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14. ABSTRACT
Forward deployed military units have a critical need for a robust, low cost, easy to use diagnostic system providing real-time, quantitative, and multiplex capability of identifying biomarkers for infectious disease, including tuberculosis. This is a project to develop a new diagnostic device for detection of a tuberculosis biomarker based on a novel "plasmonic halo" effect. Various halo nanodevices using a set of chosen metals and dielectrics were simulated and fabricated, and their plasmonic-optical response / sensitivity characterized. A major new finding is that a modified structure has been investigated and shows promise for response in the near infrared, and the architecture may be amenable to rapid detection of viruses.

15. SUBJECT TERMS
Plasmonics, Biomarker, Quantum Dot, Biosensor, Finite Element Modeling, Bioassay, Index of Refraction

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1. INTRODUCTION

There is an acute, unmet need for low cost, rapid detection of tuberculosis, as well as biomarkers of other diseases and pathogens, in a broad range of health care applications, including routine point of care (PoC) clinical evaluation, real time diagnosis and detection of infectious disease in military personnel. A critical aspect of recognizing and controlling tuberculosis in military personnel, and in future epidemics, relies on the development of such diagnostics that can be quickly deployed at multiple sites. The current project aims to develop a diagnostic device for active tuberculosis via detection of TB-specific biomarkers. In the short term, the technology will provide a rapid assay for PoC detection of tuberculosis in urine, with future goals of detecting biomarkers in blood and breath. In the long term, the developed assay will be applied to a range of infectious and noninfectious human diseases, potentially including cancer and, more recently, infectious diseases associated with viruses, in particular coronaviruses.

2. KEYWORDS

Plasmonics; Biomarker; Biosensor; Sensitivity; Functionalize; Spectroscopy; Nanofabrication; Metal Nanoparticle; Plasmon-enhanced; Materials optimization; Photolithography; Electron microscopy; Finite Element Modeling; Bioassay; Index of Refraction

3. ACCOMPLISHMENTS

Major goals of the project:

The main goal of the project is to develop a device that can quantitatively and with high sensitivity detect the presence of TB-specific biomarkers in solution (*i.e.,* urine or blood) in a compact, plasmonic halo device. The specific concept is that the optical (UV-Vis) responses of these specific biomarkers will be characterized in advance, and then plasmonic halo drumhead devices will be custom designed and fabricated based on those response characteristics. Upon narrow-band illumination at or near an absorption peak of the target molecule or tethered light absorber/emitter, with that molecule resident in the near electromagnetic field of the drumhead surface, a readily detectable change in the transmission intensity arises. This change, corresponding to the presence of the target biomarker, is detected via a change in photocurrent in a proximate photodiode. The general concept is that this scheme can be applied to a wide range of disease biomarkers, in addition to tuberculosis. High specificity for such a device is provided by matching the drumhead halo structure's resonant mode(s) with the target biomarker's absorption peak(s), while high sensitivity is aided by the extreme sensitivity of photodiode detectors. As individual drumhead devices are only a few micrometers in size, the scheme is readily amenable to multiplexing, such that combinatorial analysis (multiple absorption peaks toward fingerprinting an individual target simultaneous to multiple molecular targets) is straightforward. In early 2020, we began to consider the appropriateness of the plasmonic halo for the detection of viruses in blood, urine or breath, with particular attention to the pandemic-causing corona virus(es).

Specific Aims:

Aim 1: Select molecular targets

– Milestone 1a: Identify candidate biomarkers from a pool of emerging TB antigens, including LAM, ESAT6 and CFP10. LAM antigen has been chosen. (month 3; 100% complete, *as previously reported*)

– Milestone 1b: Identify at least two anti-LAM antibodies from a pool of commercially-available monoclonal- and polyclonal- specific LAM antibodies. We have identified NR-13811 and NR-13812 monoclonal anti-mycobacterium tuberculosis LAM, Clone CS-35 (produced *in vitro*). (month 5; 100% complete, *as previously reported*)

– Milestone 1c. Confirm sensitivity and specificity of anti-LAM antibodies on metal-attached surfaces via conventional SPR. (month 18, 50% complete)

Aim 2: Simulate/model response of plasmonic halos

– Milestone 2a. Complete 2nd generation halo computer models. (month 12, 100% complete, *as previously reported*)

– Milestone 2b. Complete prototype portable light source & light detector that could be used for halo measurements. (month 24, 50% complete)

Major Activities and Significant Results

In this reporting period, the project team modeled, made and measured a series of plasmonic halo devices in terms of their optical response in the presence of proxy biological targets. We worked on optimizing the halo structures by characterizing their performance when biofunctionalized with known analytes and antigens, with the anticipation of transferring to a molecular target once the detection scheme has been finalized. Over the last 3 months, we began to consider the appropriateness of the plasmonic halo for the detection of viruses in blood, urine or breath, ***with particular attention to the pandemic-causing corona viruses, including SARS-CoV-2.***

We used the Finite Element Methods COMSOL and CST to model and simulate the response of halo structures to incident light without and with a biological target immobilized on the surface of the halo structure metal. To this end, we used the 'standard' drumhead halo, a modified drumhead, and a 'bulls-eye' structure. In our most recent effort, we have extended simulations to the near and mid infrared regimes, with the intention of identifying structure-material-based resonant peaks that may coincide with absorption resonances intrinsic to target macromolecules.

An example of a bulls-eye plasmonic halo structure shown in the prior year report is reproduced below in Figure 1, in four different views: an electron microscope image (SEM), a COMSOL simulation of the electric field due to plasmonic interactions along with metal surfaces, and atomic force microscope (AFM) image of the structure, and an optical microscopic image.

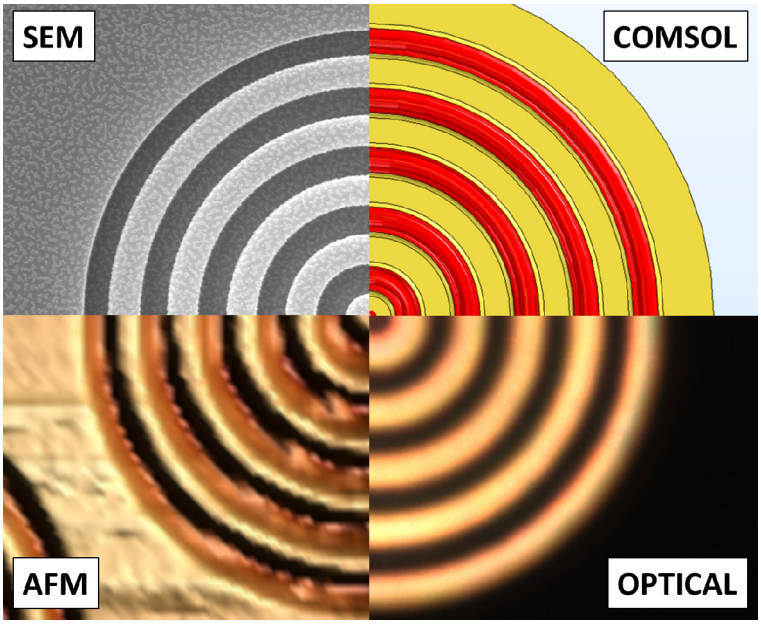


Figure 1. 'Bulls-eye' plasmonic halo structure displayed four ways. The overall diameter is approximately 10 μm.

Figures 2 and 3 below show views of COMSOL results that both depict the 3-D structure of the bulls-eye architecture and the presence of surface plasmons along the metal surfaces (plotted as power loss density), when illuminated from below with light. Figure 4 shows simulations of transmittance from the visible to the near infrared of this bulls-eye structure, with different thicknesses of metal on the halo well sidewalls, indicating that thinner wall thickness enhances light transmittance and concomitant resonant features.

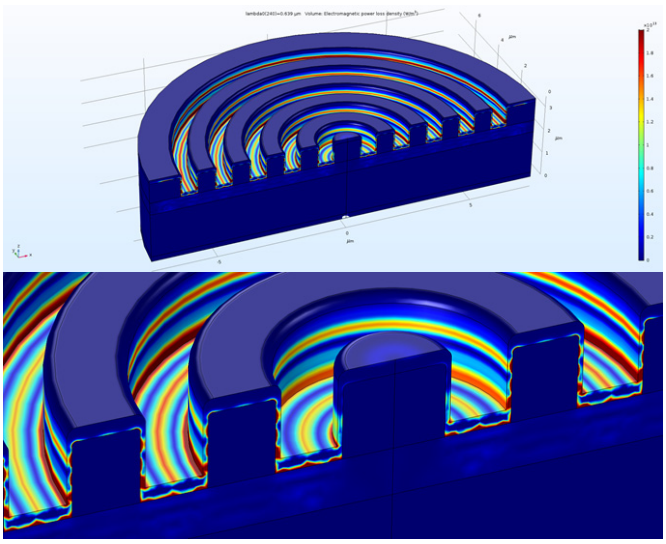


Figure 2. Computer simulation (COMSOL) of power loss density (transmitted electric field) in a 'bulls-eye' plasmonic halo structure. Both the width of each bulls-eye ring and the separation gap between neighboring rings is set to 650 nm. Surface plasmon resonances can be seen as standing waves along the metal (Au) surfaces.

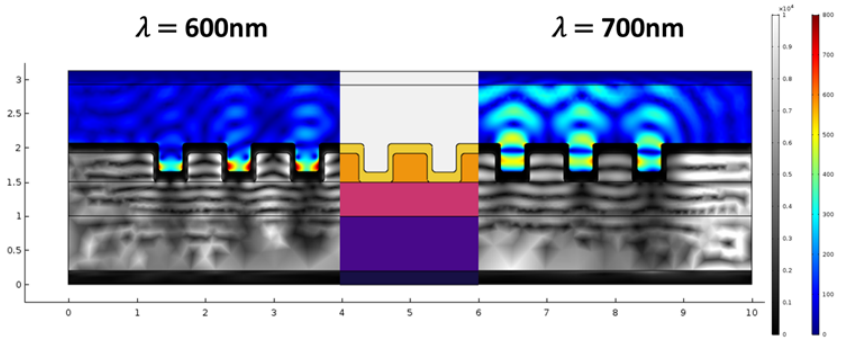


Figure 3. COMSOL images that provide additional insight into the workings of the bulls-eye halo. Cross-sectional plot showing normalized *E*-field for 600 nm (left) and 700 nm (right) incident light, and material domain (middle).

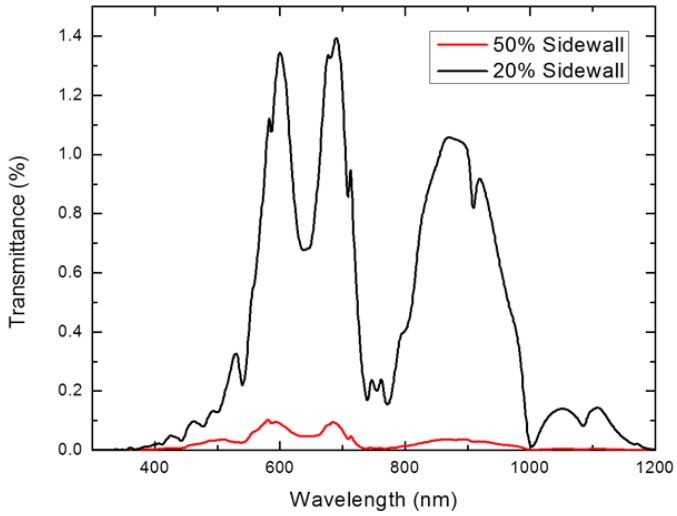


Figure 4. COMSOL results of transmittance through the structure in Figure 3, for two difference sidewall-to-base thickness ratios, showing the aforementioned role of that wall thickness in facilitating light leakage and subsequent plasmonic resonance activity.

After using modeling to predict and optimize the halo device structure and performance, we fabricated and tested devices under dry and biologically-relevant conditions. Figure 5 shows representative data for a series of devices, where the bulls-eye gap size was systematically varied, and the resulting optical transmittance recorded. The purpose of this study was to identify the dominant/characteristic absorbance and transmittance features resulting from plasmonic interactions, toward identification of size structures that optimize sensitivity.

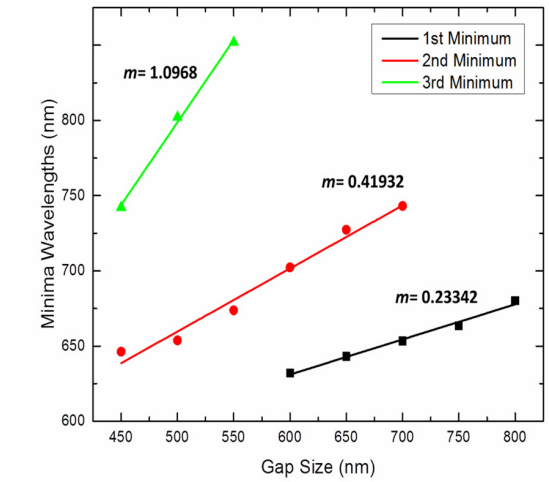


Figure 5. Varying feature size of bulls-eye plasmonic halo structure, showing wavelengths of sequential minima in transmittances showing systematic characteristics. Index *m* refers to nominal mode number.

For further characterization of sensitivity with respect to changes in index of refraction of the medium along the plasmonically-active surfaces (i.e. the base and side-walls as shown in several figures above), a particular transmittance feature (a local maximum) was monitored as the liquid medium was systematically varied. This variation led to a systematic variation of the refraction index. As such, a sensitivity in units of peak wavelength change per refractive index unit (RIU) could be calculated. Figure 6 below shows representative data.

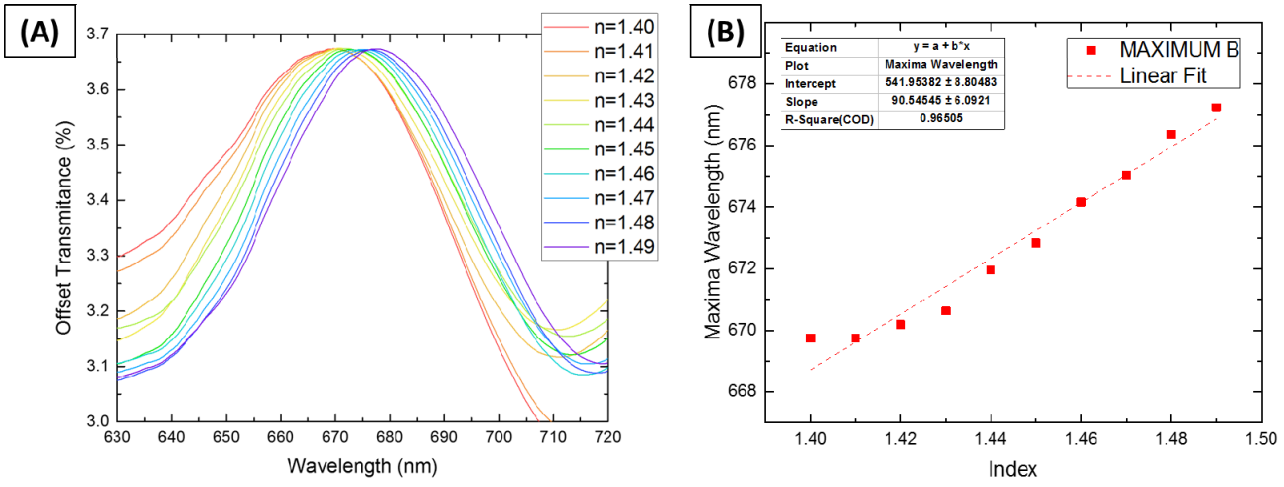


Figure 6. Y-axis shifted transmittance maxima of 650 nm gap bulls-eye sample for different refractive index immersions. (B) Plot of maximum wavelength vs. RIU. The slope is a common value of sensitivity used in literature, here ~100 nm/RIU.

Confirming that there is a shift in transmittance with a change of refractive index of the medium in the vicinity of the halo, we proceeded with a biofunctionalization scheme to test this as a sensor. A schematic of the functionalization scheme is shown below. In step (a), the sample is immersed in a physiological solution of similar composition to the solution used in subsequent steps, e.g. PBS. In step (b), thiol-conjugated streptavidin (SA-thiol) is added to the sample. The thiol conjugate forms a strong bond to the Au surface and while the binding mechanism remains fully agreed upon, the binding strength has been quantified. In step (c), biotin-conjugated immunoglobin G (biotin-IgG) is added to the sample, facilitating the immobilization of IgG antibodies through the streptavidin-biotin binding. The biotin is conjugated to the Fc region of IgG thereby facilitating the steric availability of the fabrication region, which is specific to the targeted antigen. In step (d), the targeted antigen is added and is captured by the IgG. In step (e), the final configuration is measured for both wet and dry cases.

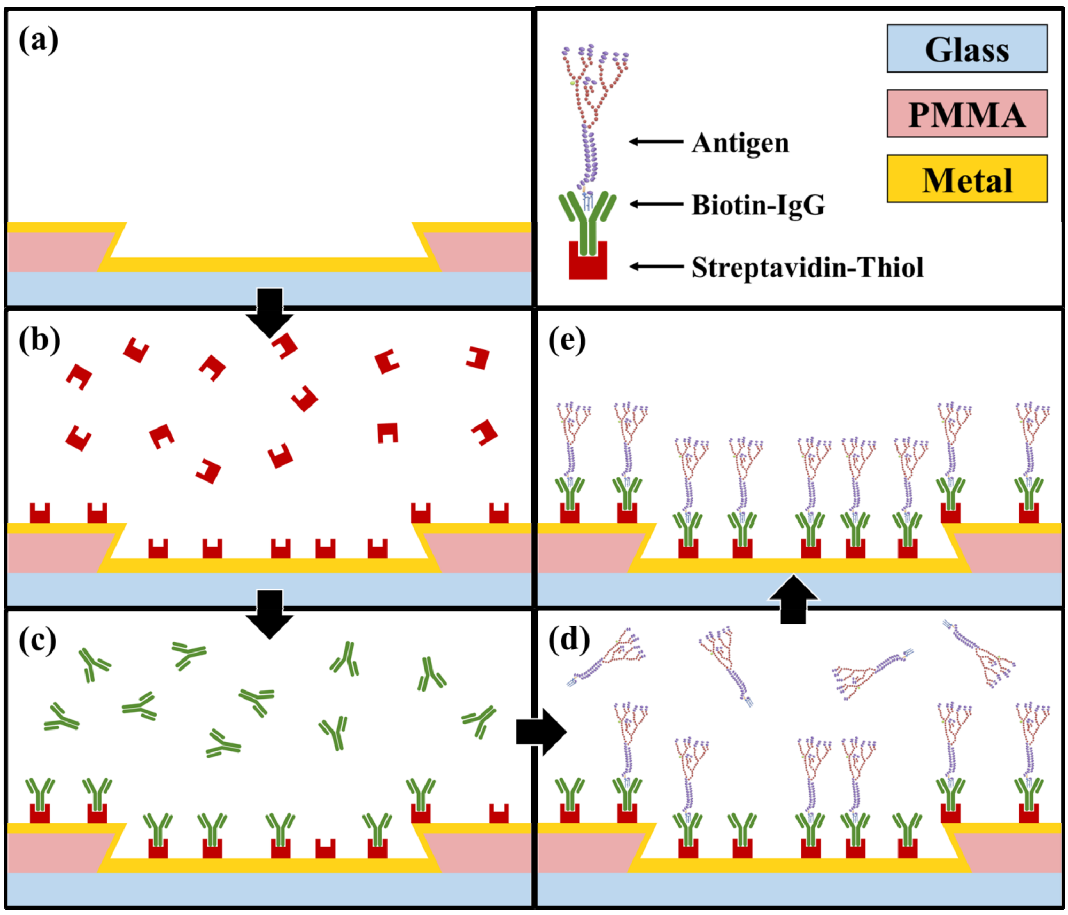


Figure 7. Antigen capture schematic. (a) Start by measuring the sample baseline with physiological liquid, (b) add SA-thiol, (c) add biotinylated-IgG specific to targeted antigen, (d) add antigen, and (e) record final configuration both wet and dry.

Experiments were conducted to show the immobilization of biotinylated-IgG for a sample with SA-thiol compared with a control sample with SA-thiol. Figure 8 shows transmittance spectra for incident white light through arrays of a bullseye with corresponding gap size 400 nm, 500 nm, 600 nm, and 700 nm. These samples have Au metallic layers and were measured with an Ocean Optics USB2000 spectrometer.

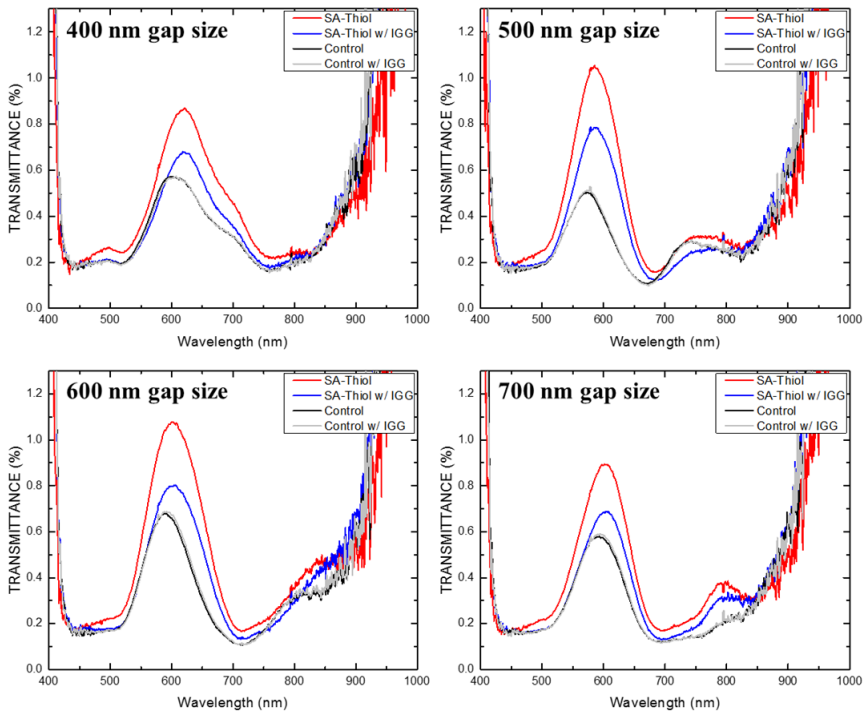


Figure 8. Transmittance before and after IgG. Plotted are the transmittances of four bullseye arrays of different gap sizes for 2 separate chips (8 regions in total). For each sizing, spectra were measured before and after the addition of biotin-IgG to a sample with previously added SA-thiol and a control sample without previously added SA-thiol.

Note that there were observable differences in the transmittance for the sample with SA-thiol compared to relatively no change for the control sample. The change in the SA-thiol-laden sample predominately preserved the wavelengths of the spectral features and therefore is not consistent with the redshift anticipated for a surface plasmon mediated changed. Additionally, since the samples were made with Au, there is a falsely inflated peak in transmittance between 500 nm and 700 nm, indicating a possible source of surface plasmon dissipation. There is a consistent observable difference in the samples with and without SA-thiol before the addition of IgG, as is expected due to the immobilization of the SA-thiol.

Similar tests were performed for different samples and equipment, primarily to investigate the potential impact of a more sensitive spectrometer. An experiment was run adding PBS to a sample, then adding SA-thiol, and finally adding biotin-IgG. Figure 9 shows the transmittance (a) before and after adding SA-thiol and (b) before and after adding the biotin-IgG. While there is a discernable shift from the binding of SA-thiol, the shift from the IgG is in the opposite direction than SPR interaction would indicate, likely due to the dissociation of unbound SA-thiol on the sample surface.

We also tested detection of a fluorescent protein perCP (peridinin-chlorophyll-protein, a 35.5 kDa fluorescent complex. As shown in Figure 10, there was, unfortunately, insufficient difference between SA-thiolated halos and SA-thiol+perCP halos.

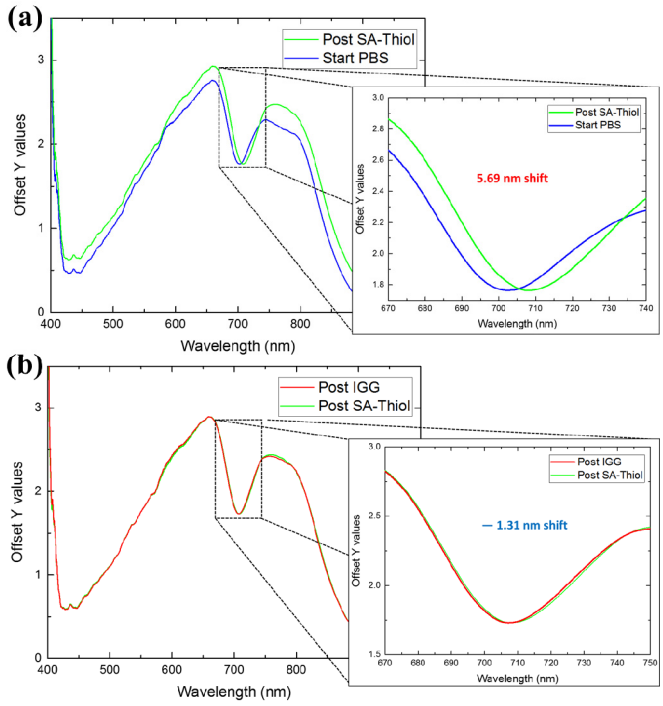


Figure 9. Transmittance pre- and post IgG. (a) before and after addition of SA-thiol and (b) before and after the addition of biotin-IgG.

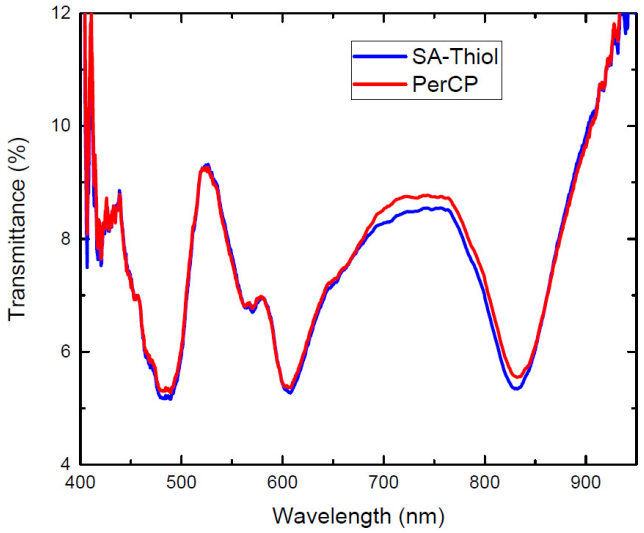


Figure 10. Transmittance pre- and post-perCP.

Since facile detection of biotin-IgG binding was not evident, we conclude that this combination of structure, biological assay and detection method were not capable of sufficiently sensitive biofunctionalized biosensing. We describe below some attempted signal enhancement schemes in efforts to realize biosensing capability.

Preliminary Conclusions

While we are confident that have our modeling, device fabrication, conjugation chemistry, and measurement capabilities under control, we remain unsatisfied with the performance of our devices. In last year's report, we identified two issues which we strove improve upon. One was in regard to absolute optical transmittance. On the one hand, we desire strong transmission of "leaked" light - that is, the light that passes into the far field, through the vertical walls of the halo structure, after being modified by the excitation of surface plasmons. On the other, we desire strong interaction of incident light with the plasmonically-active metal surfaces within the drumhead / bulls-eye structures, which naturally reduces the intensity of the leaked light. This is one reason we conceived of and introduced the bulls-eye architecture: to simultaneously increase both surface interaction and transmitted light. As such, we focused part of our effort on this modified architecture for the past year. The second issue had to do with the change in transmitted light resulting from surface plasmonic absorbance due to the presence of target biomolecules. This, in part, boils down to how large a change in refractive index is generated by the presence of captured target molecules.

To remind, the core idea is that (resonant) standing waves of plasmons are wavelength-shifted when target molecules are captured onto the halo structure surface in such a way as to be resident in the significantly enhanced electric field provided by the localized plasmon. Thus, even though the dielectric constant of the captured entity may differ only slightly from its ambient medium, the difference is amplified. This indeed occurs, and is measurable, but we anticipate that we can do significantly better than current performance results. To this end, we introduced a modified "sandwich" capture method, using the same device structure and same detection method (*i.e.*, using a primary "capturing" target antibody), but now with the addition of a quantum dot (QD) that is tethered to a secondary "detecting" antibody. With this configuration, we hoped to be able to excite the structure (i.e. the plasmon) with monochromatic light (from e.g. a laser or LED), with its wavelength chosen to match the QD absorption spectrum. With the tethered QD well within the near electromagnetic field of the plasmon, which will only occur when a target antigen is captured, its emission intensity should be amplified, and readily detected. A schematic of this scheme is shown below.

We indeed pursued this approach in parallel with our standard approach over the past year. Unfortunately, the results were not as promising as expected, as the transmitted light with and without QD attachment was about the same.

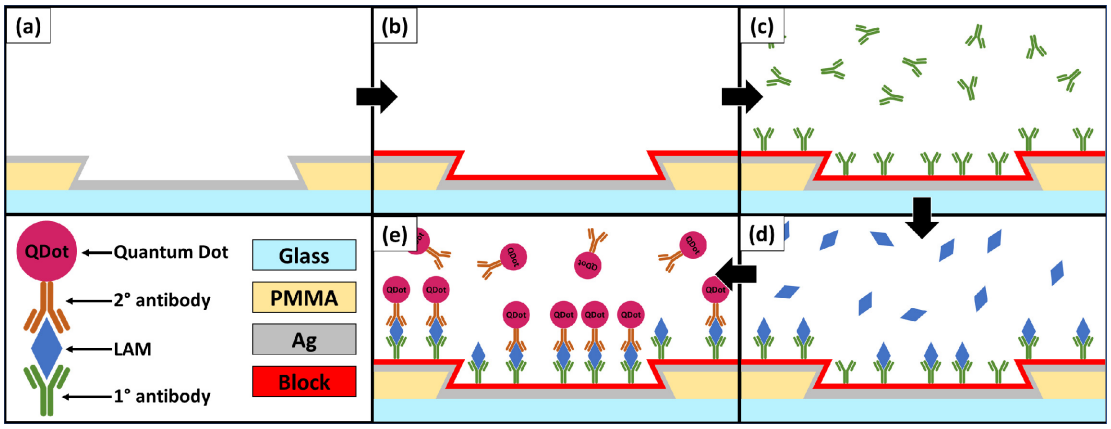


Figure 11. (a) Halo cross-section schematic. (b) Application of blocking layer for chemical protection of the Ag surface from physiological liquids. (c) Functionalize surface with conjugated primary antibody to target antigen. (d) Flow antigen-containing fluid. (e) Flow secondary antibody conjugate with a QD that will interact with plasmon for achieving sensitivities not possible with antigen alone.

In a preliminary scheme to introducing QDs, we tested the ability to bind biofunctionalized Au nanoparticles (NPs) to the bulls-eye structures. As reported last year and reproduced below, we illuminated with broadband light and recorded the transmittance spectrum. A particular absorbance peak (transmittance dip) was identified to gauge the effect of the NPs in the plasmon field. Figure 12 below shows an SEM image of a structure with a dispersion of Au NPs, a schematic representation of such, a TEM image showing the NPs, and representative transmittance data showing a shift due to the inclusion of the NPs.

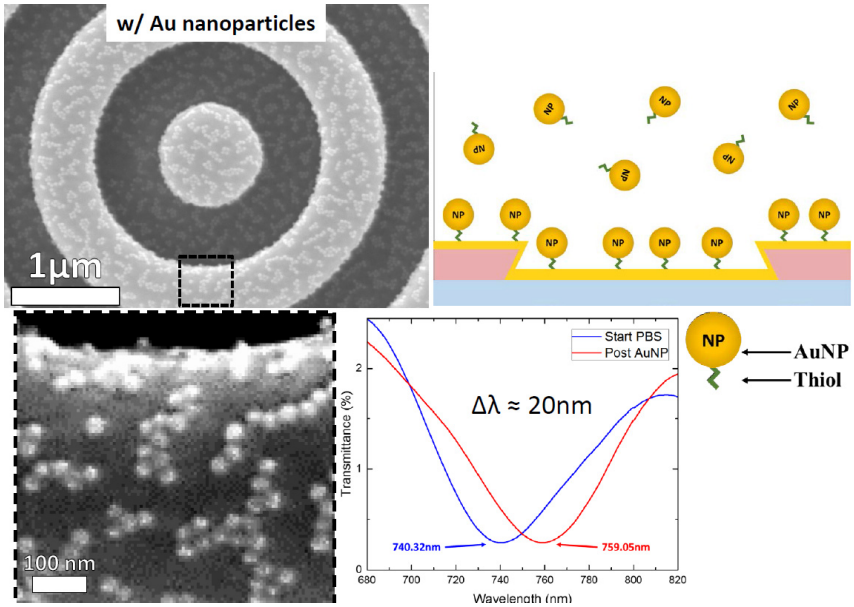


Figure 12. SEM of bulls-eye structure laden with thiolated-Au NPs, with TEM showing bound NPs (bright dots, some in small clusters). Top right shows a schematic, and bottom right shows transmittance data before and after NP attachment near a 750 nm minimum, with ~20 nm shift observed due to addition of AuNPs.

We then elaborated the AuNP capture protocol to included SA-thiol and biotinylated-IgG biofunctionalization steps to capture a AuNP conjugated 2° antibody. A 1° antibody was selected directly against the 2° antibody in order to test just the positive antigen case. There was a relatively small, though non-negligible, red-shift for transmittance features observed, as shown in Figure 13 below.

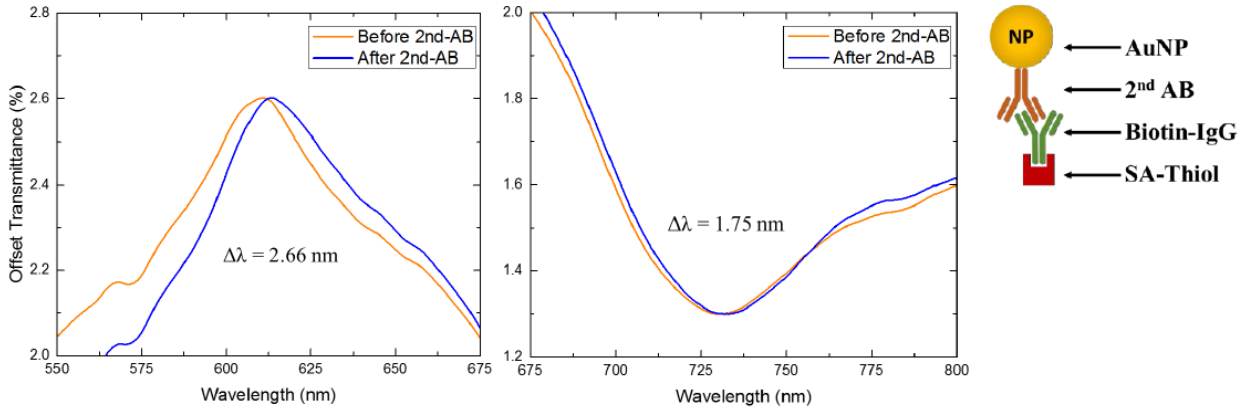


Figure 13. 2° antibody conjugated AuNP capture. Measured transmittances (offset) through a biofunctionalized bullseye array before and after the addition and capture of a secondary antibody for (a) a maximum and (b) a minimum with changes of 2.66 nm and 1.75 nm, respectively.

We followed these tests with incorporation of QDs: 20 nm diameter CdSe@ZnS core-shell dots (Thermo Fisher) that emit near 625 nm. Figure 14 shows the transmitted light for 405 nm excitation of regions centered on an array of bullseye structures (black) and for five different regions above planar metal film. All spectra show a quantum dot emission peak at 625 nm and also the tail peaks of the LED light source. Figure 15 shows again that the addition of QDs indeed changes the transmittance through the halo structure.

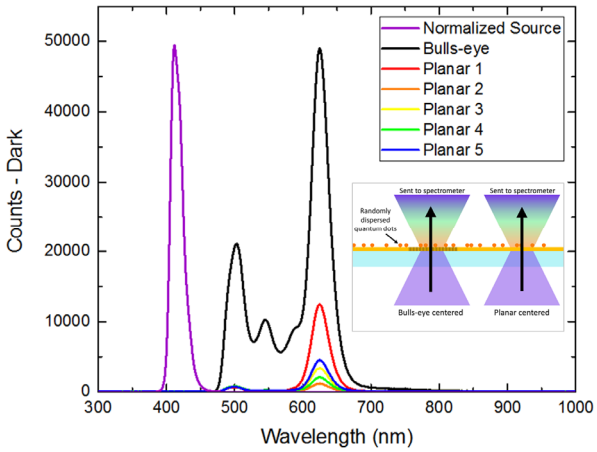


Figure 14. Quantum dots transmitted light. Shown are spectra for the normalized LED (violet), and quantum dots above a bullseye array (black) and planar regions (red, orange, yellow, green, blue).

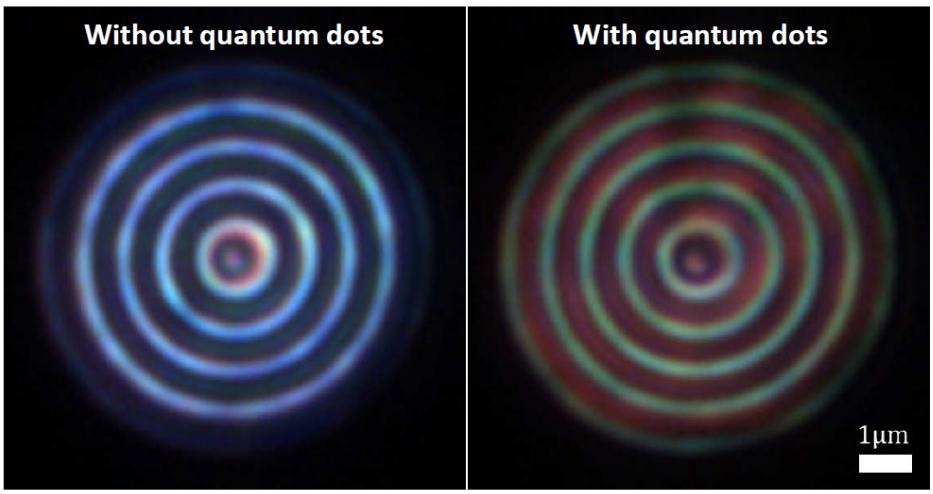


Figure 15. Bullseye with & without quantum dots. Images of transmitted light from bottom side incident white light though bullseye structure without (left) and with (right) addition of 625 nm emission peak quantum dots.

While the data above, with transmittance through the halo structure ~5 times larger than through the controls (Figure 14), initially suggested this may be a promising route to plasmonic halo biosensing, subsequent experiments with biofunctionalized QDs showed negligible difference in transmittance as compared to non-biofunctionalized QDs.

New near-infrared results.

Below, we show our recent simulations of plasmonic halos in the near IR. Figure 16 shows changes in transmittance of a halo when a simulated monolayer of viruses is immobilized on the active halo surface (green), versus no virus inclusion (red). As can be seen, the transmittance near 2350 nm wavelength increases by about 400% with virus inclusion. Moreover, there are potentially an even larger changes near 1600 nm and 1800 nm wavelengths, where the transmittances change from nearly undetectable to readily detectable levels. Similar changes are observed in the reflectance simulation, Figure 17: a nominal 300% relative increase at 1820 nm, and a 70% absolute decrease near 2350 nm. In addition to refining and expanding these simulations while we are locked out of the lab, we are investigating the robustness of the results and the potentially applicability to corona virus detection.

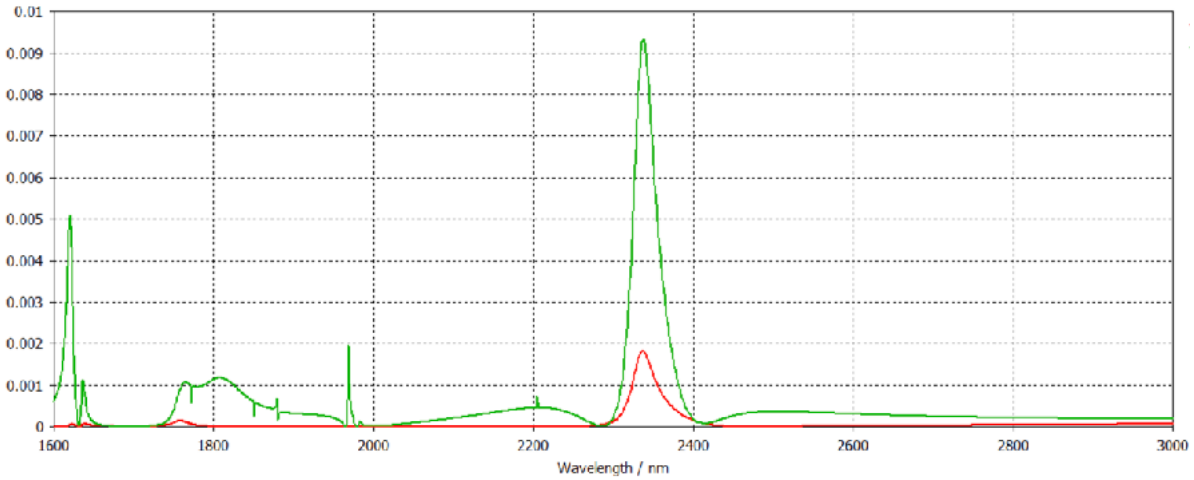


Figure 16. Transmittance simulation in a plasmonic halo microstructure in the near IR, with (green) and without (red) monolayer coverage of a virus.

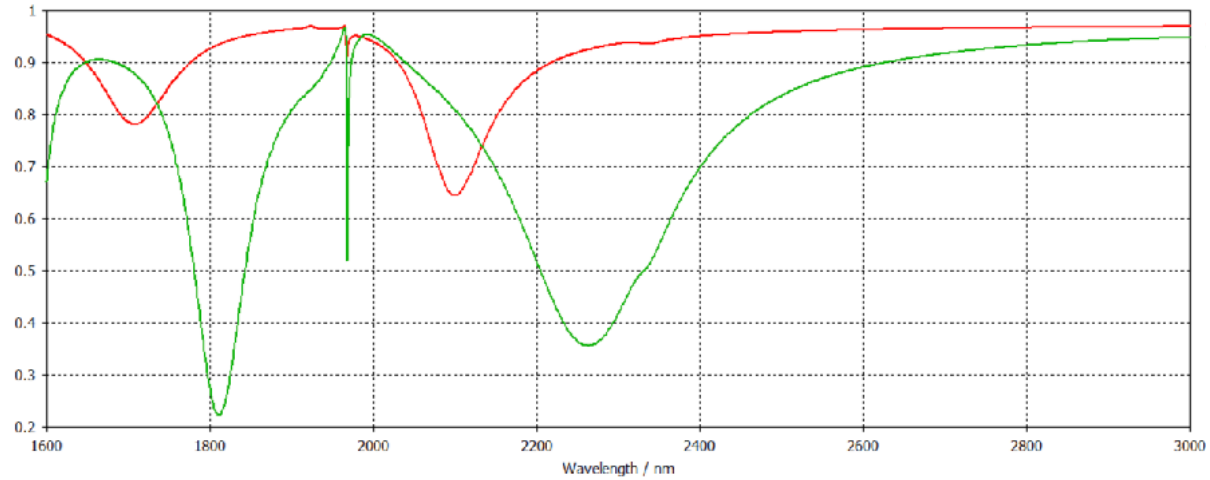


Figure 17. Reflectance simulation in a plasmonic halo microstructure in the near IR, with (green) and without (red) monolayer coverage of a virus.

Opportunities for training and professional development the project has provided

Three undergraduate students had the opportunity to develop extensive experience through involvement in this research, including training on scientific equipment, conducting experiments, preparing and presenting experimental results, and studying related materials in both physics and biology. The training and professional development for 3 graduate students involved was also extensive. These opportunities included the advising of undergraduate research activities, advancing software skills in data analysis and computer modeling, proposing and presenting design of experiments, directing and executing of experiments, designing and producing samples using an array of state-of-art cleanroom technologies, disseminating research at national scientific conferences, and preparing results to publish to the broader scientific community. One graduate student, Luke D'Imperio, completed his Ph.D. thesis, a portion of which was on the current topic. Luke is now a staff scientist at Sandia National Laboratories.

How results were disseminated to communities of interest

– Public Ph.D. Dissertation Defense: Luke D'Imperio, "Biosensing-Inspired Nanostructures", Boston College, August 2019.
– Contributed talk by Boston College graduate student Luke D'Imperio at the APS (American Physical Society) March meeting in Boston, March 5, 2019 "Plasmonic Halos Towards Molecular Sensing of Disease Biomarkers" in *Session H23: Physics in Medicine: Imaging, Therapy, and Disruptions on the Horizon*, coauthors Juan M. Merlo, Chaobin Yang, Yitzi M. Calm, Megi Maci, Michael J. Burns, Timothy Connolly, Thomas C. Chiles, Michael J. Naughton. *https://meetings.aps.org/Meeting/MAR19/Session/H23.5*

Plans during the next reporting period to accomplish project goals

For the next reporting period, which will in fact extend to the duration of the project, we intend to continue to pursue development of the plasmonic halo structure as a TB biomarker biosensor, ***with the addition of steering effort toward virus detection, in light of the Covid-2 current pandemic.***

4. IMPACT

Impact on the development of the principal discipline(s) of the project

The diagnostic nanodevice being developed, which relies on detection of specific human disease biomarkers, will address an unmet need for low cost, rapid detection of active tuberculosis ***and potentially, corona virus(es)***. If successful, the technology will provide a rapid assay for PoC detection of disease markers in blood and urine; however the technology may potentially be scaled to detect biomarkers in breath. In the long term, the developed assay can be applied to a wider range of infectious and noninfectious human diseases. If successful, the research can become a foundation for future effort aimed at emerging infectious diseases to protect our military, with eventual benefit to those in low-resource areas where access to clinical infrastructure and technology is limited, such that accurate, PoC detection is highly desired.

Impact on other disciplines

Integrating the nanofabrication techniques and materials with the biological schemes and assays necessary to achieve our targeted novel detection mechanisms and sensitivities can have a significant impact on the interdisciplinary fields of global public health, biomedicine and nanotechnology. Our research solutions to the problems of developing an impactful biosensing device can be an important to others in this growing field of interdisciplinary science.

Impact on technology transfer

Any provisional and/or utility patent applications to arise from this effort will include full attribution of the current funding.

Impact on society beyond science and technology

If successful, the research can become a foundation for future effort aimed at emerging infectious diseases to protect not only US military personnel and those in low-resource areas where access to major infrastructure and technology is limited, but to conventional clinical settings in hospitals and doctors' offices, thus providing large public health benefit.

5. CHANGES/PROBLEMS

Changes in approach and reasons for change

As discussed above, our computer simulations suggested that, in addition to the bulls-eye structures reported last year, we have investigated modified halo structures that show resonance features in optical reflectance and transmittance in the near infrared. These features suggest that these structures can be more sensitive as plasmonic biosensors than the original design, As such, we have decided to focus on this latter structure. This decision does not impact the overall approach of objectives of the project. What does change the approach somewhat is the new emphasis on promising results at near-IR wavelengths, instead of strictly in the visible.

As discussed in last year's report, we investigated, in parallel with the original biofunctionalization scheme, the incorporation of quantum dots conjugated to secondary antibodies that themselves conjugate with the target antigen, as a means to both amplify the plasmonic halo transmittance and localized the spectral width to that of the QD emitter. These changes were expected to significantly enhance the detection capabilities of the device, in terms of both sensitivity and selectivity. However, we have encountered difficulty in immobilizing the QD particles with sufficient specificity onto the plasmonic halo surfaces, and have decide to pause QD incorporation in favor of concentrating on the new near-IR capabilities, a***nd to direct effort to corona virus detection***.

Actual or anticipated problems or delays and actions or plans to resolve them

As discussed, the absolute intensity of light transmitted through the drumhead plasmonic halos has been less effective than anticipated. Our initial plan to resolve this unforeseen difficulty was to incorporate the bullseye structure, which facilitates both enhanced optical throughput and enhanced plasmonic interaction, but significantly increased the active surface that will be available to the target antigen to bind. We will continue with this direction. As for quantum dots, that effort did not show sufficiently significant promise to continue, and so will be paused in favor of pursuit of the new near-IR detection of halos (without QDs).

Changes that had a significant impact on expenditures

1. One graduate student who worked extensively on the project, Luke D'Imperio, has graduated, and gone on to work at Sandia National Laboratories.
2. A graduate student whom I had intended to take over primary effort on the project took a sudden and unanticipated leave of absence from Boston College. This left the project with no graduate student for a period of time.
3. A new graduate student, Mark Schiller, has begun work on the project in 2020. Via modeling and simulation, he has discovered already the near-IR possibility discussed above.
4. Perhaps most importantly, the global coronavirus pandemic has impacted the effort: Boston College closed down in early March, 2020, and we have been prohibited from entering our laboratories since. As such, all lab-based effort has paused for the past 3 months, and will likely remain paused for 1 to 3 more.

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. PRODUCTS

- **Publications, conference papers, and presentations**

– Contributed talk by Boston College graduate student Luke D'Imperio at the APS (American Physical Society) March meeting in Boston, March 5, 2019 "Plasmonic Halos Towards Molecular Sensing of Disease Biomarkers" in *Session H23: Physics in Medicine: Imaging, Therapy, and Disruptions on the Horizon*, coauthors Juan M. Merlo, Chaobin Yang, Yitzi M. Calm, Megi Maci, Michael J. Burns, Timothy Connolly, Thomas C. Chiles, Michael J. Naughton. *https://meetings.aps.org/Meeting/MAR19/Session/H23.5*

- **Other publications, conference papers and presentations**

Nothing to Report

- **Website(s) or other Internet site(s)**

Nothing to Report

- **Technologies or techniques**

Nothing to Report

- **Inventions, patent applications, and/or licenses**

Nothing to Report

- **Other Products**

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

Name:	**Michael J. Naughton, Ph.D.**
Project Role:	PI
ORCID ID:	0000-0002-6733-2398
Nearest person month worked:	1
Contribution to Project:	Prof. Naughton has supervised all aspects of the work.
Funding Support:	This award
Name:	**Thomas C. Chiles, Ph.D.**
Project Role:	Co-PI
Nearest person month worked:	1
Contribution to Project:	Prof. Chiles has co-supervised the biological aspects of the work.
Funding Support:	This award
Name:	**Timothy Connolly, Ph.D.**
Project Role:	Co-PI
Nearest person month worked:	1
Contribution to Project:	Dr. Connolly has contributed to the SPR experiments, bioassay development and co-supervised the bio/chemical aspects of the work.
Funding Support:	N/A
Name:	**Michael J. Burns, Ph.D.**
Project Role:	Consultant**
ORCID ID:	0000-0001-9804-405X
Nearest person month worked:	1
Contribution to Project:	Dr. Burns has contributed to the SPR experiments and co-supervised the modeling aspect. He is currently a consultant on the project.
Funding Support:	N/A **Dr. Burns' role for the remainder of the project will be Consultant. His role has changed from co-PI to Consultant, and he may advise on array fabrication and assist in the device development experimental plan. There will be no project impact and no budget impact.
Name:	**Luke D'Imperio**
Project Role:	Graduate Student
ORCID ID:	0000-0001-8281-2552
Nearest person month worked:	12
Contribution to Project:	Mr. D'Imperio was a physics graduate student on the project involved with most aspects of the research, including nanofabrication of plasmonic halo devices, FEM modeling, and SPR measurements. He completed his Ph.D. in summer, 2020, and is currently a Research Scientist at Sandia National Laboratory in Albuquerque, NM.
Funding Support:	This award
Name:	**Mark Schiller**
Project Role:	Graduate Student
ORCID ID:	N/A
Nearest person month worked:	4
Contribution to Project:	Mr. Schiller is a physics graduate student that has worked on the project, primarily on modeling and simulation
Funding Support:	This award

Name:	**Victoria Gabrielle**
Project Role:	Graduate Student
Nearest person month worked:	1
Contribution to Project:	Ms. Gabrielle is a physics graduate student involved with the project. She has been involved with device microfabrication, and biochemical aspects of the work.
Funding Support:	This award

Change(s) in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period

Nothing to Report.

Other organizations were involved as partners

Nothing to Report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *N/A*

QUAD CHART: *attached*

9. APPENDICES:

Curriculum vitae of M. J. Naughton
Updated Quad Chart

Emerging Infectious Disease Diagnostic via Novel Optoelectronic Halo Effect

Log Number PR172111, FY17 Peer Reviewed Medical Research Program, Discovery Award
W81XWH-1810102

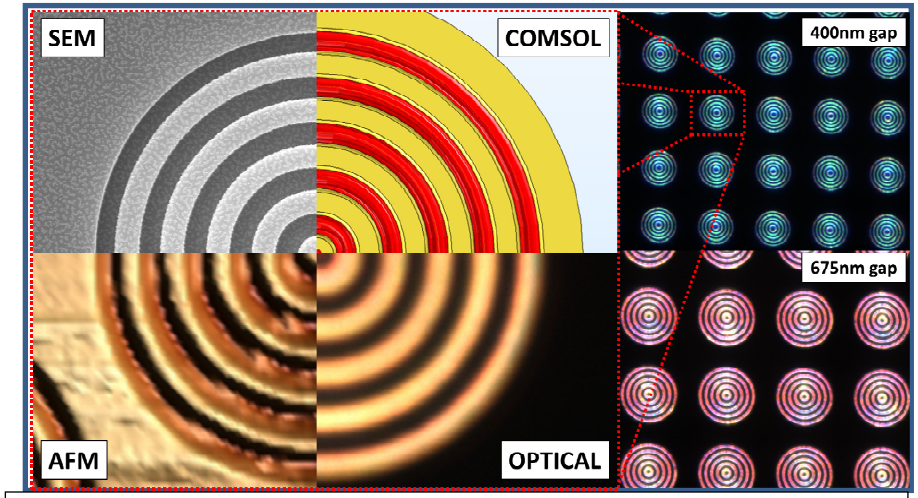
PI: Michael J. Naughton, Ph.D. **Org:** Boston College **Award Amount:** 313,000

Study Aim

• Exploit the plasmonic halo effect to develop a high sensitivity, high selectivity molecular biosensor targeting biomarker of emerging infectious diseases, such as that for tuberculosis and coronavirus.

Approach

- Model, Make and Measure plasmonic halos as sensitive biosensors.
- Simulate, using the finite element method, the interaction of light with the plasmonic halo, as a prediction tool toward optimization of the architecture as a biosensor.
- Fabricate and test devices for sensitivity and selectivity.



Left: Simulated, fabricated and characterized plasmonic halo structures for optimized design. Right: Measured the response of chemical and biological plasmonic halo assays.

Timeline and Cost

Activities CY	19	20
Identify candidate biomarkers		
Simulate plasmonic response		
Fabricate & characterize devices		
Demonstrate proof-of-concept		
Estimated Budget ($K)	**$180,000**	**$133,000**

Updated: 13 May 2020

Goals/Milestones

CY19 Goal – Optimize structure via simulation and fabrication
- Validate design architecture for enhanced sensitivity

CY20 Goal – Demonstrate proof-of-concept of halo-based detection of antigen above antigen-free control sufficient to warrant further development

Comments/Challenges/Issues/Concerns
- Advanced architecture with bullseye pursued
- Optical scheme with quantum dots not sufficiently successful
- New near-infrared detection protocol investigated
- Began development of plasmonic halo as a coronavirus detector

Budget Expenditure to Date
Projected Expenditure: $133,000
Actual Expenditure: $48,598

Michael J. Naughton

Evelyn J. & Robert A. Ferris Professor
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www.bc.edu/naughton

Education

Boston University, Ph.D. Physics 1986
St. John Fisher College, B.S. Physics 1979

Professional

Ferris Professor	Boston College	2008--
Chairman	Department of Physics, Boston College	2006-2018
CTO	Solasta Inc., Newton, MA	2006-2010
Assoc. VP Research	Office of the Academic Vice President, Boston College	2005-2006
Professor	Department of Physics, Boston College	1998--
Professor	Department of Physics, State University of New York at Buffalo	1998
Visiting Scientist	National High Magnetic Field Laboratory, Tallahassee, Florida	1996
Visiting Scientist	Service National de Champs Magnetique Pulses, Toulouse, France	1995
Associate Professor	Department of Chemistry, State University of New York at Buffalo	1993-1998
Associate Professor	Department of Physics, State University of New York at Buffalo	1993-1998
Assistant Professor	Department of Physics, State University of New York at Buffalo	1988-1993
Post-Doc	Department of Physics, University of Pennsylvania	1986-1988

Honors & Awards

Young Investigator Award, National Science Foundation, 1992
Fellow, American Physical Society, 2003
Distinguished Research Award, Boston College, 2005
Nano^{50}, Nanotech Briefs, 2006
Ignite Clean Energy, MIT Enterprise Forum (2nd place), 2006
Karl Herzfeld Memorial Lecturer, Catholic University, 2011

Professional Activities

Member, American Physical Society, Materials Research Society, American Chemical Society, Society for Neuroscience
Co-Founder, Solasta Inc.
Co-Founder, Tau Sensors LLC
Executive Committee, American Physical Society, Division of Condensed Matter Physics, 1998-2002
Chairman, inaugural National High Magnetic Field Laboratory Users' Committee, 1995-1998
Organizer, American Physical Society New England Section Annual Meeting, *Energy Matters*, 2014
Organizer, Near-Field Nanophotonics Workshop, Boston College, 2014
Member, External Academic Review Committee, University of Vermont Department of Physics, 2014
Member, Review Committee, Research Core in Interdisciplinary Science, Okayama University, 2012-2014
Participant, Ignatian Colleagues Program, 2012-2015
Proposal Reviewer, National Science Foundation, Department of Energy, National Institutes of Health
Member, Science Advisory Board, NBD Nanotechnologies, Boston, MA
Founding Member, Board of Directors, Ireland-America Science Forum

Publications

updated January, 2020

(*H*-Index 50, i10-index 112, ~7,700 citations, 204 publications, 24 issued patents, 21 pending patents)

Under Review

- *Optical confinement in the nanocoax: Coupling to the fundamental TEM-like mode*, Yitzi M. Calm, Luke D'Imperio, Nathan T. Nesbitt, Juan M. Merlo, Aaron H. Rose, Krzysztof Kempa, Michael J. Burns, Michael J. Naughton
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- *Crosstalk reduction in microelectrode arrays via shielded electrodes*, J.R. Naughton, J.R. Merlo, A.H. Rose, Y. Calm, K. Kempa, T.J. Connolly, M.J. Burns, J.R. Christianson and M.J. Naughton

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177. *Structured metal thin film as an asymmetric color filter: the forward and reverse plasmonic halos*, F. Ye, M.J. Burns and M.J. Naughton, Scientific Reports **4**, 7267 (2014). doi:10.1038/srep07267 (5 pp)

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