-value– at a volume fraction of 0. From my previous results, I knew that the swelling inhibition had a greater negative effect on sensitivity than increasing concentration did a positive one, and so the net result was unsurprising. A volume fraction of zero minimized the inhibitory effect of adding nanoparticles. This, in theory, would make for an optimally sensitive ferrogel sensor. Of course, as a ferrogel sensor would be incapable of detecting anything without any nanoparticles, a certain threshold of iron was required to ensure that the sensor can function as intended.

**Results:**

**Optimal Design:**

The ultimate result of my project is that an optimal ferrogel sensor has been designed: the volume fraction of iron nanoparticles should be kept as close to zero as possible to ensure maximum effectiveness for said sensor. Though the theoretically highest sensitivity is reached at 0, a ferrogel sensor has to have a detectable amount of maghemite within it to report any change. That said, the threshold at which it is “possible” for a magnetometer to detect changes in permeability and hence report the sensor’s activity varied from model to model. In my circumstance, and using a relatively unsophisticated magnetometer, an optimal volume fraction was calculated to be approximately 1\*10-5. This was verified by the machine’s own specifications, which stated its sensitivity to be 10-5 to 10-7. Given that my device was not a superconducting quantum interference device, a vibrating sample magnetometer, or a torque magnetometer, and that such machines are unlikely to be used in measuring simple ferrogel sensors it can be asserted with reasonable certainty that a concentration of 10-5 is the lowest detectable volume fraction and the ferrogel sensor is thus “optimized.” The originally predicted and actual sensitivities of a ferrogel at specific volume fractions can be seen in Figure 5:



*Figure 5: Sensitivity of any Ferrogel as Volume Fraction Rises*

*Net sensitivity being the red line, blue the calculated sensitivity without swelling inhibition, and magenta the theoretical base sensitivity with no nanoparticles*

*represents the volume fraction of nanoparticles in hydrogel*

The optimal sensitivity (derivative of permeability with respect to volume fraction) of a theoretical ferrogel as the volume fractions approach 0 was calculated as 8.9465\*10-3, while the 0.002221 volume fraction yielded a sensitivity of 8.9442\*10-3. The 0.01 ferrogel gave a sensitivity of 8.9426\*10-3. Unfortunately, for the volume fraction of 0.000162, congelation of the maghemite solution within its container was such that a negligible amount was transferred into the pregel solution, and the resulting ferrogel was thereby rendered worthless, having no measurable magnetic susceptibility. Alternative means of dispersing the maghemite particles are thus required for further exploration with extremely small concentrations of iron. However, for this experiment, it can be safely concluded that the measurements would conform to the Bruggeman equation predictions and simply provide verification that smaller concentrations equate to higher sensitivity.

**Measurement Data and Meaning:**

The magnetometer measurements at 0.221% concentration yielded an average permeability of 1.000303, while 1% gave an average of 1.001393. As mentioned before, 0.0162% gave no significant readings. From these results, I calculated the gain in sensitivity as volume fraction increased. As can be seen by the “Predicted” curve in Figure 5, the increase in sensitivity granted by additional nanoparticles is monotonic, with the slope being 5.35\*10-7. Integrated, this reflects the quadratic increases in permeability as a function of volume fraction (Figure 2). In total, from a volume fraction of 0 to 1, a ferrogel would gain a sensitivity of approximately 5.35\*10-5 from the added nanoparticles, or 5.35\*10-7 per percent of increased SPMNP concentration. Thus, higher concentrations of iron would also increase the sensitivity of the ferrogel to volume– and therefore pH– changes.

For the gel diameters, 0.352 mm was the average loss in diameter of swelling or shrinking with an iron concentration of 0.221%, while 1% gel yielded an average diameter loss of 0.787 mm. These measurements were used to calculate the loss in swelling with an increase of iron. Much like the increase in sensitivity from added nanoparticles, the decrease in sensitivity from the same was monotonic, with a slope of 0.558 mm. At a volume fraction of 1, the ferrogel would lose 5.575 mm diameter in swelling compared to a pure hydrogel, with a loss of 0.558 mm per percent of increased SPMNP concentration. When this loss in swelling is converted to loss in volume (via V=(d/2)2)) and plugged into the Bruggeman equation, a ferrogel at a volume fraction of 1 would experience a total loss in sensitivity of 2.149\*10-3. By percent of increased nanoparticles, the loss would be 2.149\*10-5. As the losses in sensitivity as a result of increasing SPMNP concentration outweighed the gains by nearly two orders of magnitude, the conclusion reached in “Optimal Design” are clearly justified.

**Proof of Hypotheses:**

My first hypothesis was that: “An increase in the concentration of magnetic ferroparticles will be mirrored by a rise in ferrogel sensitivity.” As shown in the above “Model Verification” subheading of “Materials and Methods,” the opposite, that an increasing ferroparticle concentration will decrease sensitivity, is true. This hypothesis is hence proven false.

My second hypothesis was that: “The relationship between ferroparticle volume fraction and ferrogel sensitivity will be mathematically-expressible.” The findings detailed under the “Materials and Methods” subheadings “Model Verification” and “Designing an Optimal Sensor” show that the above relationship can indeed be mathematically expressed, and within an error range of 0.05% as well. This hypothesis is therefore proven true.

**Consistency of Measurement:**

For the magnetometer measurements, the 0.221% had a mean permeability of 1.000303, with a standard deviation of 4.453\*10-5. All repeated measurements at all frequencies fell between -1.50 and 1.59 standard deviations. The 1% measurements gave a mean of 1.001393, with standard deviation 1.634810-4. Repeated measurements at all frequencies were within -1.35 and 1.67 standard deviations. In margin of error, the data at 0.221% was 1.0003030.0000708, while at 1%, it was 1.0013930.000273 permeability. Future measurements are therefore likely to be consistent with my own. All hydrogel capillaries were measured by visual alignment on a screen and were thus unaffected by measurement error.

**Discussion:**

**Ferrogel Applications:**

The results reached in this project demonstrate a simple, yet effective means by which ferrogel sensors may be optimized and hence used. The medical– and other– implications are enormous. An operational sensor of this type permits the facile measurement of literally any substance that there exists a suitable hydrogel. In other words, as long as there is a measurable quantity that a hydrogel will react to, it can be measured using this sensor. And of course, the nature of the project’s methodology ensures that nanoparticle material is in no way limited to ferrous substances. So long as its permeability is known, any magnetic ore, be it nickel, cobalt, or whatever else, can be substituted; the efficacy of optimization and the accuracy of the Bruggeman equation will be undiminished. In that regard, the term ferrogel is something of a misnomer.

Of course, the practical scope of an optimized ferrogel sensor is not quite so sweeping. There is no need, after all, to supplant sensors which already perform their job perfectly well with a new, recently-perfected, ferrogel one that may have unrealized difficulties and would, in all likelihood, do no better (though also no worse) a job than its predecessor. For instance, by using thermosensitive hydrogel (such as poly(N-isopropylacrylamide)), a ferrogel can easily be used to detect the temperature change as a beaker of water is heated. But a simple thermometer already serves that purpose, and clearly enough, replacing it with a ferrogel is pointless. Such applications, however, do show the versatility and widespread application of ferrogel sensors.

Even disregarding the redundant, ferrogels still have very broad potential for use, notably when sensors grow more indirect and complicated than a thermometer in water. Their unique structure permits them to be used in more complex environments, where other sensors face difficulties. In conditions where delicacy and elaborate construction are weaknesses, yet accuracy is paramount, ferrogels’ simple composition and straightforward operation are assets.13 An obvious application– and indeed, the original focus of this project, mentioned several times above– is within the human body itself. A lengthy list of quantities essential for human well-being must be measured within the body. Blood pressure, blood pH, cholesterol levels, the list goes on. Most must be either measured externally, meaning with a drawn blood sample or elaborate methodology; or via an implanted, usually microelectromechanical (MEMS) sensor with all its assorted costs and complications.14 A prime example is the case of diabetes mellitus and blood glucose.

A critical part of treating diabetes of both types is accurate information on a patient’s blood glucose levels. Traditionally, those levels are measured by extracting a blood sample via a needle-pricked finger.15 However, this is both painful and imprecise, the latter because it measure only the glucose concentration in a tiny sample at a single time, and the former for self-evident reasons.15 A ferrogel sensor, in this case, would demonstrate a marked improvement over the current method. By using a glucose-sensitive hydrogel (like acrylamide-co-methylphenylboronic acid), ferrogel could easily react blood glucose concentration and changes thereof; the sensor works both accurately and painlessly. Its location within the patient’s hypodermis permits it to collect blood samples without stabbing the fingers, while its permanence allows it to give constant readings over whatever period of time the patient desires. Reading the data is accomplished by a simple, external, magnetometer measurement. Thus, a ferrogel glucose sensor would provide diabetics with a facile means of gleaning accurate information on their own well-being, while simultaneously relieving them from their unpleasant duty of finger-stabbing. Just as clearly as ferrogels were utterly useless in the thermometer case above, they are very clearly the opposite with regard to diabetics. And blood glucose is hardly the limit of ferrogel sensing. All the quantities mentioned above– blood pressure, blood pH, cholesterol levels– and far more may be effortlessly monitored with a ferrogel implant.

Admittedly, a ferrogel sensor must be first implanted before being effective, but cutting a few layers of skin to access the hypoderm is hardly on the level of open-heart surgery.16 Any patient that must measure a particular internal quantity on a regular basis would benefit from utilizing this sensor. Professional athletes, for instance have to undergo frequent chemical tests to verify that they are free of performance-boosting drugs.17 A single implant of a ferrogel could facilitate faster, more accurate tests than the traditional urine ones, as well as remove the risk of tampering with samples. And they are but one example. Another can be found in HIV patients, who must keep a constant watch on the number of T-cells in their bodies.18 Yet another in recovering addicts, who can be easily monitored with ferrogels to ensure they don’t relapse.19 To reiterate, as long as there exists a reactive hydrogel– and designing them is simple enough– any condition may be detected and quantified. With regard to internal conditions, as exemplified by the diabetes case above, ferrogel sensors have the potential to greatly simplify the process of collecting formerly hard-to-gather data, from drugs to diabetes.

**Bruggeman Implications:**

During the process of determining an optimal design, I also showed that the permeability of any homogeneously-dispersed magnetic hydrogel can be predicted with reasonable accuracy by a modified version of the Bruggeman effective medium approximation. (Appendix A) Non-homogeneously dispersed magnetic hydrogels may also be modeled by the further-modified Bruggeman equation. (Appendix D) So long its permeability is known, any magnetic ore can be substituted for maghemite in the nanoparticles without losing accuracy. However, it is important to remember that the total change in volume of the hydrogel swelling is altered with the addition of more nanoparticles, so the volume fraction must be adjusted to reflect this, or an inaccurate prediction (Figure 5 “Predicted”) will be made. Given said adjustment, and a known quantity for the chosen material’s permeability constant, my version of the Bruggeman equation will likely be successful in modeling the actions of nearly all synthesized ferrogels.

**Relation to Prior Literature:**

As previously mentioned, the only paper to deal explicitly with ferrogel sensors is Ziaie (2013).3 Others employ ferrogels, nanoparticles, and hydrogels, but for a variety of purposes like single-use drug delivery, tissue engineering,4 electrocatalysts,5 and quantum dots.6 The greatest difference between those and my own project is that they focus on treatment, rather than data collection.5 Protecting new tissue, dispensing drugs, catalyzing reactions and particle-tracking are active measures, performed after having gathered the kind of information my project seeks to use ferrogels to gather. That said, my results corroborate and expand upon those detailed by Ziaie.3 Certain results he suggested qualitatively were quantitatively verified by my own project; for instance, that gel swelling outweighs ferroparticle density when determining greatest inductance (or permeability, in my case). My project, by optimizing the initial concept of a ferrogel sensor for actual usage, could thus be seen as a continuation and refinement of Ziaie’s original proposal of a ferrogel sensor.

**Conclusions and Future Work:**

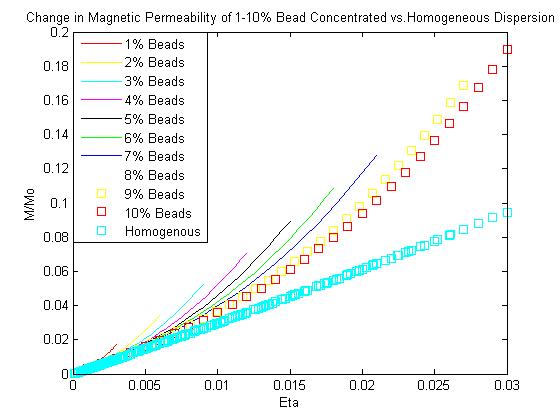
**Accomplishments:**

This project has shown that an optimized ferrogel sensor can be achieved, and that its implications for all science, especially medicine, are substantial. Experimental results show that an optimized ferrogel has a minimal concentration of iron, with a suggested volume fraction of 1\*10-5. Also, two variations of the Bruggeman equation were derived and shown to be accurate in predicting ferrogel permeability. My two hypotheses were disproved and proven, respectively, and a justification provided for each.

Further investigation of this concept could involve the testing of varying hydrogel and nanoparticle materials, to verify that the conclusions reached in this report apply to all ferrogels.20 Also, my own ferrogels exhibited no measurable decay over a period of three months in buffer, but an experiment to test the longevity of hydrogels within the bloodstream would be worthwhile. Researching a means to disperse extremely small quantities of iron into hydrogels without significant losses during transfer would also aid in ferrogel synthesis.

**Reflections:**

Time permitting, I would have liked to explore the latter of the proposed ideas above; as mentioned, that project branch was ended due to several difficulties, but its line of thought appeared promising. On a different note, if I had to restart my project today with the lessons learned from my project; I would favor experimental work over theoretical, instead of the 50/50 split I originally adopted. Unforeseen obstacles, like complications with equipment, materials, and procedure are far more common and obstructionary in the experimental stage. Further optimization might also be achieved by altering the dispersion of nanoparticles within hydrogel instead of keeping it homogenous. A modification to the originally derived Bruggeman equation was made to permit it to report permeability in hydrogels with non-homogeneous dispersions. (Appendix D) Preliminary calculations via this version of Bruggeman equation suggest that concentrating the nanoparticles within microcapsules (e.g. ProMag Bangs Laboratories, 1m spheres) could at least double the permeability, permitting a smaller concentration for the detection threshold. Unfortunately, transferring difficulties and limited materials put an end to further testing. The eventual prospect of ferrogel sensors used in hospitals and such requires considerable development beyond the scope of this project.21



*Figure 6: Predicted Benefits of Concentrating Nanoparticles Within Beads*

*being volume fraction and M/Mo the total added permeability (to 1)*

This project, though concluded, leaves many aspects of ferrogels unexplored. Besides the further research needed to refine the conclusions presented here, the practical, legal, and commercial facets of actually producing a viable sensor for use by physicians are unaddressed. The intermediate steps between this project and a widely-used sensor require aid from across multiple disciplines. Not only scientists and academics, but lawyers, manufacturers, and patients themselves have major roles to play in answering the questions posed by this still-imperfect innovation.21

**Appendices:**

**Appendix A: Bruggeman Effective Medium Approximation Derivation:**

Original Equation: i i(i - e) /[i + (n - 1)e ] = 0

was switched for , for , and set n = 3, because the desired model is in three dimensions.

Thus, the new equation: \* (n - e) / (n + 2e) + (1 - )(0 -e) / (0 +2e) = 0

A common denominator, (n + 2e) \* (0 + 2e), was applied to both sides, which yielded:

\* [(n - e)(0 + 2e)] / [(n + 2e)(0 + 2e)] + [(1-)(0 - e) (n + 2e)] / [(n + 2e)(0 + 2e)] = 0

Both sides were multiplied by the common denominator, which simplified the expression to:

\* [(n - e)(0 + 2e)] + [(1-)(0 - e) (n + 2e)] = 0

Both sides were then multiplied by 1 / 0, giving \* [(n - e)(0 + 2e)] /0 + [(1-)(0 - e) (n + 2e)] /0 = 0

For simplicity’s sake, x was substituted for , y for e / 0, and z for n / 0.

The equation was thus: x(z - y)(1 + 2y) + (1 - x)(1 - y)(z + 2y) = 0

Expanding the left gives: -xy + xz - 2xy2 + 2xyz + z + 2y - yz - 2y2 -xz - 2xy + xyz + 2xy2 = 0

Factoring: -2y2 + (-x + 2xz + z - z - 2x +xz)y + z = 0

Rearranging the middle expression yields: (3x - 1)z + (2 - 3x)y, whose coefficient is set equal to “m”

With the original quadratic equation, apply the quadratic formula to get the positive root:

y = (-m + sqrt[m2 - 4(-2)(1)]) / 2(-2)

Simplification gives: y = ¼(m + sqrt[m2 + 8z], given that m = (3x - 1)z + (2 - 3x)

And converted back to the original variables:

e/0 = ¼ \* (((3 - 1) \*n / 0 + (2 - 3)) + sqrt(((3 - 1 )\*n / 0 + (2 - 3))2 + 8 \*n / 0))

The above form was used in calculating all predictions, with e / 0 as the magnetic permeability of the ferrogel with respect to that of the pure hydrogel, n / 0 as the permeability of the iron nanoparticles with regard to that of the pure hydrogel, and as the volume fraction of the nanoparticles.

**Appendix B: Magnetometer Readings:**

Magnetic Susceptibility of 0.00221 Ferrogel (Field = 300 A/m for all measurements)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **X’ (\*10^-6) Sample 1** | **X’’ (\*10^-6) Sample 1** | **Freq (Hz) Sample 1** | **X’ (\*10^-6) Sample 2** | **X’’ (\*10^-6)**  **Sample 2** | **Freq (Hz) Sample 2** |
| 370.1 | 43.0 | 30.518 | 374.0 | 32.4 | 30.518 |
| 373.7 | 33.3 | 46.387 | 366.4 | 44.0 | 46.387 |
| 350.0 | 39.5 | 108.642 | 311.9 | 35.3 | 108.642 |
| 332.7 | 36.4 | 205.078 | 333.7 | 37.4 | 205.078 |
| 322.8 | 37.6 | 305.176 | 324.2 | 38.3 | 305.176 |
| 313.2 | 38.1 | 488.281 | 310.8 | 37.4 | 488.281 |
| 296.5 | 37.4 | 804.443 | 295.8 | 37.7 | 804.443 |
| 293.3 | 38.0 | 1030.273 | 291.8 | 37.9 | 1030.273 |
| 264.9 | 38.5 | 2010.498 | 277.4 | 38.9 | 2010.498 |
| 264.2 | 38.5 | 3012.695 | 271.2 | 40.1 | 3012.695 |
| 257.7 | 41.6 | 5002.441 | 266.3 | 40.2 | 5002.441 |
| 237.8 | 37.9 | 8002.929 | 228.5 | 36.0 | 8002.929 |
| 237.6 | 35.9 | 9901.123 | 244.5 | 37.0 | 9901.123 |

Magnetic Susceptibility of Maghemite Nanoparticles (Field = 300 A/m for all measurements)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **X’ (\*10^-6) Sample 1** | **X’’ (\*10^-6) Sample 1** | **Freq (Hz) Sample 1** | **X’ (\*10^-6) Sample 2** | **X’’ (\*10^-6)**  **Sample 2** | **Freq (Hz) Sample 2** |
| 12412.3 | 1882.4 | 30.518 | 12427.5 | 1918.5 | 30.518 |
| 11726.7 | 1609.2 | 46.387 | 11703.6 | 1599.1 | 46.387 |
| 10970.0 | 1413.1 | 108.642 | 10993.9 | 1469.4 | 108.642 |
| 10487.4 | 1330.4 | 205.078 | 10464.4 | 1323.3 | 205.078 |
| 10203.6 | 1262.5 | 305.176 | 10141.4 | 1254.0 | 305.176 |
| 9818.7 | 1194.6 | 488.281 | 9841.9 | 1197.3 | 488.281 |
| 9519.8 | 1151.8 | 804.443 | 9478.0 | 1144.9 | 804.443 |
| 9291.1 | 1125.6 | 1030.273 | 9287.0 | 1124.0 | 1030.273 |
| 8958.1 | 1121.6 | 2010.498 | 8850.1 | 1107.9 | 2010.498 |
| 8604.2 | 1118.0 | 3012.695 | 8594.7 | 1115.5 | 3012.695 |
| 8308.8 | 1137.5 | 5002.441 | 8288.0 | 1133.5 | 5002.441 |
| 8035.6 | 1093.0 | 8002.929 | 8011.6 | 1089.1 | 8002.929 |
| 7908.3 | 1101.1 | 9901.123 | 7961.0 | 1018.3 | 9901.123 |

All susceptibilities were converted into relative permeability by the equation: e / 0 =+1, where X’ is in-phase susceptibility, X’’ is out-phase susceptibility, and e / 0 is the relative permeability of ferrogel with respect to pure hydrogel.

**Appendix C: Swelling Measurements**

Day One Measurements, after 24 hours in buffer

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **pH** | **Diameter (Grid)** | **Diameter (mm)** | **pH** | **Diameter (Grid)** | **Diameter (mm)** |
| 4.20 | 37.9 | 2.060 | 4.16 | 36.7 | 1.995 |
| 4.20 | 39.4 | 2.141 | 4.16 | 36.1 | 1.962 |
| 4.20 | 40.5 | 2.201 | 4.16 | 33.4 | 1.815 |
| 7.29 | 55.5 | 3.016 | 7.19 | 47.1 | 2.560 |
| 7.29 | 47.6 | 2.587 | 7.19 | 36.7 | 1.995 |
| 7.29 | 54.3 | 2.951 | 7.19 | 45.0 | 2.446 |
| 9.89 | 59.9 | 3.255 | 9.95 | 51.1 | 2.777 |
| 9.89 | 57.5 | 3.125 | 9.95 | 47.0 | 2.554 |
| 9.89 | 61.9 | 3.364 | 9.95 | 48.2 | 2.620 |

Day Two measurements, after 48 hours in buffer

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **pH** | **Diameter (Grid)** | **Diameter (mm)** | **pH** | **Diameter (Grid)** | **Diameter (mm)** |
| 4.14 | 31.8 | 1.728 | 4.14 | 33.7 | 1.832 |
| 4.14 | 36.6 | 1.989 | 4.14 | 36.1 | 1.962 |
| 4.14 | 35.3 | 1.918 | 4.14 | 33.5 | 1.821 |
| 7.4 | 55.9 | 3.038 | 7.4 | 46.0 | 2.500 |
| 7.4 | 57.4 | 3.120 | 7.4 | 45.7 | 2.484 |
| 7.4 | 53.0 | 2.880 | 7.4 | 48.6 | 2.641 |
| 9.87 | 56.8 | 3.087 | 9.79 | 50.5 | 2.745 |
| 9.87 | 53.1 | 2.886 | 9.79 | 52.7 | 2.864 |
| 9.87 | 55.8 | 3.033 | 9.79 | 55.1 | 2.995 |

Day Three Measurements, after 72 hours in buffer

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **pH** | **Diameter (Grid)** | **Diameter (mm)** | **pH** | **Diameter (Grid)** | **Diameter (mm)** |
| 4.18 | 38.0 | 2.065 | 4.17 | 33.9 | 1.842 |
| 4.18 | 31.2 | 1.696 | 4.17 | 35.7 | 1.940 |
| 4.18 | 33.2 | 1.804 | 4.17 | 28.3 | 1.538 |
| 7.34 | 58.5 | 3.179 | 7.37 | 44.3 | 2.408 |
| 7.34 | 56.1 | 3.049 | 7.37 | 44.7 | 2.429 |
| 7.34 | 57.6 | 3.130 | 7.37 | 45.7 | 2.444 |
| 9.87 | 57.3 | 3.114 | 9.88 | 54.5 | 2.962 |
| 9.87 | 64.6 | 3.511 | 9.88 | 52.4 | 2.848 |
| 9.87 | 62.1 | 3.375 | 9.88 | 50.7 | 2.755 |

The buffers’ original pH was 4, 7.4, and 10, respectively. They were changed with fresh buffer each day immediately after measuring. A weighted average of the difference in swelling between pure and ferro- hydrogels at various pH values was calculated to quantify the loss in sensitivity (see “Results”).

**Appendix D: Bruggeman Effective Medium Approximation Derivation (For Non-Homogenous Dispersions)**

Given the original derivation:

e/0 = ¼ \* (((3 - 1) \*n / 0 + (2 - 3)) + sqrt(((3 - 1 )\*n / 0 + (2 - 3))2 + 8 \*n / 0))

and converted back to

y = ¼(m + sqrt[m2 + 8z], given that m = (3x - 1)z + (2 - 3x)

with x substituted for , y for e / 0, and z for n / 0.

The above equation (for homogeneous dispersion) is then solved for each bead (with nanoparticles concentrated inside) within the hydrogel. The results are then put through the Bruggeman equation again, in place of the permeability constant, with the volume fraction being the concentration of beads in hydrogel, to yield:

¼ \* (((3b - 1) \* (¼ \* (2 \* x - 1) + sqrt((2 x - 1)^2 + 8 z))+(2 - 3b)+sqrt((((3b - 1) \* (¼ \* (2 x - 1)+sqrt((2 x - 1)^2 + 8 z)) + (2 - 3b))^2 + 8(¼ \* (2 x - 1) + sqrt((2 x - 1)^2 + 8 z))))))

with b =b, x = , the volume fraction of the nanoparticles in beads, and z = n / 0, the permeability constant

And converted back into original terms:

e / 0 = ¼ \* (((3b - 1) \* (¼ \* (2 \* - 1) + sqrt((2 - 1)^2 + 8 n / 0))+(2 - 3b)+sqrt((((3b - 1) \* (¼ \* (2 - 1)+sqrt((2 - 1)^2 + 8 n / 0)) + (2 - 3b))^2 + 8(¼ \* (2 - 1) + sqrt((2 - 1)^2 + 8 n / 0))))))

with b being the volume fraction of the beads in hydrogel, the volume fraction of the nanoparticles in beads, and n / 0 the permeability constant

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