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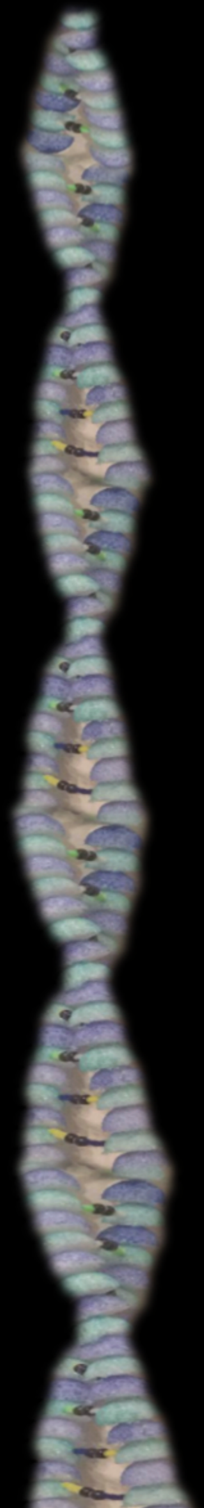

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Undergraduate Envision

Non-invasive Technique for Determining the In-situ Temperature of Ferrofluid in Magnetic Hyperthermia Treatment

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Context

The use of magnetic hyperthermia in the treatment of tumors has become a rapidly growing field. The technique involves the injection of magnetic nanoparticles like Ferrofluid into tumor cells followed by the application of an external alternating magnetic field. The resulting temperature rise in the Ferrofluid is utilized to destroy the tumor cells.[1] One of the obvious parameters researchers are interested in, is the temperature achieved in-situ and the time needed for this temperature to be reached. Knowing these parameters will facilitate the optimization of the treatment by preserving normal cells while also providing important temperature feedback. It is vastly preferable to determine the temperature non-invasively for several reasons. Measuring the temperature of the Ferrofluid inside the body is a complex problem since there are many dynamic variables involved, such as capillary flow, the thermal properties of tissues, and location among others.[2] In this paper, we present a new, non-invasive method to determine and control the temperature of Ferrofluid in a tumor located within the body. The experimental results indicate that this is a viable method. Additionally, an exciting result has emerged, shedding new light on the exact mechanism of heating on which there has previously been much speculation. It has been found that most of the heating effect in Magnetic Ferrofluid is related to the viscosity of the oil used in the synthesis of the Ferrofluid.

Vision

Magnetic Nanoparticle Therapy is a growing area of research. The technique involves the injection of Magnetic Nanoparticles, like Ferrofluids, into tumor cells. Next, the Ferrofluid is heated by applying an external AC magnetic field. This field excites the Ferrofluid, sufficiently increasing its temperature to kill the tumor. One of the issues on which there has been much debate is the exact temperature achieved within the tumor. It happens to be a complex process to predict the temperature. Many papers, both theoretical and experimental have tried to determine this. However, this is a complex process as there are many dynamic variables involved, such as capillary flow, mix of tissues with different thermal properties, location, shape and volume of the tumor, etc.[3] For example, adipose tissues might be better insulators compared to other types of tissue. Computer simulations are only as good as the input parameters. However, there are a large number of parameters and a lot of variation in any practical situation. The results may be deceptive. Another technique may be to embed a thermal probe; however, this would defeat the purpose of a non-invasive treatment. Additionally, most physical probes are localized and have thermal mass which obfuscates the measurement process. Infrared thermal imaging may also be considered, but it too is dependent on many factors. In this paper, we have developed a non-invasive technique to determine the temperature of the Ferrofluid deep inside the body. To verify certain results, Bismuth, a diamagnetic substance was used as a control. An exciting result indicates that the temperature rise in Ferrofluids aligns with the temperature dependent viscosity of the oil used to synthesize the Ferrofluid. The temperature rise mechanism has been speculated upon thus far. This could lead to important practical significance in the usage of Ferrofluids in Magnetic Hyperthermia treatment.

The setup of the apparatus is shown in the schematic Fig. 1. A simple oscillator operating around 200 kHz is connected to a variable power supply source Model PS (0-30A, 0-10A). Both the current and the voltage were simultaneously measured to determine the power. A base reading was taken with no Ferrofluid in the test tube, corresponding to the power level with no sample absorption.

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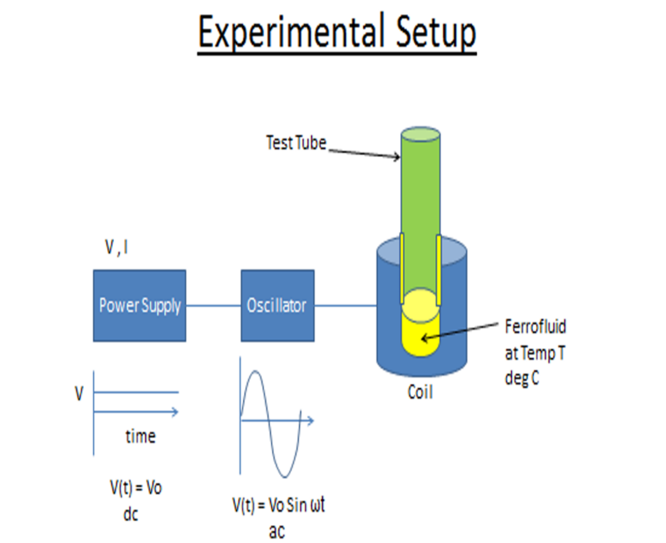

Next, the Ferrofluid was poured into the test tube, with its volume being kept constant. It was experimentally observed that the power absorbed by the sample increased from its base level. However, as time passed, this power level decreased and finally ended at a level close to the base level, indicating that zero power was being drawn by the sample. Since it was also observed that the sample temperature was increasing with time and leveling out at a final temperature, a method was established to try correlate these two factors. Thus, the plot of power absorption versus temperature rise in the sample was used to non-invasively determine the temperature inside the sample. A further simplification for the power absorption was achieved by keeping the voltage constant. Since the oscillator power is the product of the voltage and current, P=VI, keeping the voltage constant meant that the power would follow the current value. Thus, the change in the current input to the oscillator would be proportional to the power absorbed by the sample. A plot of this current change and the temperature of the sample was graphed. This correlation plot allows for the temperature of the Ferrofluid to be non-invasively determined just by looking at the oscillator current.

The initial procedure was to try and measure the temperature of the Ferrofluid and the current at the same time. However, this did not work as both these variables were changing too rapidly. Thus, the temperature was fixed by placing the Ferrofluid test tube in a water bath to fix its temperature. Next, it was quickly transferred to the

Table 1. The Effects of Increasing Temperature on Oscillator Current

Sample Temp. deg C	#1	#2	#3	#4	#5	Avg. Current Change mA	% Current Change with Ref. at Room Temp.
18 (Room Temp.)	3105	3105	3105	3104	3105	3104.8	104.8
25	3090	3090	3090	3089	3088	3089.4	89.4
30	3074	3073	3073	3073	3072	3073	73
35	3061	3061	3061	3061	3062	3061.2	61.2
40	3050	3050	3049	3049	3049	3049.4	49.4
43.5	3044	3045	3043	3044	3044	3044	44
50	3035	3035	3034	3035	3035	3034.8	34.8
60	3016	3016	3017	3016	3016	3016.2	16.2
70	3000	3000	2999	3000	2999	2999.6	-0.4

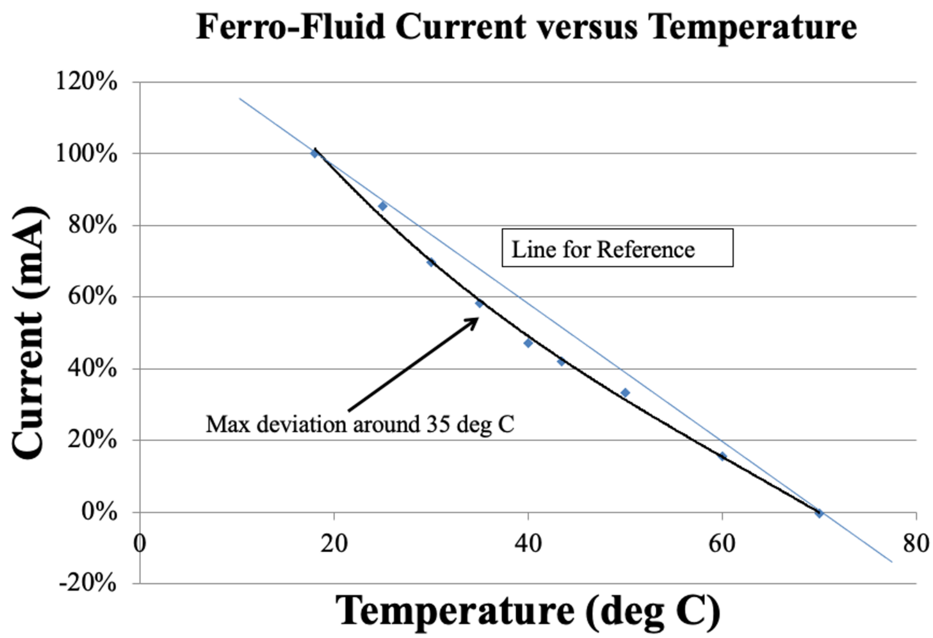

Fig 2. Plot of Oscillator Current versus Temperature for Ferrofluid.

inside of the oscillator coil and the maximum absorption current was recorded. Note, that this initial current corresponds to the absorption at the temperature of the water bath. Subsequently, with the passage of time this current would decrease to its base level as the Ferrofluid heated up. The temperature and the peak current values were recorded for several temperatures ranging from 18 to 70 deg C. Each data point was repeated five times for averaging.

Analysis

Results obtained using this method are tabulated in Table 1. Figure 2 shows that the power absorbed by the Ferrofluid has a slight deviation from the linear relation line drawn for reference. Note, the data point error bar is about or less than the size of the point drawn. In order to relate this to the vegetable oil used in making Ferrofluids, a comparison graph, Fig. 3a, of Vegetable Oil viscosity versus Temperature is shown below.[4] Note that there is a similar dip in values around the interest region of 35 deg C as well. An enlarged graph for the experimental region is shown in Fig. 3b below. As we can see, there is an interesting correlation between the graphs around the same temperature regions. Thus, it can be deduced that the viscosity plays a critical role in determining the final temperatures reached by the Ferrofluids. Using this method, the current in the power oscillator can be used to determine the temperature of tumor deep inside the body.

In order to verify the validity of our method, a control sample of Bismuth was also measured. Bismuth Pellets were put in the test tube, along with water as a medium to distribute the temperature uniformly within the region. The test tube was then placed in the water bath. The temperature of the Bismuth was adjusted by varying the temperature of the water around it. The results of this control experiment are shown in Table 2 below. As we can see from the plotted data, Bismuth, which is diamagnetic, has a linear power absorbtion curve. This is as expected. Thus, the experimental method is acting in the way that it should, with no deviation, unlike the Ferrofluid case. The magnetic heating in Ferrofluid and Bismuth may be explained through the contribution of a variety of factors:

Heating in Ferrofluid

1. Viscosity Loss: The nanoparticles are small and have a magnetic moment which aligns with the applied field. As the applied field switches direction, the nanoparticles rotate to follow the field. This back-and-forth motion of the nanoparticles in the surrounding fluid causes heat to be generated due to the viscosity

Table 2. The Effects of Increasing Temperature on Oscillator Current

Sample Temp. degC	#1	#2	#3	#4	#5	Avg. Current Change mA	% Current Change with Ref. at Room Temp.
18 (Room Temp.)	3155	3154	3155	3155	3154	3154.6	154.6
22.5	3150	3151	3150	3150	3149	3150	150
31	3144	3144	3143	3144	3142	3143.4	143.4
45.5	3135	3138	3138	3138	3138	3137.4	137.4
52	3138	3138	3136	3136	3136	3136.8	136.8
67	3128	3128	3130	3128	3130	3128.8	128.8
75	3125	3126	3127	3126	3126	3126	126

*Sample: Bismuth Pellets (Water)

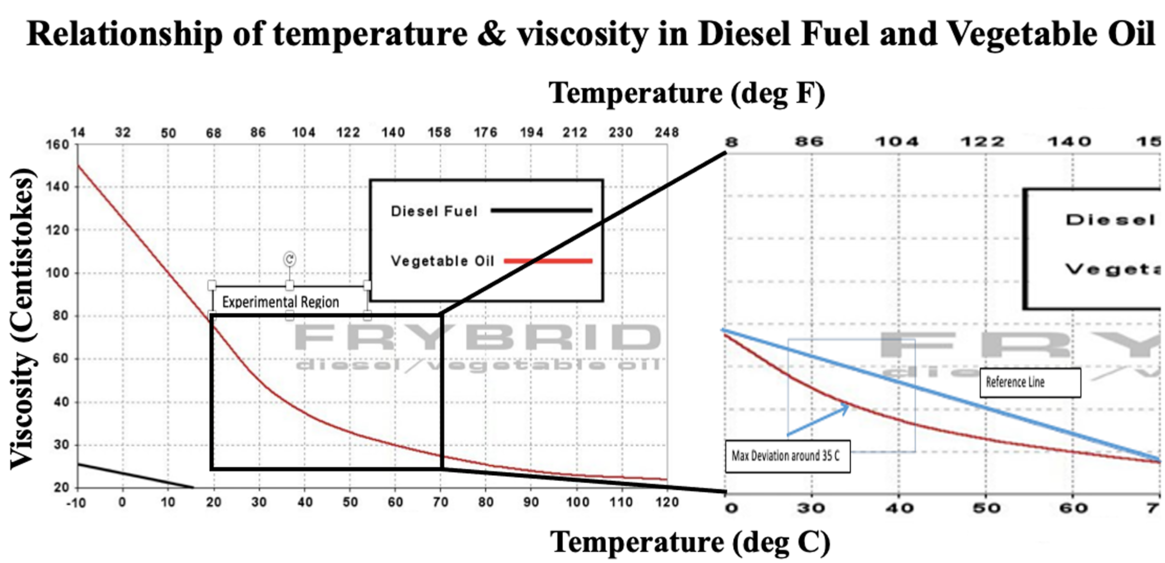

Fig. 3. ***A.*** Viscosity of Vegetable oil from Reference[3]. ***B.*** Enlarged inset showing the variation in the 20 to 70 deg C temperature range

of the fluid.[5] The fact that the ferromagnetic nanoparticles rotate is important. The power needed to rotate the nanoparticle is evidently related to the viscosity of the local fluid media due to viscous coupling between the particle and the fluid. Thus, the temperature-dependent viscosity of the fluid tracks the power absorbed. The viscosity of the vegetable oil decreases by 75% with a temperature rise from 20 to 70 degrees. As a result, this is the main reason for the drop in current/energy with temperature.

2. Eddy Current Loss: There will be an eddy current setup inside the nanoparticles.[6] These losses will decrease as the resistance increases with temperature and as the current is decreased. The resistivity coefficient of iron is 0.168% per deg C. This means the total eddy current contribution from 20 to 70 deg C is 0.168*(70 -20) =9%.

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3. Curie Point: The magnetization is also reduced as we approach the Curie Temperature for iron, T_c= 750 C. From the graph, this contribution is about 1-2%.
4. Hysteresis Loss: Since the nanoparticles are around 10nm in size, they are much smaller than the domain size of 50 to 100nm. Thus, there will be negligible hysteresis loss and these particles will behave as a single domain or like a super paramagnet.[7,8] temperature is related to the viscosity properties of the oil used, thus different oils can be used to change the treatment temperatures. A future experiment may also involve the placement of Ferrofluid in a glassy media (e.g., a cross-linked media or frozen oil), that does not flow, in which the eddy current losses could be calculated more accurately due to the elimination of the viscosity effect. The Bismuth control data showed that the experiment generated data reasonable with the theory.

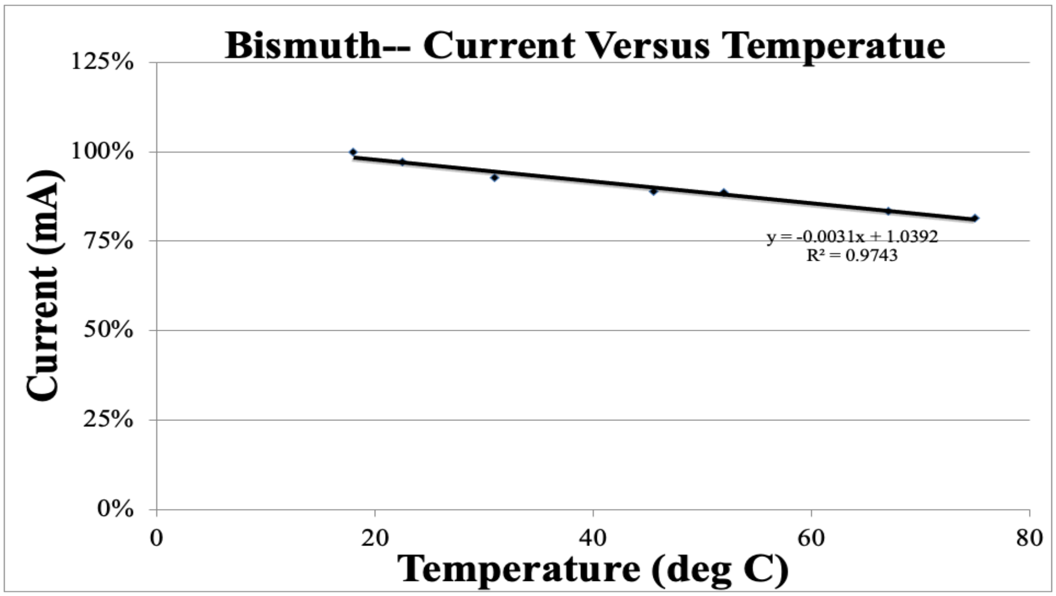

Fig. 4. Plot of Oscillator Current versus Temperature for Bismuth.

5. This covers about 90% of the losses compared to the 100% which we are observing. The remaining 10% could be due to errors or inexact estimates.

Heating in Bismuth

1. Bismuth is diamagnetic and its magnetic properties do not change with temperature.
2. There is only eddy current losses present, which decrease with temperature as the resistance of bismuth increases. The coefficient of resistivity of bismuth is 0.42% per deg C. So, for a temperature change from 20 to 75 deg C the loss is about 0.42*(75-20) = 23 %.
3. We observe a drop of 18% in our data, which is reasonably within the error range.

Implementation

This experiment was successful, and we have presented a technique to correlate the temperature to the current change in percentage. This allows us to non-invasively determine the temperature of the Ferrofluid from the oscillator current drop. A majority of energy loss with

Additionally, in this paper, the test tube ferrofluid media is globally heated during the calibration process. Thus, there is no significant viscosity gradient in the fluid within the test tube. However, in actual operation, when the particle rotates in a biological semi-solid or liquid media, such as a tumor, there may be a significant viscosity gradient within the tissue. The current in that real situation will best correspond to temperatures in the immediate vicinity of the nanoparticle because the temperature gradient follows the viscosity gradient. These "higher-order" effects may need to be considered in more advanced in situ applications of this newly developed technique.

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Conflict of Interest

None

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