Naval Information Warfare Center PACIFIC

TECHNICAL REPORT 3285
JULY 2022

Biological Brain Microtubules Interfaced with Semiconductor Qubits

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Administrative Notes:

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ADMINISTRATIVE INFORMATION

The work described in this report was performed by the Cryogenic and Quantum Research Branch, (Code 71730), Dr. Joanna Ptasinski, branch head, Naval Information Warfare Center (NIWC) Pacific, San Diego, CA. The NIWC Pacific Naval Innovative Science and Engineering (NISE) Program, Dr. Dave Rees and Dr. Ryan Lu provided funding for this Basic Applied Research project.

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Editor: MRM

EXECUTIVE SUMMARY

This technical report presents the results of recently executed research at NIWC Pacific on the topic of “Quantum Monitoring and Control of Biological Cells”. The primary objectives were to develop quantum biology chips with biological elements, i.e. brain microtubules interfaced in nanoscale proximity to semiconductor spin qubits (an option for quantum computing/networking applications). The motivation was to advance fundamental knowledge on biological elements to advance the field of brain-inspired electronics/neuromorphics and brain-electronic interfaces as well as to explore nano-scale interactions, which may be relevant to viral processes and thus current global health challenges such as COVID-19. The research will ultimately enable the design of new information systems with features of what is referred to as “consciousness” by taking the step of providing an unprecedented ability to monitor and control changes in these biological elements at the nanoscale.

The scientific literature is currently very active with several studies focused on the key role of nanoscale effects including those dominated by quantum physics in understanding consciousness; these are including coherent energy/charge transfer, entanglement, tunneling, and spin processes that are assisting to understanding brain function.

The specific steps taken in this work include: (1) Synthesizing a series of microtubules (MTs) with native surface chemistry as well as surface modified chemistry to induce selective photoluminescence, from commercial tubulin precursors; (2) Depositing these microtubules on semiconductor spin qubit chips where the microtubules are in nanoscale proximity to optically active qubits formed from vacancy states in silicon carbide crystals; (3) Performing advanced spectroscopy of these MT-qubit chips under vacuum and cryogenic conditions spanning 4-10K to study the impact of charge/energy transfer between the MTs and the qubits and the resulting impacts to the composite spectra when taking a scan of the system response. In addition to this technical report, a U.S. patent disclosure was filed on the concept and technology.

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ACRONYMS

RNA	Ribonucleic acid
DNA	Deoxyribonucleic acid
COVID-19	Coronavirus disease
MTs	Microtubules
CCD	Charge-coupled device
SIC	Silcon Carbide Crystal
QUBIT	Quantum Bit

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CONTENTS

FIGURES

TABLES

1. INTRODUCTION

Biological proteins/microtubules and RNA/DNA are amazing systems at the nanoscale that have very complex tertiary structures, i.e. folding into three dimensional sheets and helixes and having nanoscale spatial configurations. The translation of DNA drives complex expression and tertiary structures of proteins that are an essential part of cellular function. Viruses can infect cells, altering their information processing capabilities, impacting protein expression and/or microstructure and thus cellular functions. In addition, proteins on their own i.e. tubulin proteins, assemble into microtubules, cytoskeleton structural components which in addition to playing a key role in mechanical support, and cell migration, couple to and regulate neural-level synaptic function. Other proteins, i.e. metallo-proteins, contain metal centers such as Cu ions and can be used for targeting cancerous cells in order to induce apoptosis. Other proteins such as the Spike protein on the COVID-19 virus are on the order of 2-3 nanometers and are critical for interacting with the human ACE-2 enzyme and nanoscale changes result in devastating new mutations of the virus. The physical processes described are being actively studied for the classical and quantum physical effects involved including conduction, energy transfer, optical emission and quantum entanglement in the operation of these bionanomaterials. It is therefore important to understand the physics of these hybrid systems in order to design new designer proteins or to modify existing proteins-qubit complexes that could be used to monitor and control biological processes by means of electronic/optical/or other stimuli.

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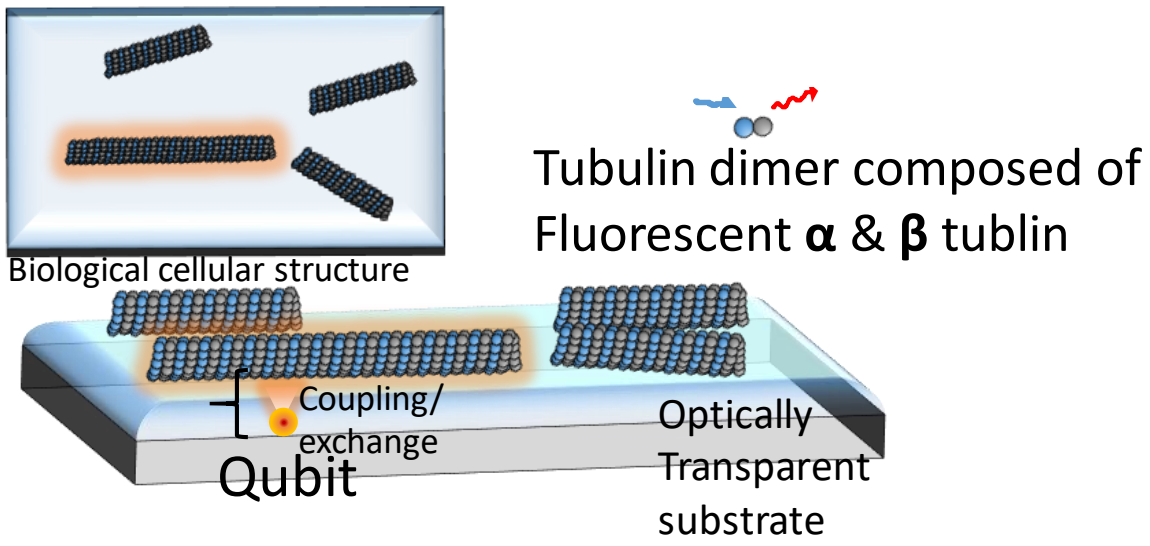
2. CHIP PRODUCTION PROCESS AND CHEM/BIO SAFETY & HAZCOM PROTOCOLS

We developed a process for the construction of the experimental device, i.e. MTs interfaced with semiconductor spin qubits. A schematic of the chip is shown in Figure 1. The key elements of the process were the synthesis of the microtubules via the polymerization of fluorescent tagged and, or native tubulin precursors, procured from Cell, Inc. In order to prevent depolymerization of the microtubules after synthesis, they are drop-casted on silicon carbide qubit substrates and dried under vacuum at room temperature. Substrates contain qubits formed near the surface via ion implantation and annealing i.e. in the top 5 nm near the interface. The short nanoscale distance is key as the qubits need to be in nanoscale proximity to the microtubules in order to ensure efficient energy transfer, dominated by quantum physical processes occurring between these elements. Following synthesis of the microtubules and drop-casting on the qubit substrates, the bio-chips are transferred to the quantum lab where the chips are loaded in the vacuum chamber of a cryo-magneto-optical probe station and vacuum pumped and cooled to the 10-4 Kelvin range. At this stage advanced characterization via spectroscopy is conducted.

Approach:

- Procure brain tubulin monomers and polymerize a series of microtubules
- Develop deposition process for attaching microtubules to qubits
- Liquid nitrogen freezing of qubit-cellular biological chips
- Dry cryogenic cool of chips in cryo-magneto-optical station under vacuum
- Imaging and spectroscopic/electronic characterization to examine feasibility of process
- Refinement of invention disclosure Navy Case 111354



- The nanoscale proximity of the microtubules and the qubits enable coupling/exchange of energy between these elements from electrostatic charge transfer mediated by high speed tunneling processes.

Figure 1. Illustration of the experimental chip design where the microtubules are deposited and interfaced directly with a solid-state silicon vacancy spin qubit formed in an optically transparent crystal substrate, i.e. Silicon Carbide.

Table 1. Summary of Qubit-MT configurations that were formed and experimented with on SiC crystals.

	Qubit	Microtubule
1	Silicon vacancy in Silicon Carbide (Vsi)	Zero microtubules, i.e. control sample
2	Silicon vacancy in Silicon Carbide (Vsi)	Unmodified microtubules i.e. native
3	Silicon vacancy in Silicon Carbide (Vsi)	Fluorescein labeled microtubules
4	Silicon vacancy in Silicon Carbide (Vsi)	Rhodamine labeled microtubules
5	Silicon vacancy in Silicon Carbide (Vsi)	HiLyte labeled microtubules

3. MICROTUBULE RE-POLYMERIZATION

Microtubule Polymerization was performed according to the vendor *Cytoskeleton, Inc.* instructions with minor modifications to control for density of surface fluorescent tags:

Microtubule assembly:

Freshly prepared MTs in solution are stable for several hours for typical characterization at room temperature, but will depolymerize at lower temperatures. Dried microtubules are stable for extended times. Microtubules added to substrates through liquid deposition can be dried to impart longer term stability for cryogenic analysis.

Polymerization Method:

1. Defrost the taxol solution; this solution can be kept at room temperature during the course of the experiment as it will be needed throughout the procedure.

2. Aliquot 200 µl of General Tubulin Buffer into a labeled centrifuge tube and place at 35°C.

3. Defrost one 20 µl aliquot of Tubulin Protein by incubating for several minutes in a room temperature water bath. Once thawed IMMEDIATELY transfer to ice, add 2 µl of Cushion Buffer
    a. Typically, at this point reactions are incubated at 35°C for exactly 20 minutes, allowing tubulin to polymerize to microtubules (MTs). In this particular case the reaction was monitored in real time by carrying out the incubations in 96 well plates and observing optical density at regular intervals until polymerization rate was observed to plateau in the native microtubules (encouraging longer microtubules).

4. In this case, after 60 minutes incubation, remove the 200 µl of General Tubulin Buffer from 35°C and add 2 µl of 2 mM Taxol stock solution (green cap). Mix well.

5. Immediately remove the MTs from incubation and dilute with the 200 µl of General Tubulin Buffer plus Taxol. Mix thoroughly but gently and leave the MTs at room temperature. The Taxol will stabilize MTs.

6. You now have a population of stable MTs that are –approximately 10-15 µm in length and that are at a concentration of approximately 3.0 x 1011 MT/ml. This is equivalent to 5 µM tubulin dimer or 0.4 nM microtubules.

The ease of characterization, both due to stability, and available excitation sources, made the rhodamine samples ideal for further optical characterization. Their emission would also align well with the absorbance of the Si vacancy qubits for future optical coupling characterization. The deposited rhodamine labeled microtubules are approximately 10-15 um in length (Figure 4a) in good agreement with the observed optical density. Images were obtained using a 64x immersion lens on a fluorescence microscope. The high quantum yield allows visualization of these fluorescent structures, but native microtubules are not visible at this magnification.

The growth curves collected (Figure 1) show reproducible growth using native monomer with an enhanced nucleation with the addition of 12% rhodamine, evidenced by an earlier onset of growth.

Logically, the increase in the number of nucleation sites results in an increased concentration of microtubules, and thus ultimately shorter structures, corresponding to the lower equilibrium optical density. The even faster nucleation observed in the HiLyte microtubules also appears to lead to a slow decrease in average microtubule length. This effect is more obvious in the AMCA based microtubules where there is a significantly lower peak in microtubule size, and what appears to be a degradation of the microtubules over time. Under standard conditions, typical microtubules are fairly stable at room temperature, but can de-polymerize at lower temperatures if not chemically stabilized with a species such as taxol. The seemingly rapid degradation observed here suggests a destabilizing effect of the blue fluorescent label. This result implies that either improved chemical stability, or adjusting the chemistry of the blue dye would be necessary for further studies of that particular system.

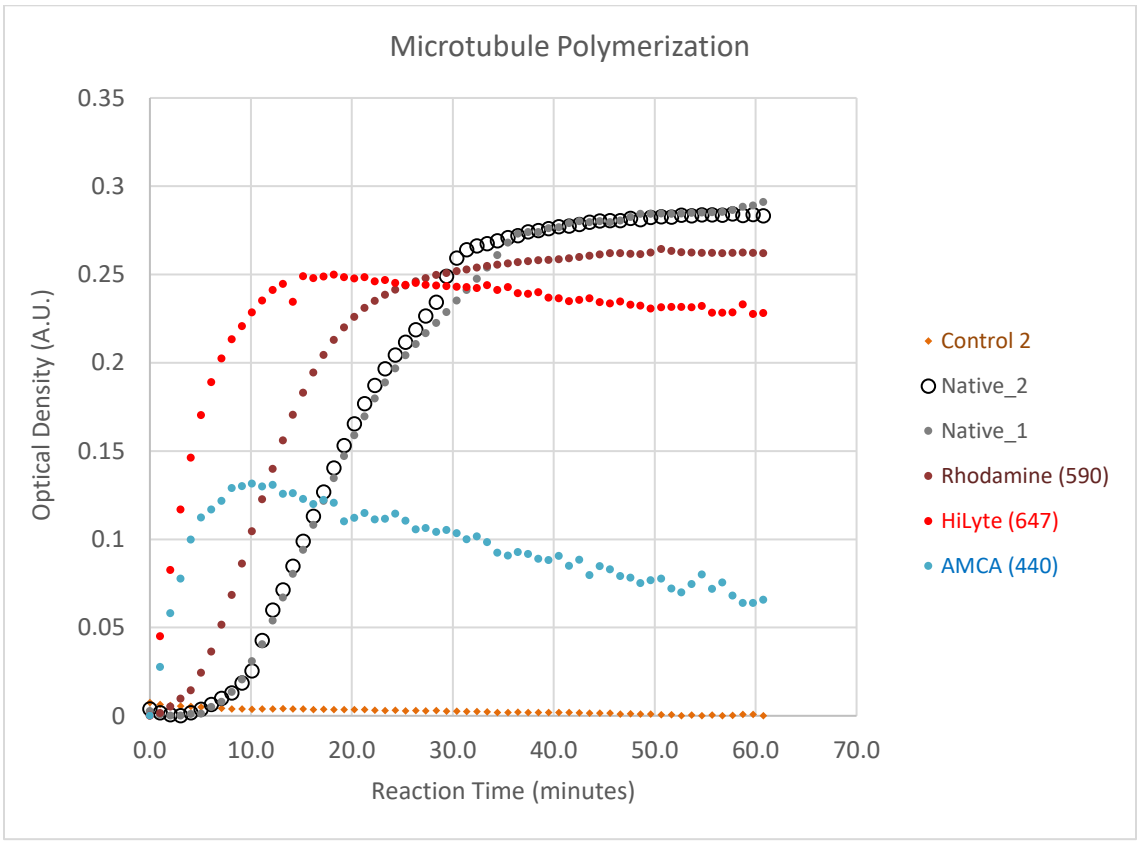


Figure 2. Polymerization of microtubules from tubulin monomers monitored by absorbance at 350 nm. Microtubules were synthesized from native tubulin as well as from native tubulin doped with 12% w/w fluorescent tag labeled tubulin.

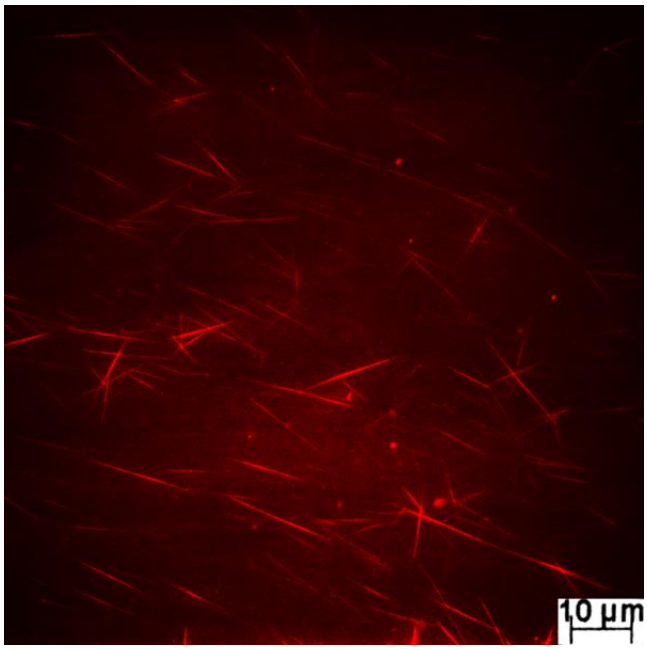


Figure 3. Fluorescent image of Rhodamine labeled microtubules.

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4. DEPOSITION OF MICROTUBULES ON QUBIT CHIPS

In accordance with the experimental illustration (Figure 1), all four varying microtubules were deposited onto a qubit substrate (Figure 2). A micropipette was used to extract a micro-liter of the MT material including taxol. The micro-liter was drop-casted in a fume hood directly on the qubit substrate. Following deposition, the remaining taxol was allowed to air dry and the samples were placed in a vacuum oven for 15 minutes at 80 degrees Celsius.

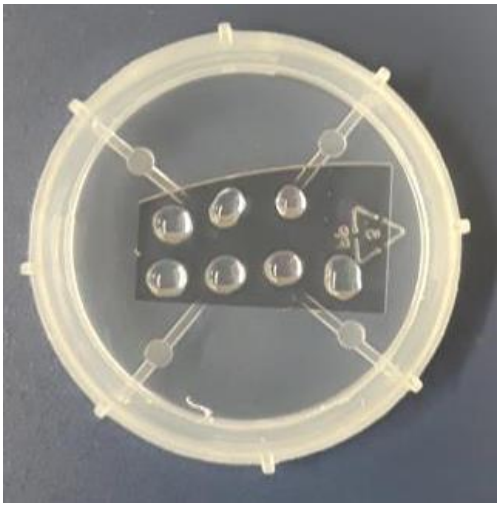

Figure 5. Photograph of the Silicon carbide qubit substrate with the regions deposited with microtubules in accordance with the list in Table I.

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5. VACUUM PUMP DOWN AND CRYOGENIC COOLING OF CHIP

Safety protocols were developed for characterizing the qubit-microtubule chips in the quantum lab. This required adhering to guidance on the PPE required and the handling and disposal of the chips.

Chips were transferred from the bio lab to the quantum lab in a sealed petri dish and inserted in the cryo-magneto-optical probe station, MicroXact Inc. Vacuum was established, pumping down with a roughing/turbo pump combo. Next, dry cooling via two Sumitomo Helium compressors was done to reach a base temperature of 8 Kelvin. At this point spectroscopy was done according to the experimental arrangement in Figure 4. A multimode fiber installed inside the vacuum chamber was used to excite the various samples with 532 nm laser light with an excitation power of 40 mW and also a 785 nm laser light with a maximum power of 250 mW. The fiber was brought in near proximity to the surface using a micro-manipulator probe arm and producing a 500 micron spot size as shown in Figure 6.

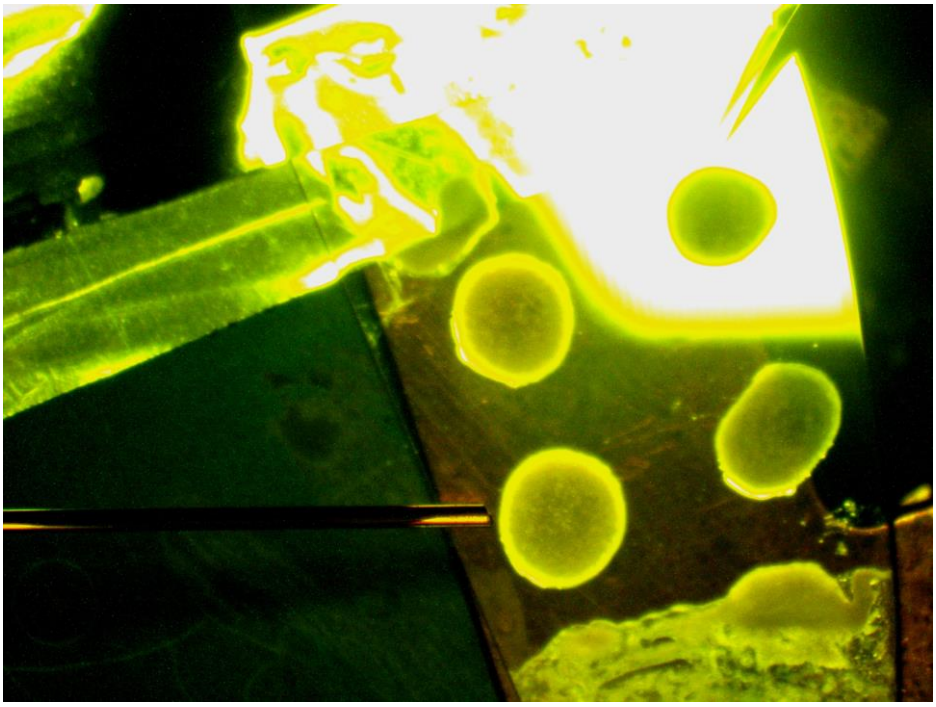

Figure 5. Image of the chip while under vacuum and cryogenic conditions. The fiber probe can be seen in the bottom left.

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6. OPTICAL SPECTROSCOPY AT CRYOGENIC TEMPERATURES

Our experimental arrangement for cryogenic optical spectroscopy is shown in Figure 6**.** A microscope is used to collect the optical emission through a quartz window of the station. A beam splitter is used so that concurrently a CCD camera is enabled to simultaneously view the region of interest. After beam splitting a long pass filter is used to filter out the excitation light and a Horiba ihr-550 equipped with cooled CCD camera is used to detect the spectrum spanning a wide band of wavelengths. The emitted signal is routed via fiber to the spectrometer. This arrangement also enables the use of various detectors such as avalanche photo-diodes, photo-multiplier tubes and nanowire single photon detectors.

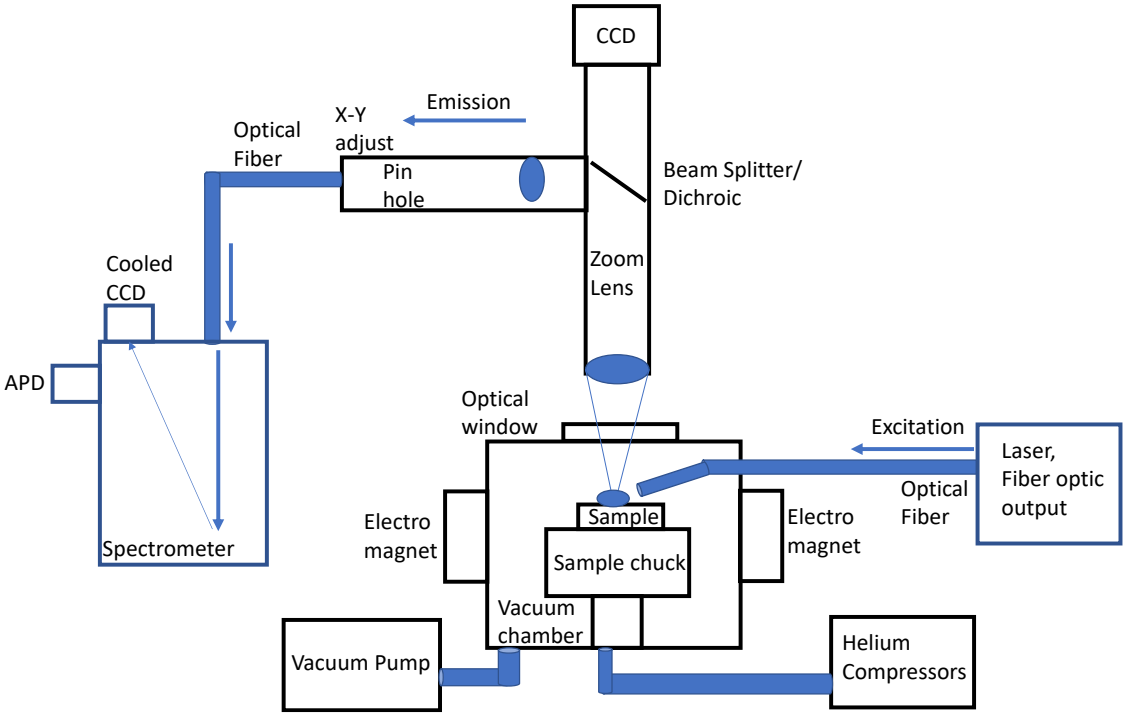


Figure 6. Schematic of the experimental spectroscopy setup. Key features are the sample in cryo-magneto-optical chamber under vacuum. Excitation is performed with a fiber probe inside the chamber and collection takes place via a zoom lens. The collected emission is sent via fiber to a spectrometer with a cooled CCD camera to extract spectra.

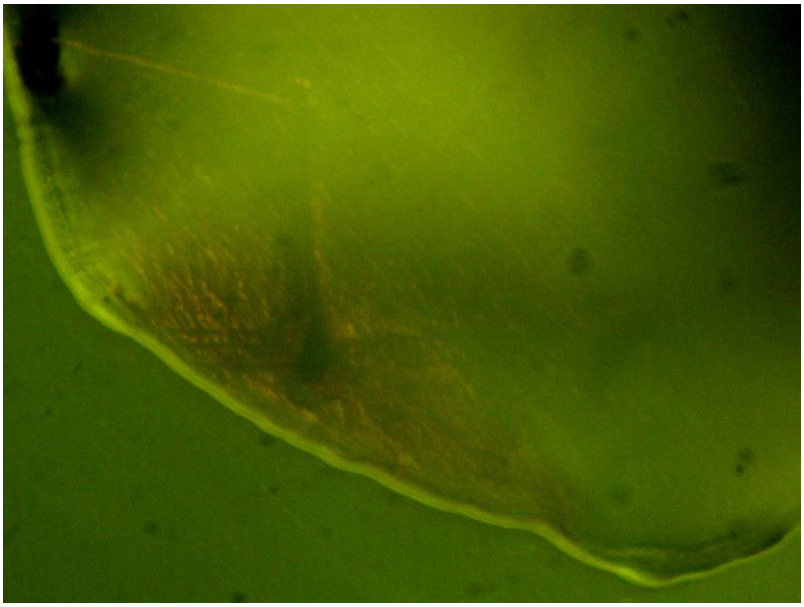


Figure 7. Close up image of a microtubule region of the chip.

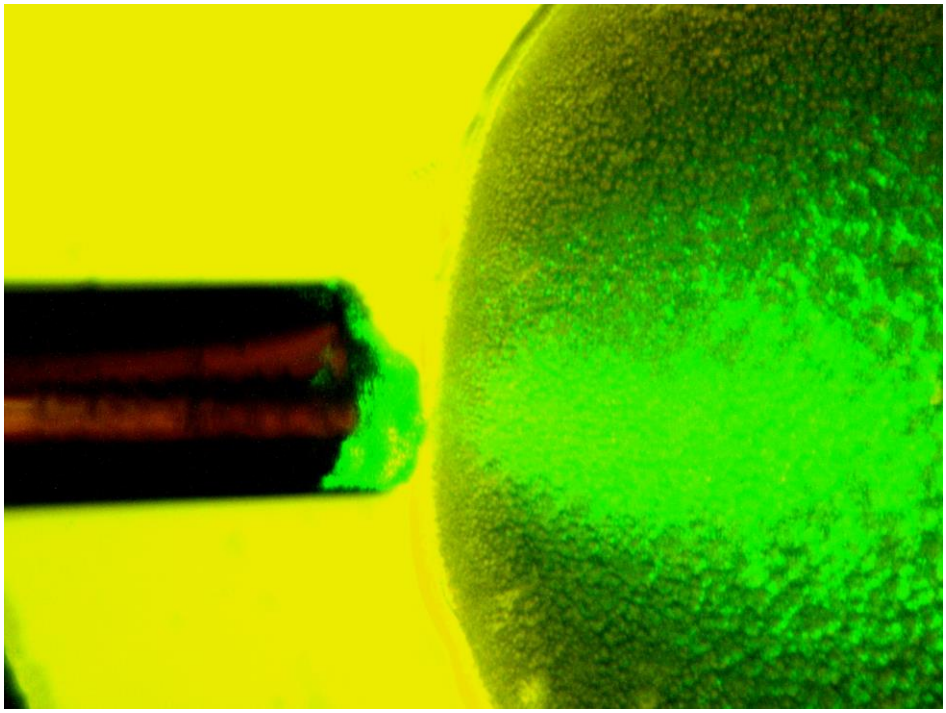


Figure 8. Close-up image showing an example of how collection takes place where the fiber probe is brought in near proximity to the surface to produce a 50 micron excitation region. Extensive calibration and optimization of the optics is done to collect the emission.

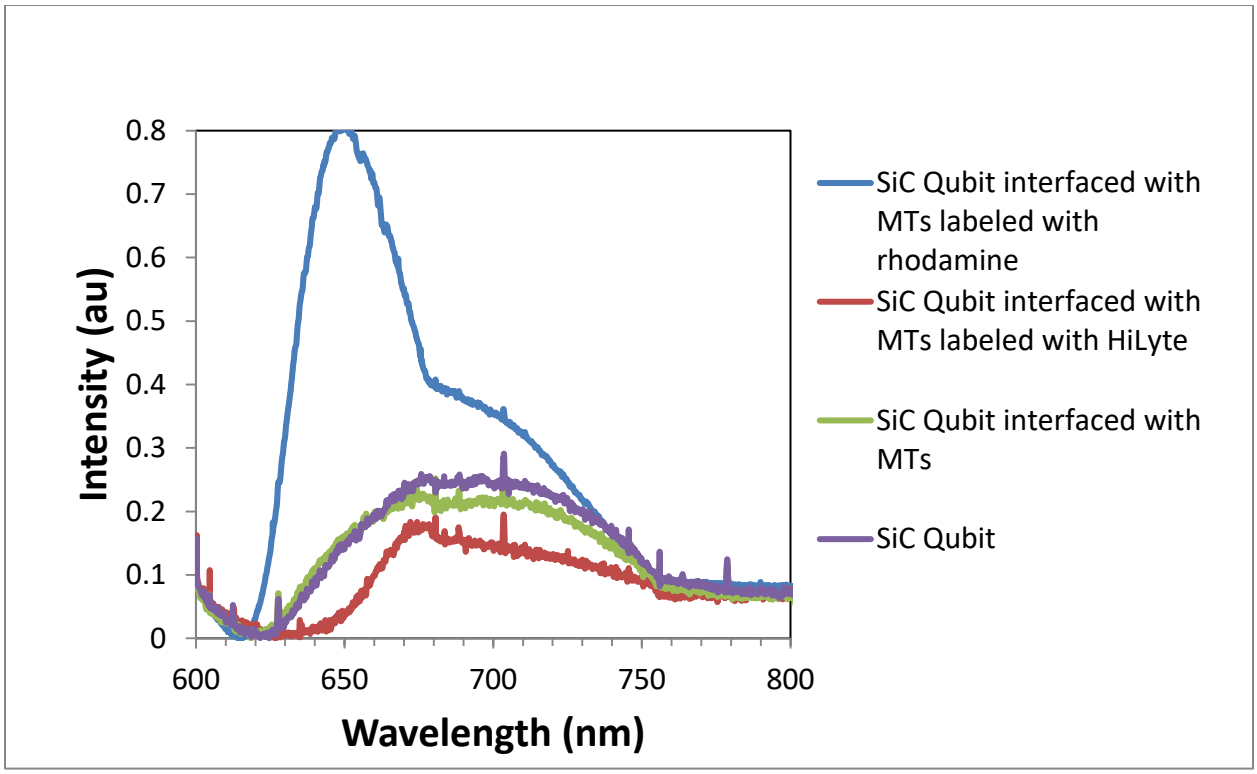


Figure 9. Spectra collected with excitation at 532 nm and 40 mW power. Shown are the spectra for a) SiC qubit ensemble interfaced to MTs. (b) SiC qubit ensemble interfaced to native MTs i.e. without any additional fluorescence labeling (c) SiC qubit ensemble interface with MTs functionalized with Rhodamine and (d) SiC qubit ensemble interfaced to MTs functionalized with HiLyte Flor.

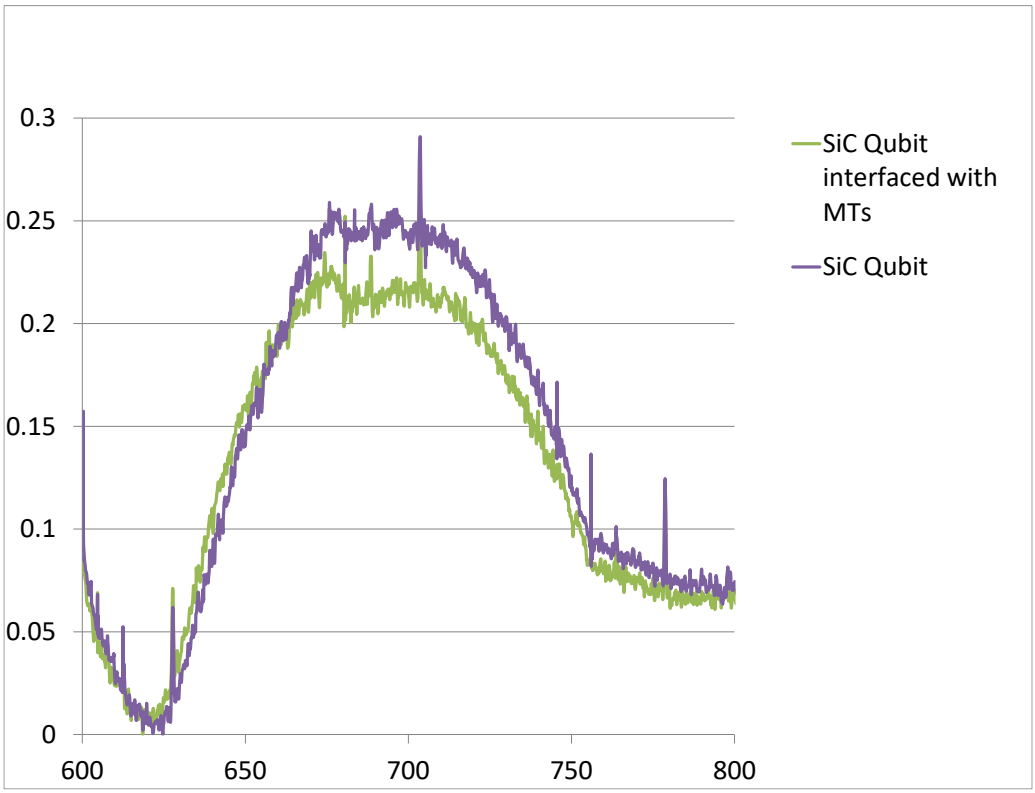


Figure 10. Difference in the spectra collected with and without microtubules that demonstrates the impact due to the interfacing of the qubits with the MTs.

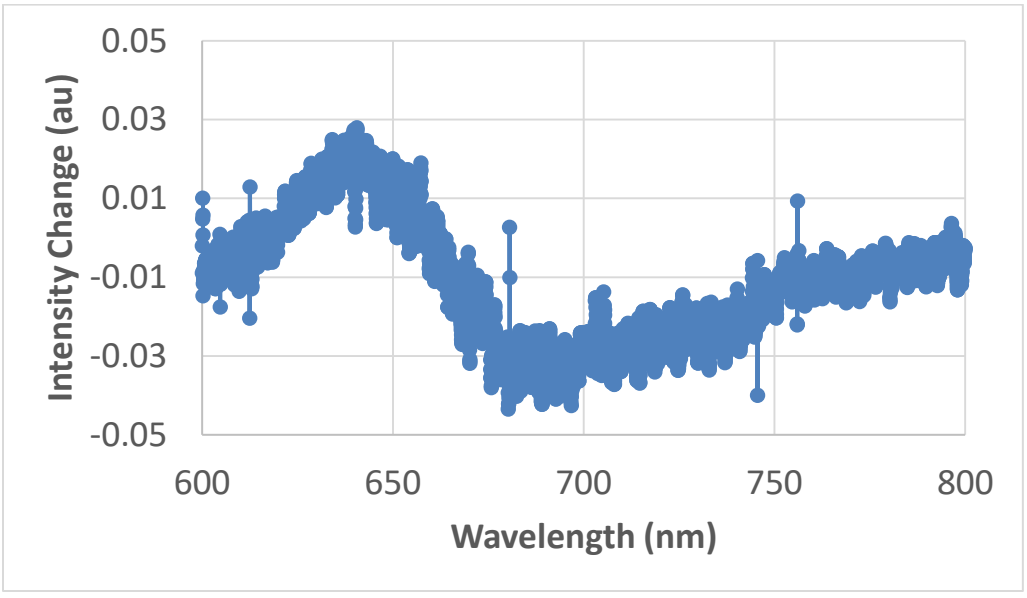
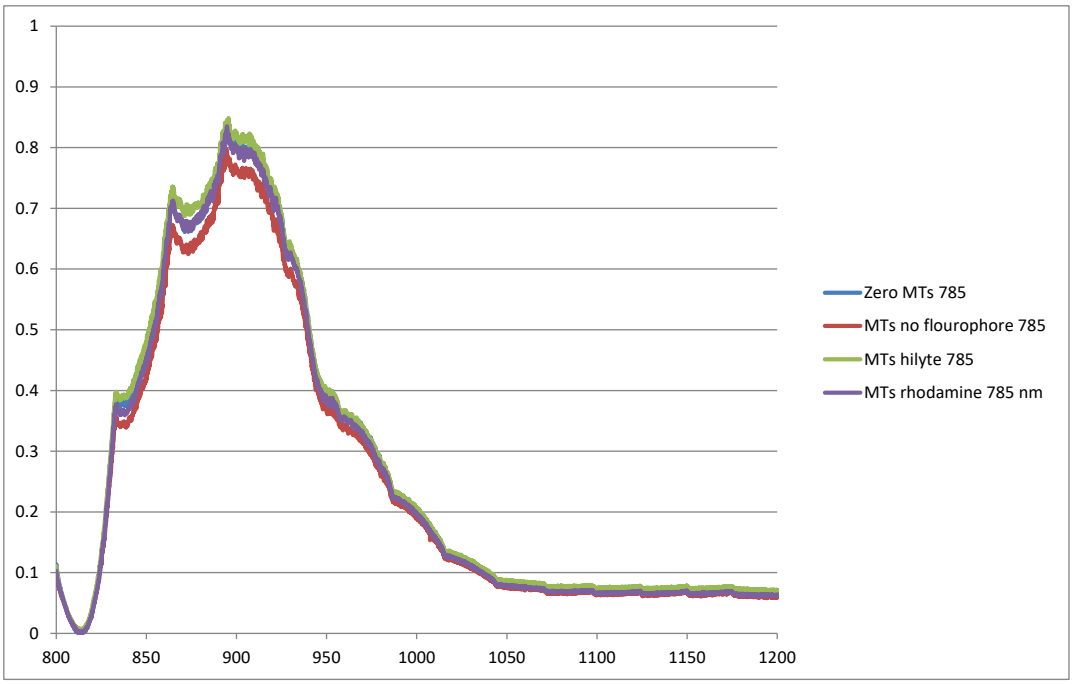


Figure 11. Difference in the spectra collected with and without microtubules that demonstrates the impact due to the interfacing of the qubits with the MTs.



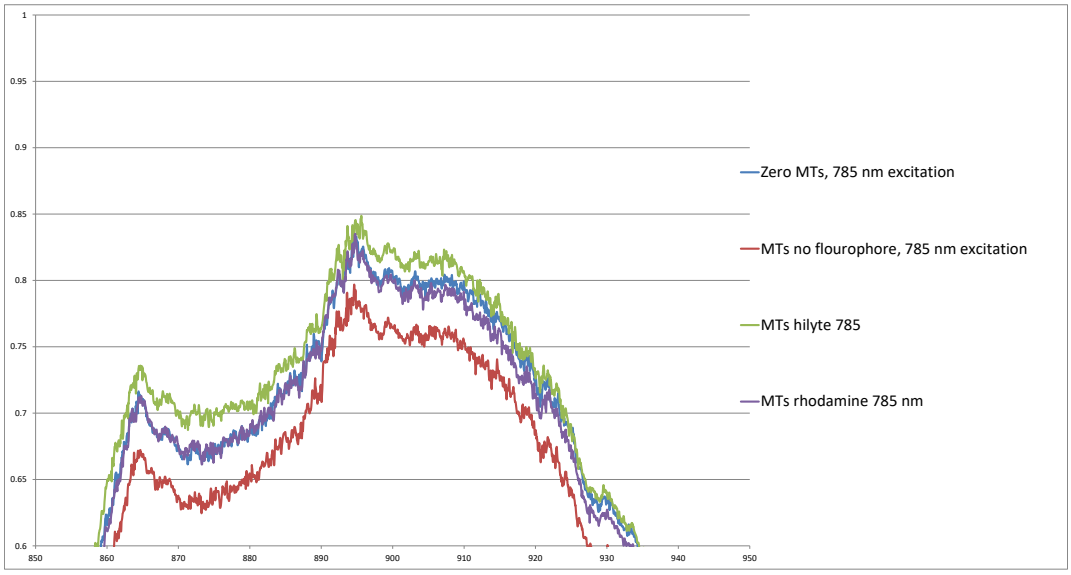


Figure 12. Spectra collected with excitation at 785 nm and 250 mW power. Shown are the spectra for a) SiC qubit ensemble interfaced to MTs. (b) SiC qubit ensemble interfaced to native MTs i.e. without any additional fluorescence labeling (c) SiC qubit ensemble interface with MTs functionalized with Rhodamine and (d) SiC qubit ensemble.

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7. DISCUSSION AND ANALYSIS

In analyzing the microtubule-qubit interaction and interface it is helpful to look at the molecular reconstruction including at the atomic level of MTs and qubits. Figure 12 shows the ball and stick and cartoon visualizations of MTs. The visualizations were formed from configuration files available on the protein data bank. In analyzing the interactions of MTs with qubits, it is important to consider the surface of the MTs and the presence of c-termini. These c-termini can be clearly identified on the MTs structure as shown in Figure 13. Numerous biological and neurological studies in the literature have highlighted the key role of c-termini in the electronic and opto-electronic properties of MTs. In this analysis we therefore focus on the interaction of the atoms of the c-termini with the atomic states that form the qubits operation i.e. the potential to form a charge transfer complex involving the c-termini with the charged vacancy atomic center in the silicon qubit. The possible mechanisms for this interaction are described as a nanoscale interaction where short-range coupling can occur and be a dominant mechanism as well as an energy band diagram in Figure 15 that considers the current understanding of the atomic energy levels of both MTs and vacancy qubits. It should be noted that long range interactions could also occur between atomic states in the MTs and the qubits, though in analyzing these experimental results where there is predominately surface interaction between the MTs and qubits due to the type of design structure i.e. MTs interfaced with qubits formed at the surface of a bulk substrates. In considering the surface interaction of MTs with qubits several mechanisms can be considered for this coupling including excitation and subsequent electron transfer tunneling, effects as well as resonant energy transfer. The processes can be modulated via the collective or individual optical excitation of the MTs and qubits depending on the energy of the light utilized and our experimental results demonstrate a key step in this effort. The vision is where this coupling can be optimized to modulate the quantum optical activity of these complexes to alter the quantum computing behavior via the spin-photon properties used in addressing qubit control including rotations and entanglement.

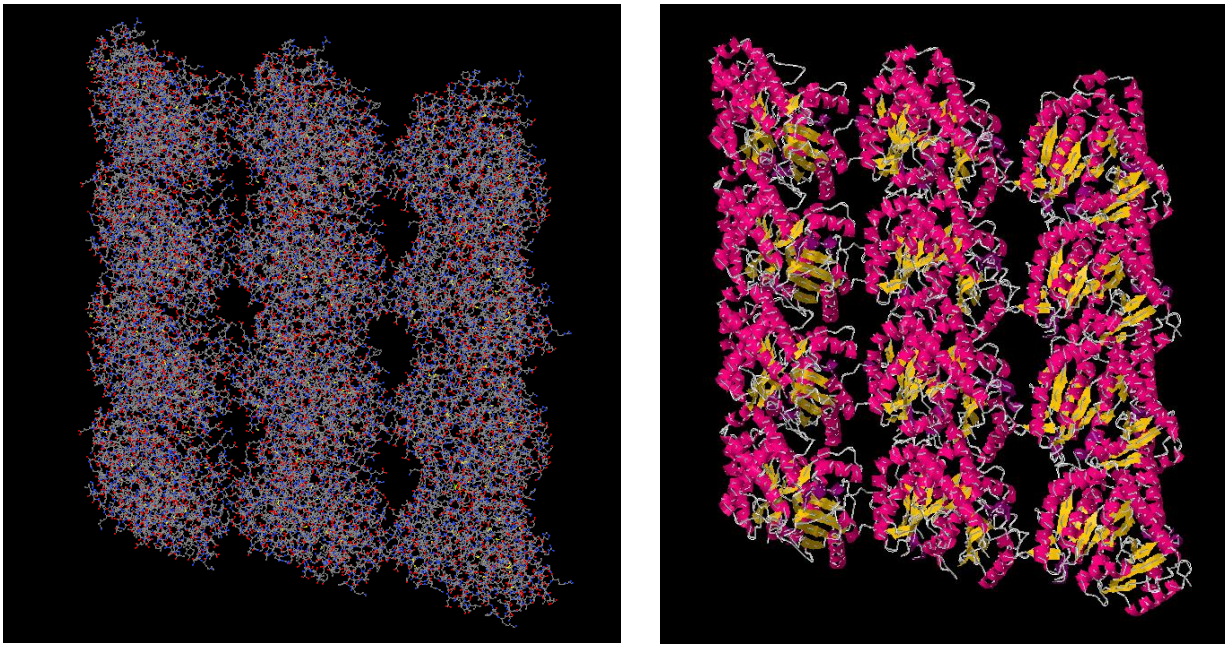

Figure 13. Molecular reconstruction of tubulin protein dimer in a cluster array of microtubules.

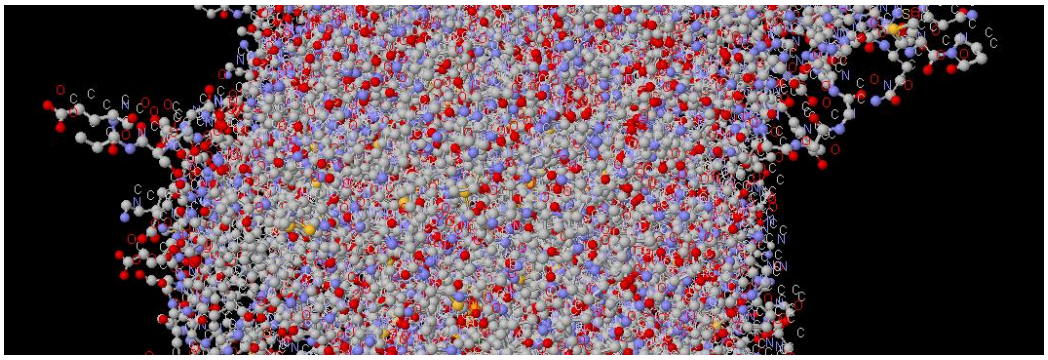

Figure 14. Molecular reconstruction of tubulin protein dimer showing the c-termini.

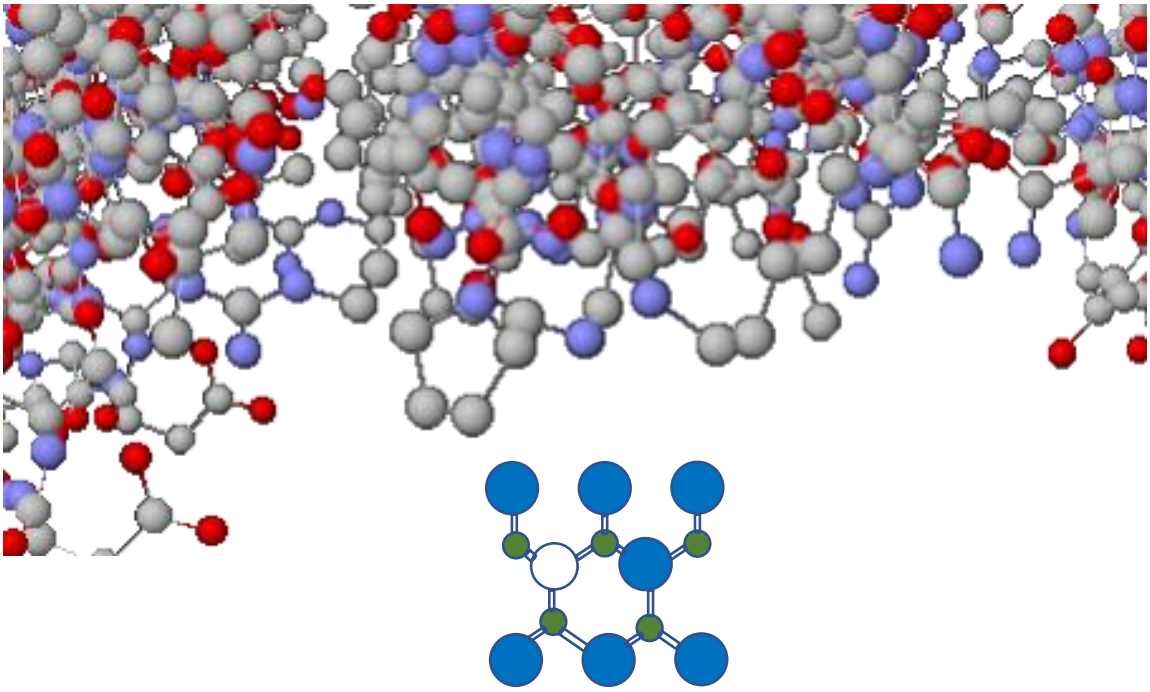

Figure 15. Molecular reconstruction of tubulin protein dimer showing the MTs c-termini interaction with the qubit.

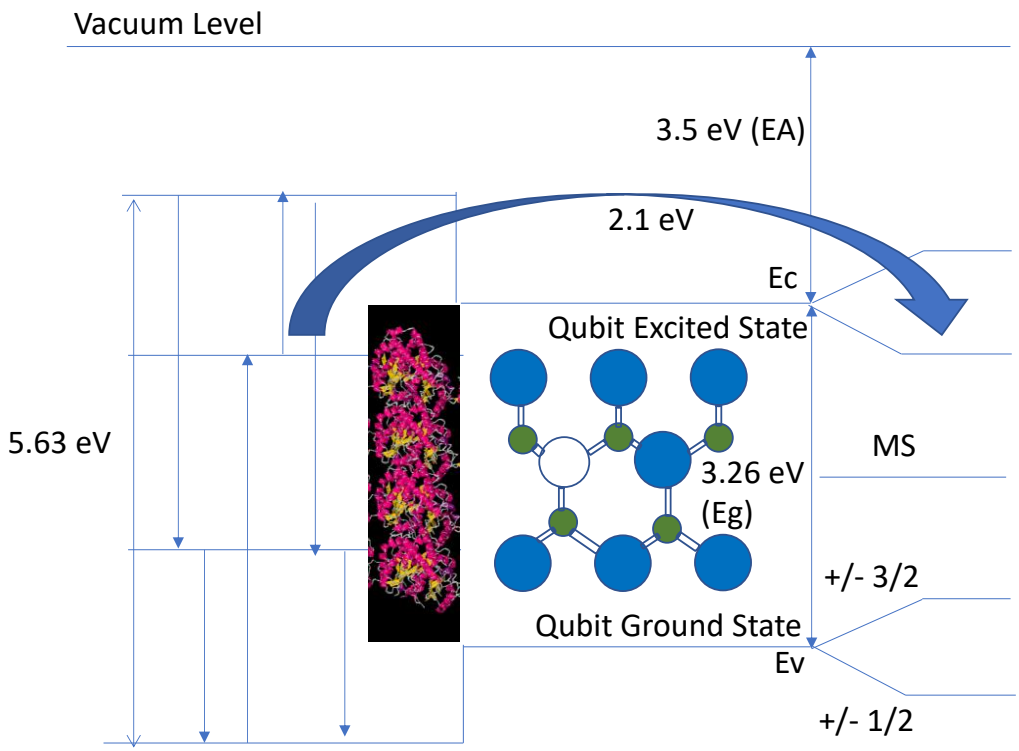

Figure 16. Proposed energy band diagram of the microtubule-qubit interface.

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8. SUMMARY

The ability to prepare synthetic microtubules at NIWC was established. The four target microtubule structures were successfully synthesized, and their polymerization kinetics characterized through optical absorption studies. Fluorescently modified microtubules were deposited onto prepared substrates and confirmation of their presence and structure obtained by collection of fluorescence microscopy images. A qubit-cellular interface substrate was prepared containing four types of microtubules then loaded under high vacuum into the cryo-magneto-optical station and advances spectroscopy performed of the resulting system.

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

This technical report presents the results of recently executed research at NIWC Pacific on the topic of "Quantum Monitoring and Control of Biological Cells". The primary objectives were to develop quantum biology chips with biological elements, i.e. brain microtubules interfaced in nanoscale proximity to semiconductor spin qubits (an option for quantum computing/networking applications). The motivation was to advance fundamental knowledge on biological elements to advance the field of brain-inspired electronics/neuromorphics and brain-electronic interfaces as well as to explore nano-scale interactions, which may be relevant to viral processes and thus current global health challenges such as COVID-19 and their pharmaceutical and other solutions. The research will ultimately enable the design of new information systems with features of what is referred to as "consciousness" by taking the step of providing an unprecedented ability to monitor and control changes in these biological elements at the nanoscale.

15. SUBJECT TERMS

Biological; Quantum; Neuromorphics; Qubits; Microtubules; Control

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