Development of a Digital Continuous Wave NMR for Search for Hemoglobin Patterns - A Feasibility Study

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Introduction

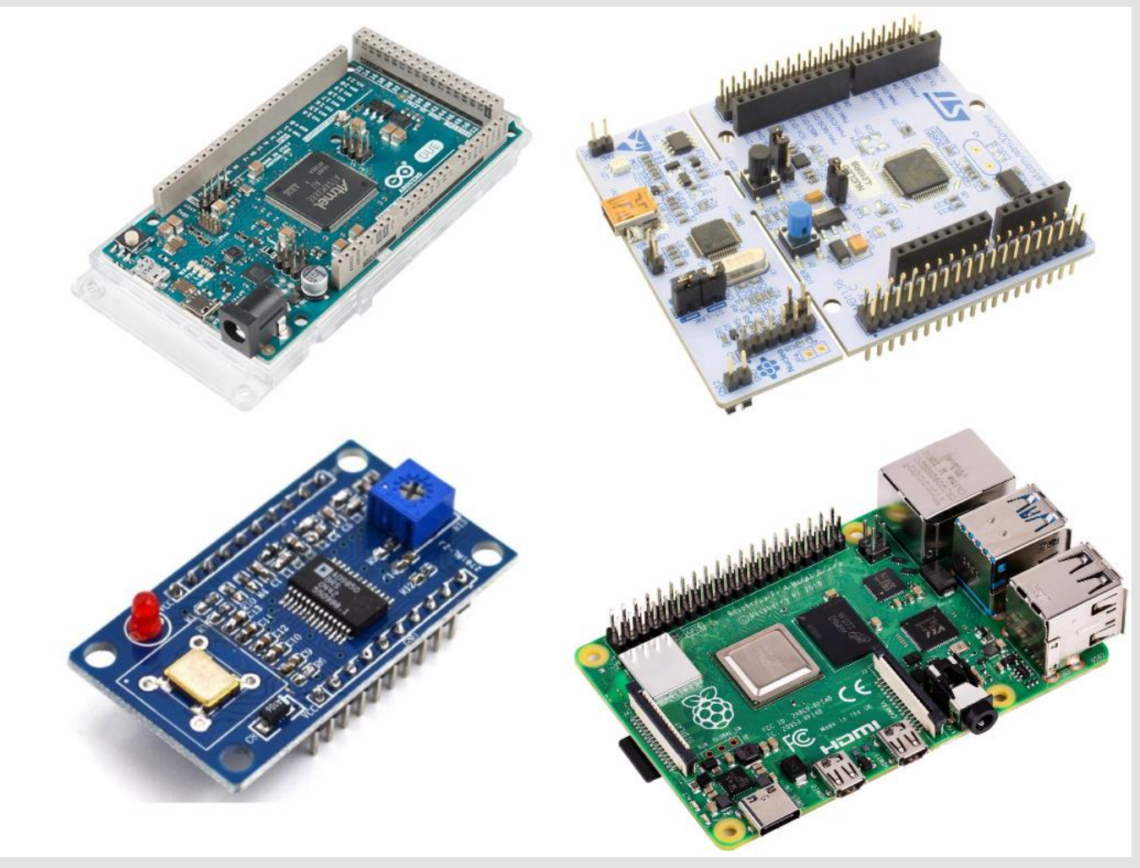
This poster outlines the feasibility of constructing a benchtop Continuous Wave (CW) Nuclear Magnetic Resonance (NMR) machine for mobile spectroscopy. Compact, low-field instruments are allowing for mobile testing and faster analysis times. Benchtop NMR machines are being used in the field for identifying metabolic diseases, suggesting a potential for disease outbreaks and access to advanced testing equipment for more

This poster serves as an initial study and feasibility report. This paper will not deliver a full outline for the technological solutions for all requirements. As a first project of its kind for this lab, the requirements are not formed from a perspective of expertise but rather a position of exploration.

Pictured left: an education level CW-NMR device. It is designed to demonstrate NMR resonance in a classroom setting through manual adjustment. This is the device to be automated and ultimately replaced.

Materials

There are several development components used for this project. These are electronic systems designed for a wide range of applications that were adapted to satisfy system requirements.



The Arduino DUE (top left) has a faster clock speed (84MHz) than most other Arduinos and entry level micro-controllers. The STM32 (top right) has an even faster clock speed (100MHz) but is programmed in C language. The AD9850 (bottom left) is a Digital Synthesis (DDS) device that generates a signal of up to 30MHz. The Raspberry Pi (bottom right) functions as a microprocessor, capable of faster calculations and data handling.

Methodology

- **Chemistry of Hemoglobin**

Human blood consists of red blood cells containing oxygen-carrying hemoglobin. Chemical changes, such as anemia, to hemoglobin affect the amount of oxygen it can carry. Studies have confirmed the link of Anemia to Covid-19. These changes can be detected by NMR spectroscopy.

- **NMR Spectroscopy**

The device that this paper outlines is a benchtop CW-NMR machine. CW-NMR is the oldest technology of NMR, allowing it to be the least expensive and an appropriate development baseline. Advances in all aspects of the technology (magnetic induction, Microcontrollers, HF-signal generators) greatly shrink these devices in size (benchtop) and cost.

- **NMR Metabolomics**

The final consideration into the efficacy of benchtop CWNMR is its potential for application in Metabolomics. Metabolomics is the. The general baseline for NMR-based metabolomics is a 600MHz system [7], because spectral dispersion is sufficient above 600MHz. Benchtop CWNMR falls well short of this, and most systems no longer use CW technology.

Requirements

- Benchtop NMR capable of detection within blood
- Perform a pattern search to analyze data patterns
- Generate analog signals need for resonance
- Operate current coils, probe, and setup and produce:
    - Up to 500 mT for the B0 field
    - A 20-30 MHz sinusoidal signal
    - A variable circuit
- Amplify and attenuate signals appropriately
- Function automatically without manual adjustment
- Convert analog output (16kHz) into digital output
- Store digital data
- Perform a pattern search to analyze data patterns

- **Requirements**

From these fundamentals, a list of requirements for building a digitized, benchtop NMR device are outlined (left). Though not all the technical specification for every requirement was found, this poster can serve as a roadmap that guides to that eventual solution. A final note: the conclusions and recommendations outline a more thorough explanation of challenges to be addressed in the next steps.

Results

Results are discussed at the subsystem level: Microcontroller and ADC; DDS, Amplification, and Filtering; NMR Hardware and Power Supply; Data Storage and Pattern Recognition.

- **Microcontroller and ADC**

This subsystem includes the microcontroller and the analog-to-digital converter (ADC). This is all included on the Arduino DUE and the STM32. The microcontroller controls the settings and the inputs/outputs to the system. The Analog-to-Digital Converter (ADC) on the micro-controller converts the signal returned from the NMR device into digital data. The analog-to-digital converter (ADC) must do this at the signal speed (~16kHz). The Arduino DUE is hamstrung by the slow Arduino programming language. The clock speed of the STM32 is higher (100 MHz) and it is programmable through the C Programming language. The STM32 ADC conversion requires 12.5 clock cycles, which is roughly 8 MHz of sampling frequency.

- **DDS, Amplification, and Filtering**

From the microcontroller, the digital control signals must be transferred to analog signals used for the NMR Probe and the oscillation field. The DDS module outputs a clean signal up to 30MHz. Two DDS modules are required: DDS 1 for the high frequency signal to later generate the BR field and DDS 2 to generate the signal for the B0 oscillation field. The details for the circuitry of the NMR signal is the most technically challenging aspect of future development. More on this in the conclusion and recommendations.

- **NMR Hardware and Power Supply**

The NMR signal creation occurs within the NMR Hardware and Power Supply. All hardware is used from the initial analog NMR unit. The power supply can be successfully communicated with (via SPCI) to sweep through the range of currents to find the resonance spectrum.

- **Data Storage and Pattern Recognition**

Data Storage and Pattern Recognition can be handled by a Raspberry Pi. This board can control the microcontroller, store all data to an onboard SD card, handle interfacing (wired, wireless, and via onboard display), and run machine learning models for pattern recognition. The data packages for each sample are less than 1kB. For 100 repeats per sample and 100 sequences per repeat, the data package for any material sample is around 10GB. SD card capacity has greatly surpassed this. The data must be sequenced and turned into a spectrum after storage. Each repeat of the samples stacks and creates the same amount of data as one sample. This reduces the total data size from the above estimate to 10MB, easily fit on 1GB of RAM on the Raspberry Pi tested. The roughly 10MB sequence can then be fed into a machine learning model for evaluation. Small AI models can be implemented easily on the Raspberry Pi.

Conclusion

After the completion of this project, several paths can be followed for a successful outcome. Incites about the future opportunities and challenges were obtained from the technical accomplishment limitations. Furthermore, these requirements are fulfilled in part. A separate task is to integrate these subsystems together.

There are several challenges ahead. The greatest of these challenges are a pattern and recognition search capable of determining the reading from different materials. The next are improvements to the data pipelines. Under current architecture, these channels are much slower than possible. However, optimistically this is a promising start to the development process.

- **Recommendations**

The main limitation found was with the high frequency NMR signal. Appropriate prototyping HF signals requires advanced equipment. Traditionally, PCBs are used are for high frequency signal handling. It is thus recommended to create a partnership with an institution or research group with these capacities.

On the task of Hemoglobin-Oxygen pairing analysis, CW-NMR machines are not capable. It is thus the recommendation of this paper to include FT-NMR in future iterations of this system development.

Acknowledgements

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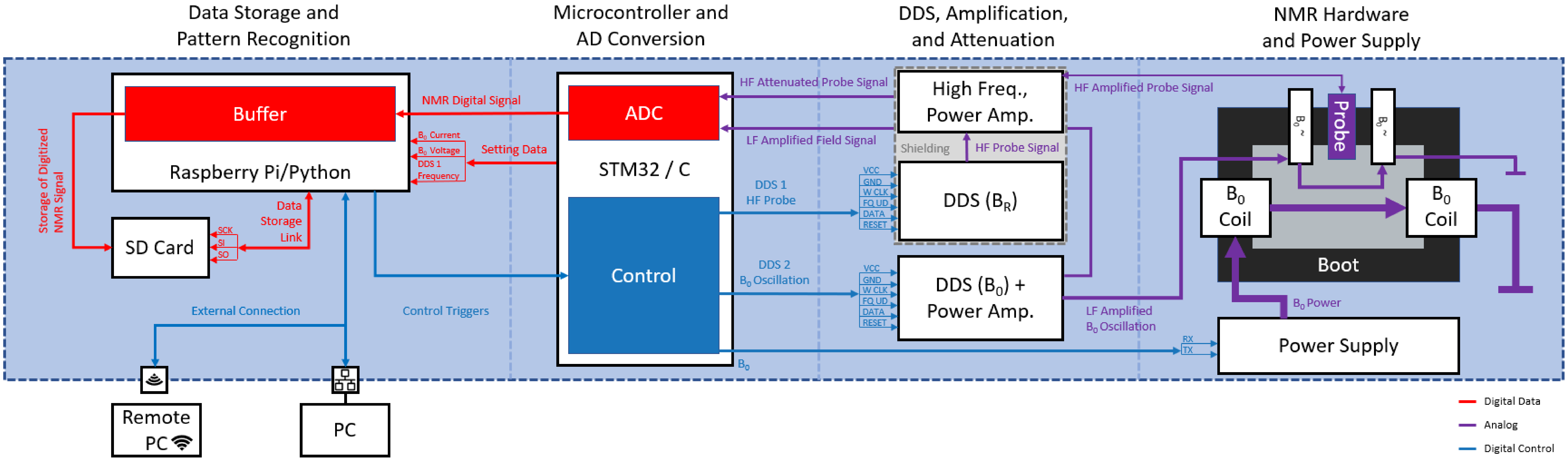

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