Optical Fiber Sensors for Biomedical Applications

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Outline

1. Introduction to our group
2. Brief overview of projects
3. Projects
   - ❑ A fiber optic pressure sensor for blood pressure measurement
   - ❑ Fiber optic biosensors
   - ❑ A fiber optic pressure sensor for blast wave measurement
   - ❑ Fiber optic temperature sensors
   - ❑ A fiber optic ultrasonic generator
4. Conclusions
5. Acknowledgements

Introduction

People

Dr. Xingwei Wang:
Optical bio/medical sensors; optical fiber sensors; MEMS

NSF CAREER Award;
MLSC Young Investigator Award

1 Postdoc: Dr. Hongtao Zhang
Optical fiber sensing technology; quantum physics

7 PhD students with various background; 1 Master student and 2 REU students

9 journal publications in 1.5 years.

Equipment & Facilities

Optical sensing analyzer
Micron Optics Si720

Optical fiber splicer
Furukawa S177A

Tunable laser
NewFocus TLB-6600-H-CL

Access to Focus ion beam (FIB) in UML Zeiss AURIGA ($ 1.15M)

Access to the Cleanroom in Harvard Center for Nanoscale Systems (CNS)

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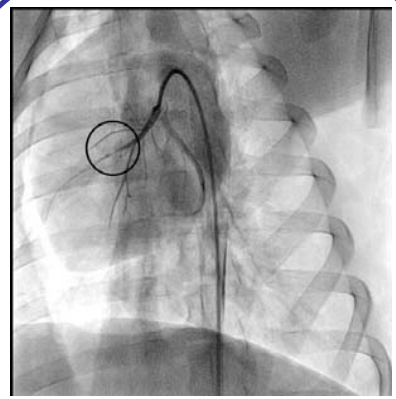
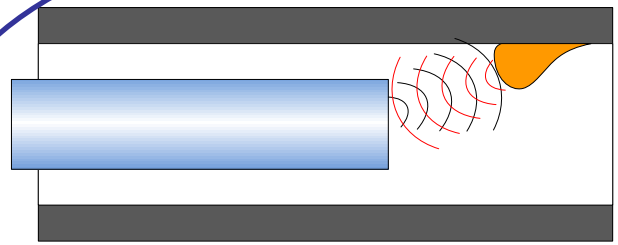
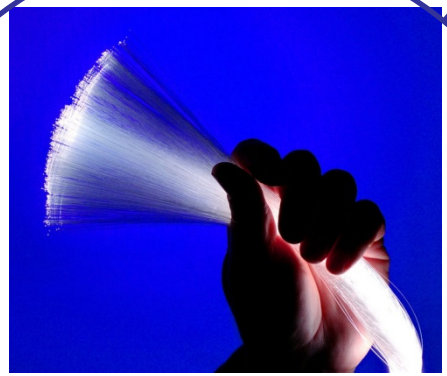
Projects Overview



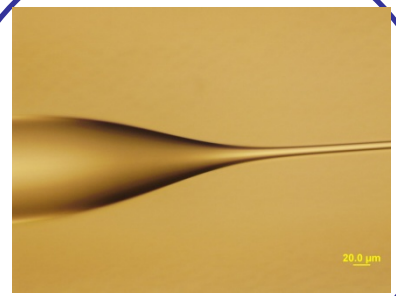
In-vivo blood pressure measurement



Ultrasonic generator for imaging

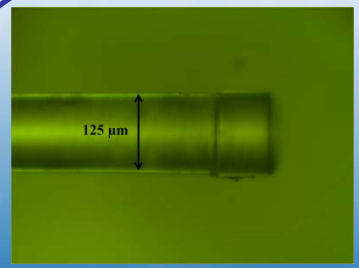


Optical fibers



Biosensor

Blast wave measurement



Temperature sensor

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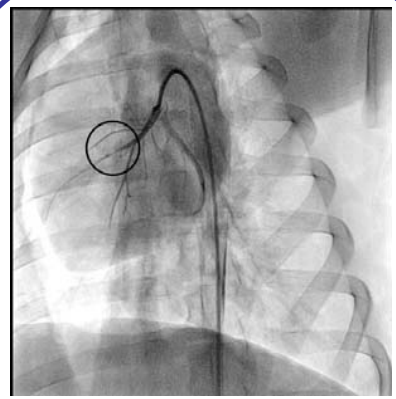

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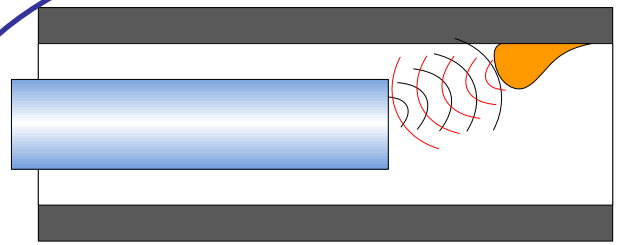

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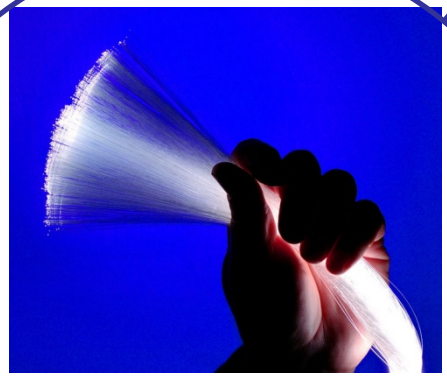
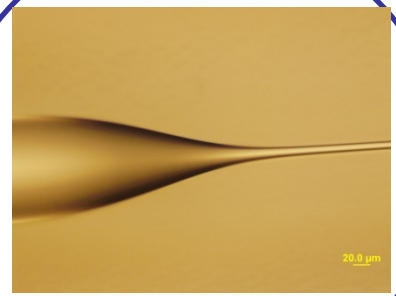
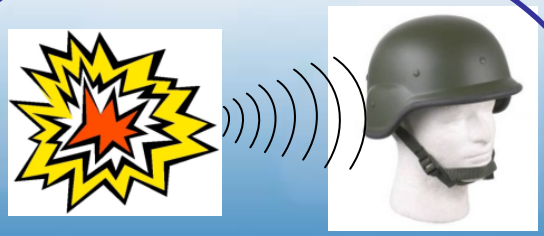


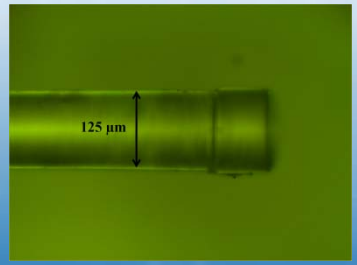
Optical fibers



Biosensor



Blast wave measurement



Temperature sensor

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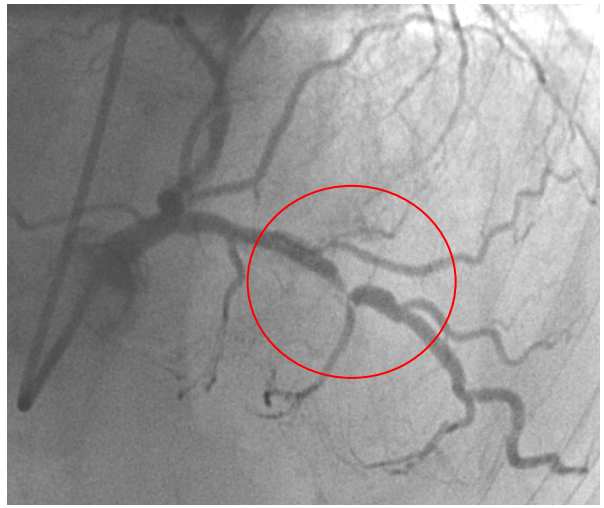
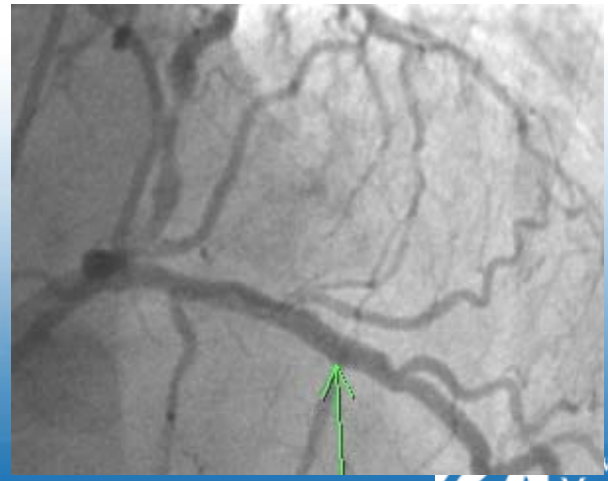
Coronary Artery Disease (CAD)

- 14 million patients
- $100 Billion annually



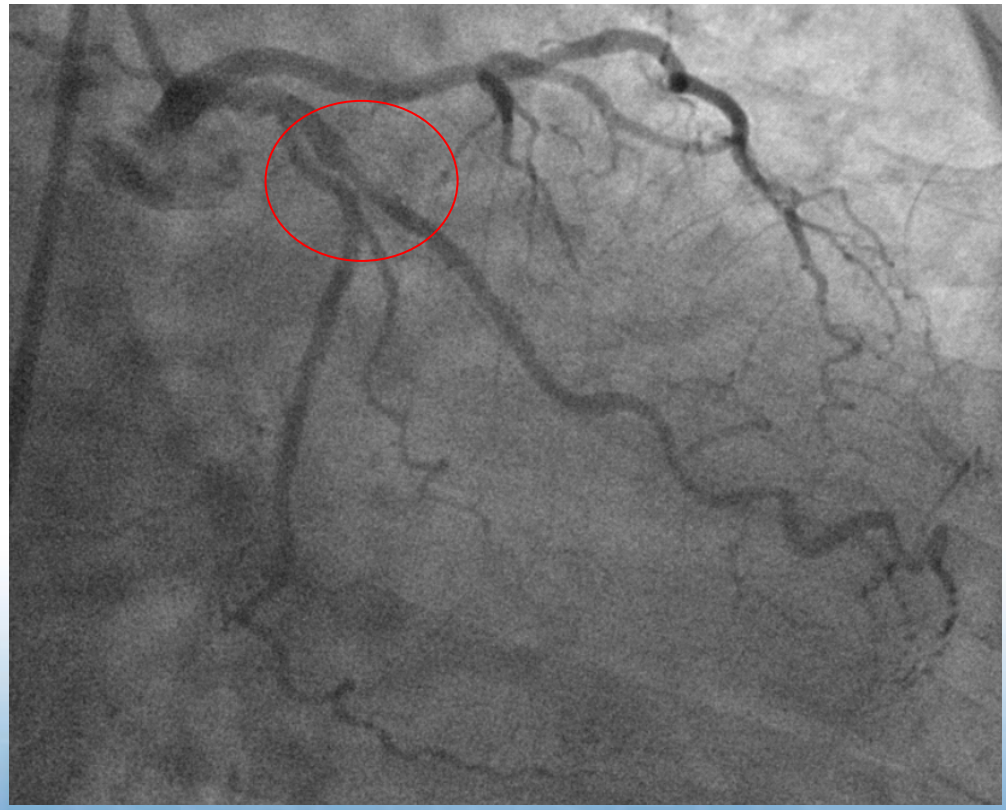
- Percutaneous Coronary Intervention (PCI)
  - Angioplasty with or without stent (90%)
  - Over 1 million/year
  - $8 billion/year



CAD: PCI vs Medical Therapy

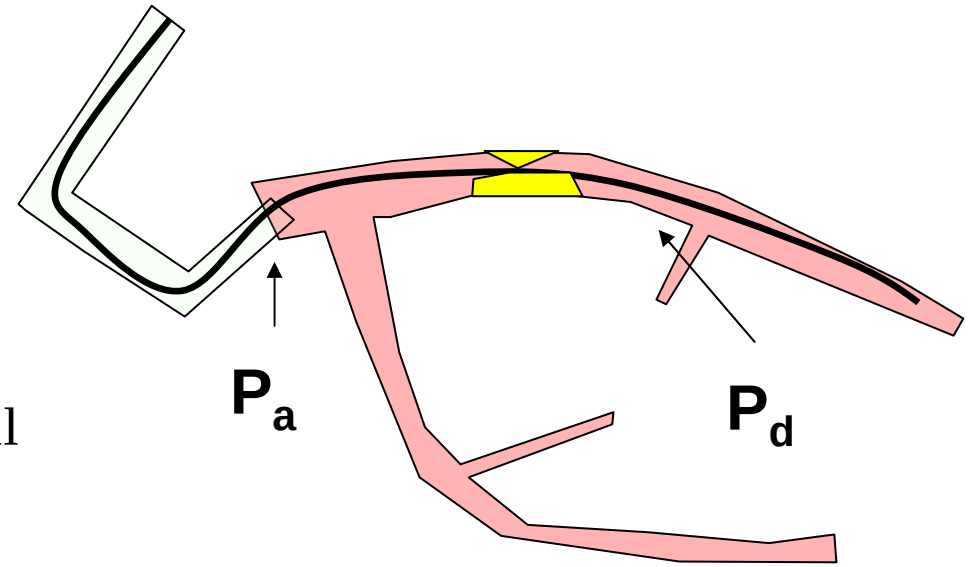
- PCI Limitations
  - Not helpful if stenosis is <40%
  - Expense
  - Renarrowing or occlusion
- Medicines often effective
  - Many PCIs may not be needed
  - Medical savings: $2.1 Billion
- Intermediate Lesions may not be responsible for symptoms
  - Proceed with PCI

    vs
  - Determine coronary blood flow (FFR)

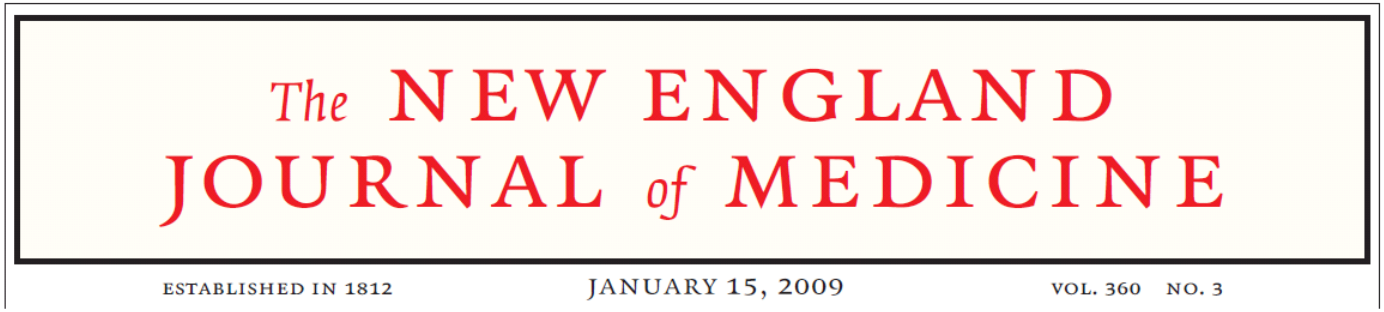


Fractional Flow Reserve (FFR)

- Means of determining coronary blood flow
- Defined as the pressure before a stenosis divided by the pressure beyond a stenosis during maximal dilation of the artery
- Current Market: $600 million/year
  - St. Jude; Volcano
  - Clinical adoption ~10%
    - Wire expense
    - Device delivery



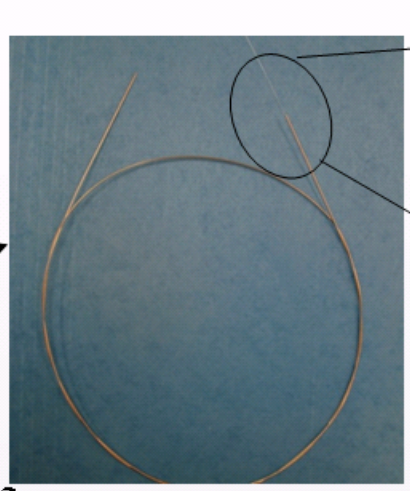
- Fractional flow reserve (FFR) = P_d/P_a
  - P_d = blood pressure beyond stenosis
  - P_a = blood pressure before stenosis
- Abnormal FFR < 0.75



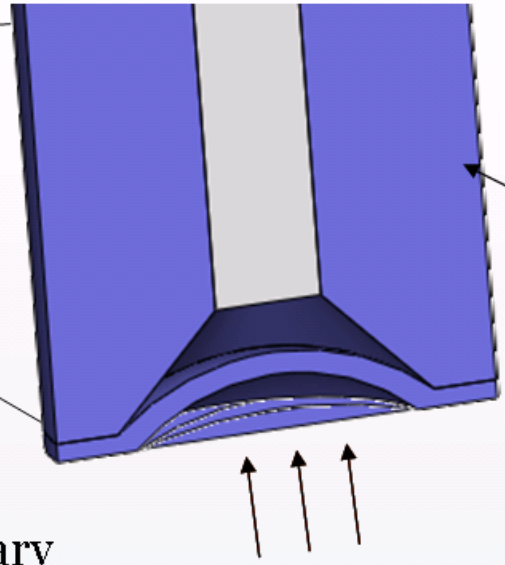
Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention

- FFR-guided approach reduces
  - Number of stents deployed
  - Procedural expense
  - Death/myocardial infarction (MI)
- Optical sensor guidewire
  - Decreased expense
  - Improved steerability

UML Optical Pressure Sensor



Standard guidewire
OD: 356µm
ID: 254 µm



Our sensor
OD: 125µm

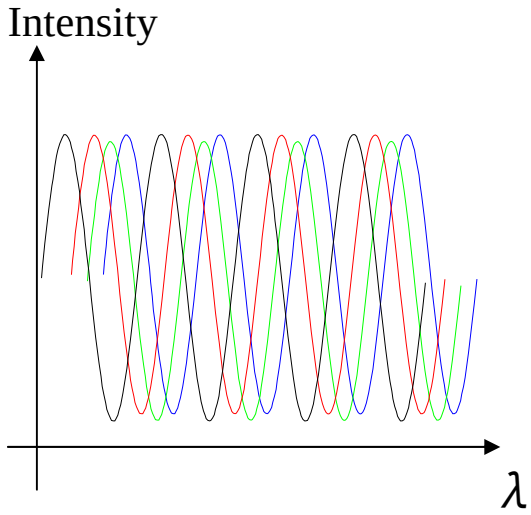
UML proprietary

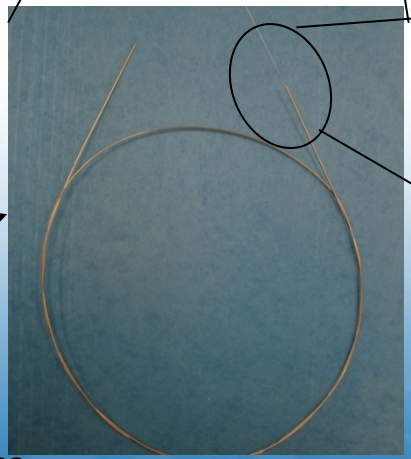
Cross-Campus Development and Commercialization Team:

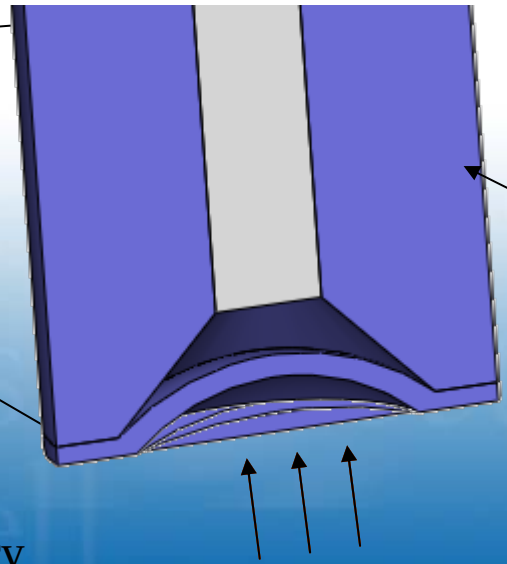
Xingwei Wang, PhD	UML	Principal Investigator	Sensor Fabrication
Kurt Barringhaus, MD	UMMS	Principal Investigator	Animal/Human Testing
Jill Murthi, et al	UML	CVIP Office	Tech Transfer, IP
Effraim Herskovic	UMass	President's Office	Commercialization

Fiber optic blood pressure sensor

Principle & Structure





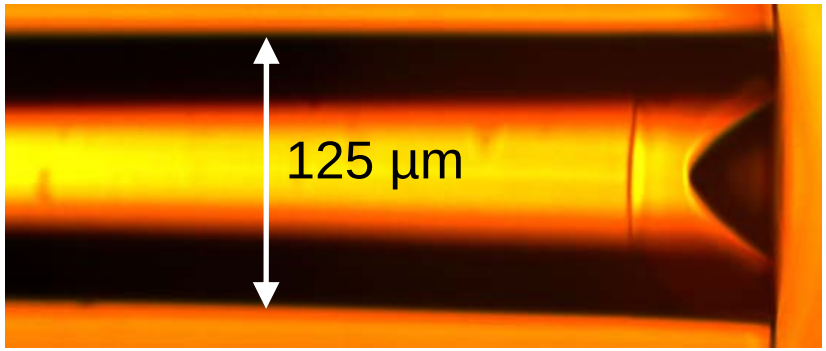


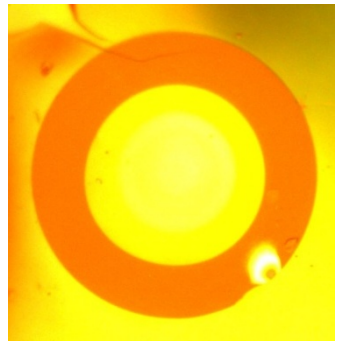
Standard guidewire
OD: 356 μ m
ID: 254 μ m

Our sensor
OD: 125 μ m

Fiber optic blood pressure sensor

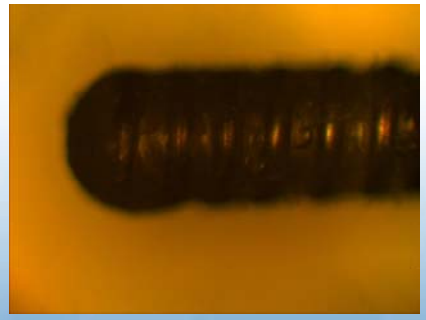
Bare fiber optic sensor



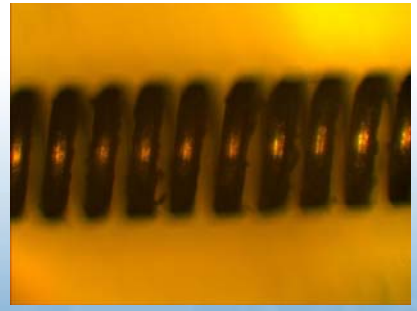


The thickness of the diaphragm is 1.5 µm

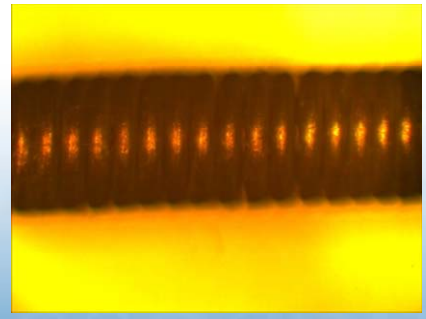
Packaged sensor



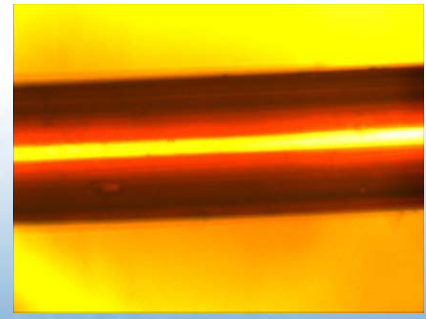
Biocompatible polymer bead



Stretched stainless steel coil



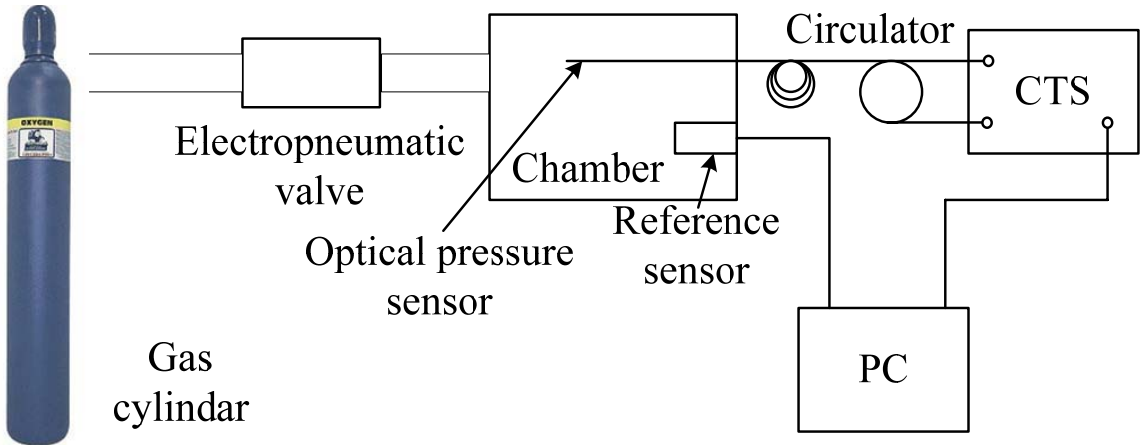
Unstretched stainless steel coil



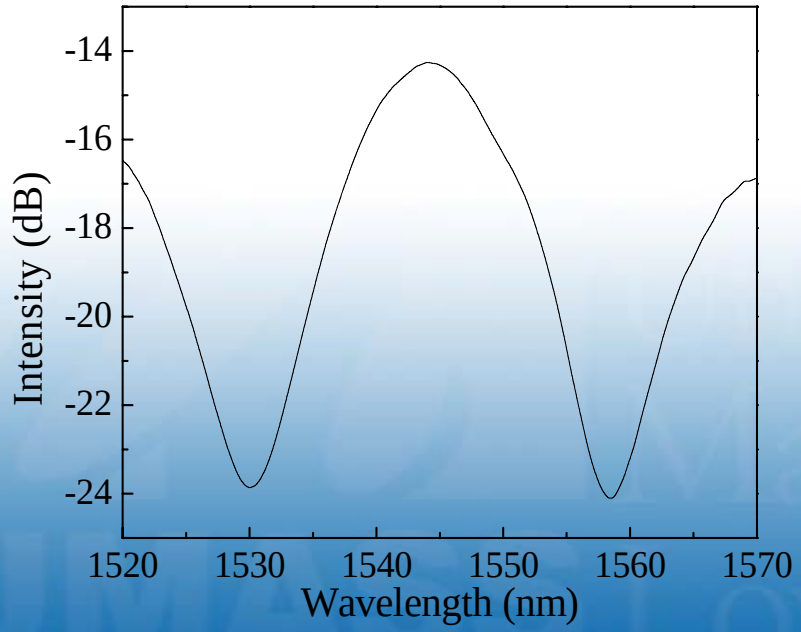
Kapton tube

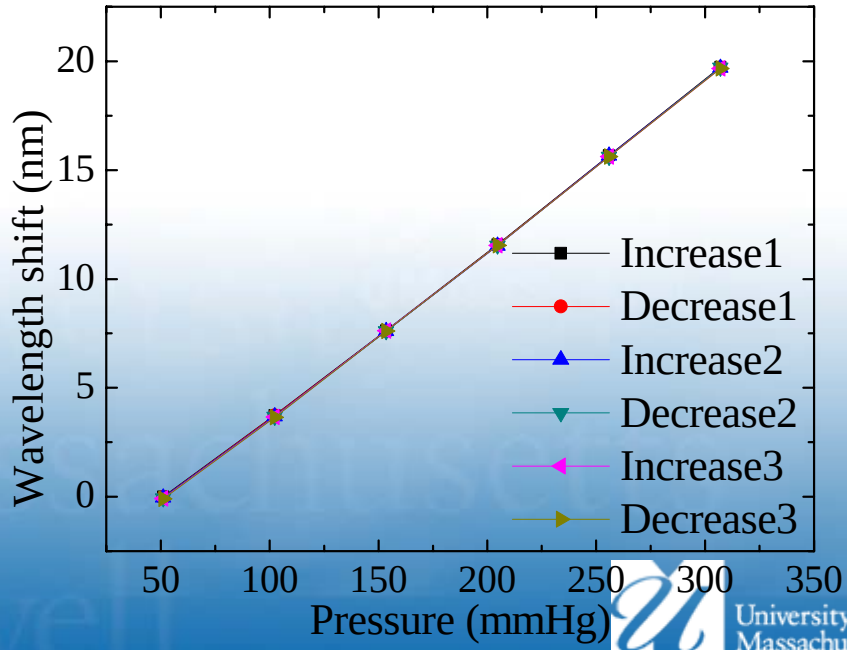
Fiber optic blood pressure sensor

Sensor characterization

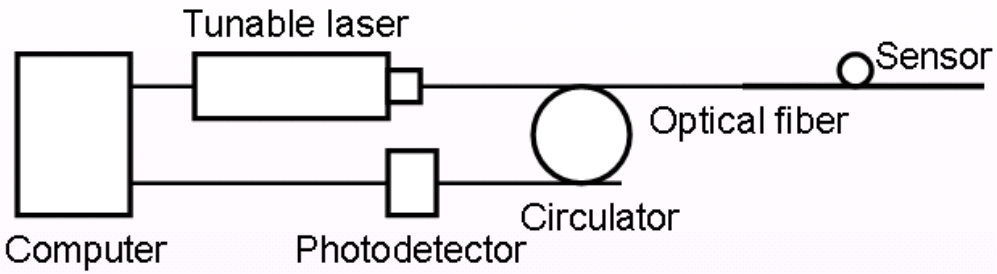


Sensitivity: 0.033 nm/mmHg – 0.039 nm/mmHg
Resolution (under 30pm tunable laser accuracy) :
0.77 mmHg – 0.87 mmHg
Dynamic range: 1500 mmHg

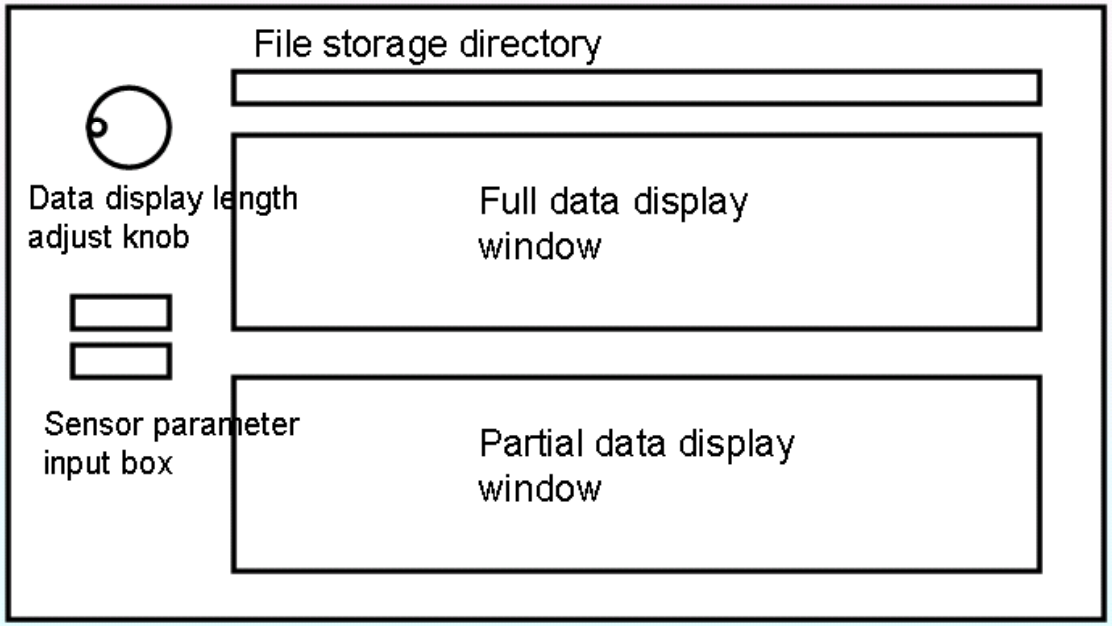


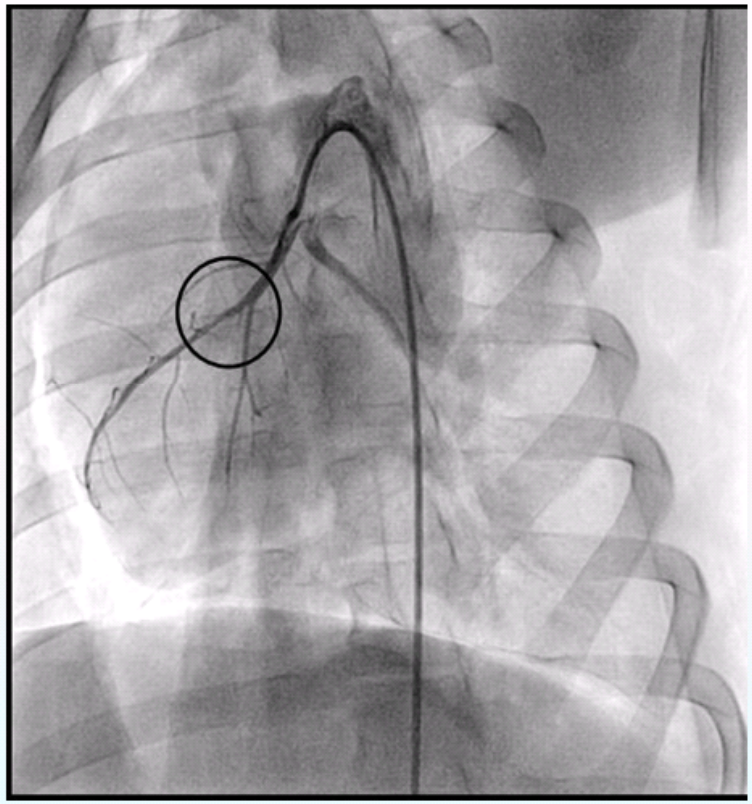


Optical Fiber: Proof of Concept



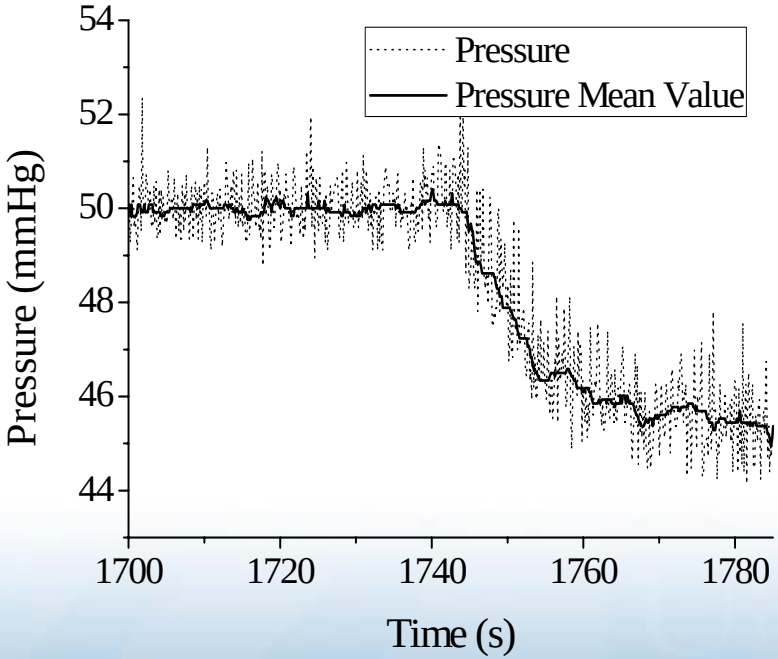
Schematic diagram of experiment setup.

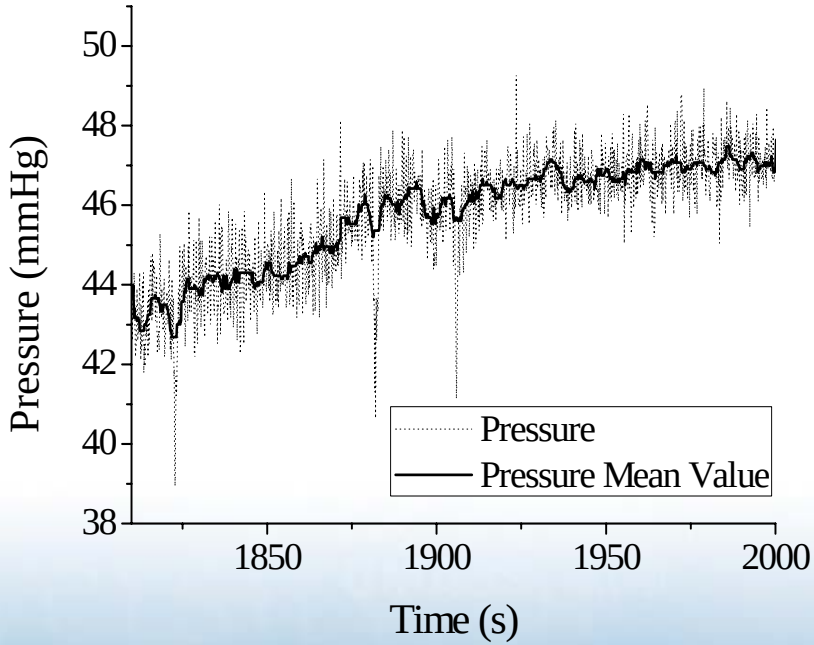




Coronary angiography following introduction of the UML fiber pressure sensor into the LAD.
(left anterior descending coronary artery)

UML Optical Sensor Identifies Coronary Stenosis-Induced Arterial Pressure Gradient





Pressure measured by UML pressure sensor decreased from 50 mmHg to 45 mmHg, caused by complete occlusion of coronary vessel.

Blood pressure measured by UML sensor increased gradually following partial deflation with resolution of the occlusion.

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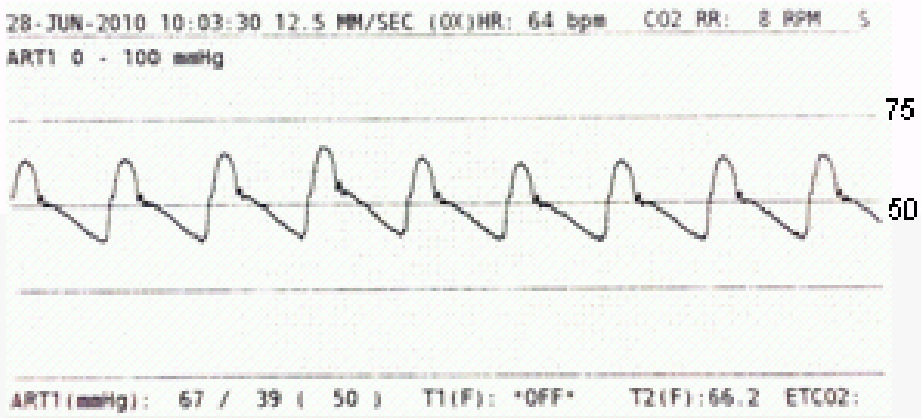
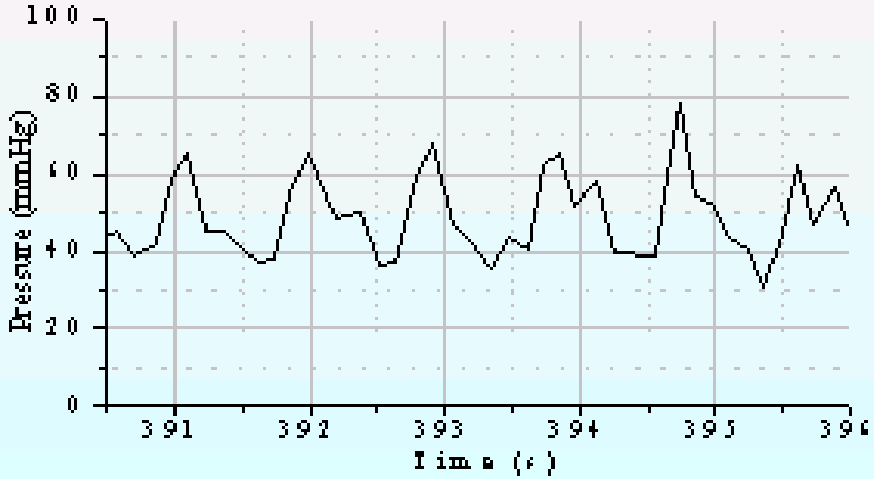
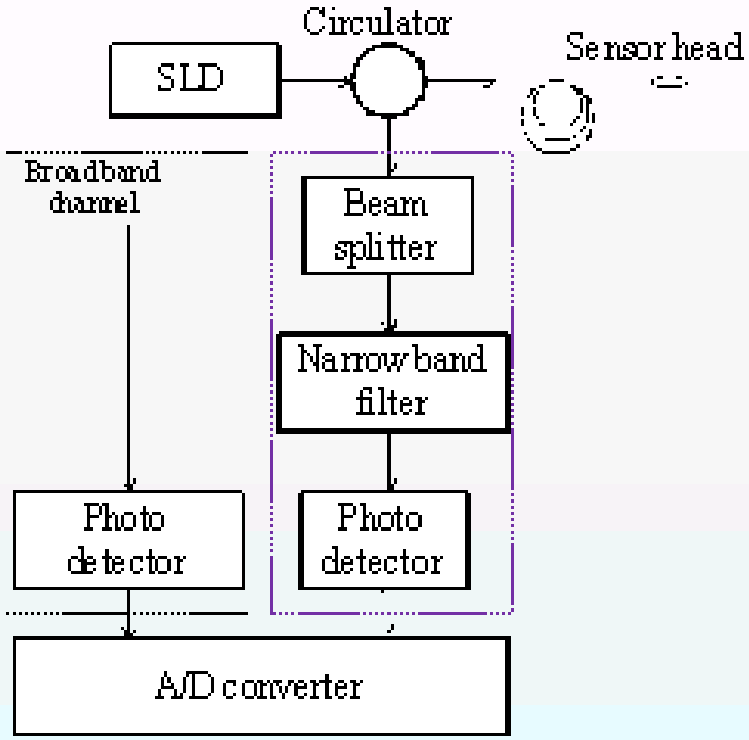
UML Optical Sensor Accurately Reflects Systolic and Diastolic Blood Pressure



Catheter transducer: 67/39



Optical sensor: 65/38



SCIIB system schematic

Fiber optic blood pressure sensor

Summary

Parameters	Value
Sensitivity (fringe shift)	0.033 nm/mmHg – 0.039 nm/mmHg
Sensitivity (diaphragm deformation)	0.82 nm/mmHg – 0.99 nm/mmHg
Resolution (under 30 pm tunable laser accuracy)	0.776 mmHg – 0.879 mmHg
Dynamic range	0– 1550 mmHg
Temperature cross-sensitivity	1.034 mmHg/° C
Rise time	0.4 μ s

Comparison with current pressure sensor

UML Sensor	PressureWire® (St. Jude Medical)**
Optical	Electrical
Immune to EMI	Susceptible to EMI
Biocompatible material	Electrical wires inside the patient body
~ a few dollars (material cost)	~ $600

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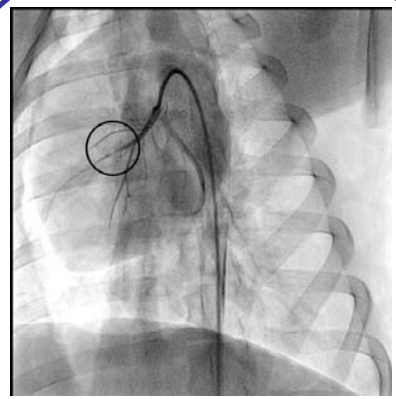
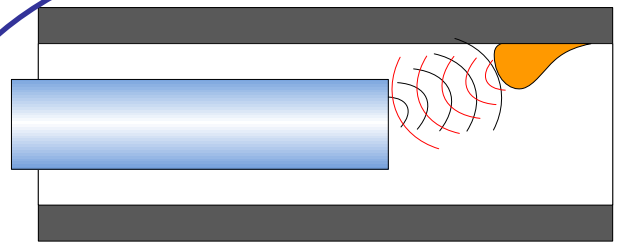
Summary

- UML optical sensor will advance care of patients with coronary artery disease in a cost-conscious manner
- Wire and system refinements are planned but preclinical studies require additional support
- Results from preclinical studies will set the stage for clinical studies and FDA approval
- Expansion into other clinical environments and take advantage of the optical sensor's superior accuracy and resistance to electromagnetic interference

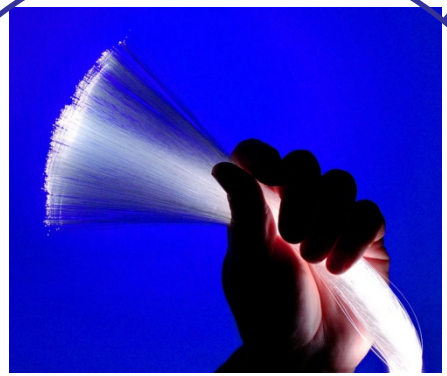
Overview of projects



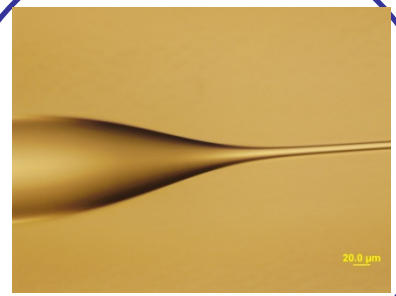
In-vivo blood pressure measurement



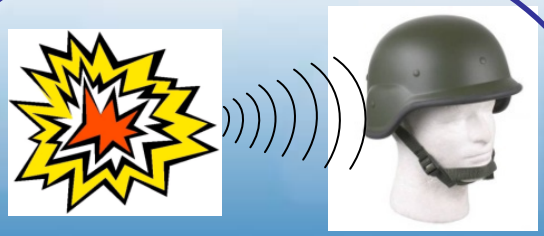
Ultrasonic generator for imaging



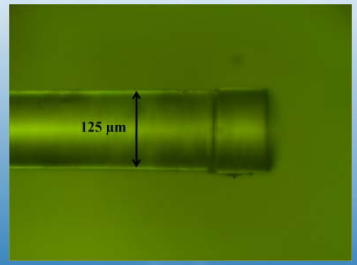
Optical fibers



Biosensor



Blast wave measurement



Temperature sensor

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Fiber optic biosensor

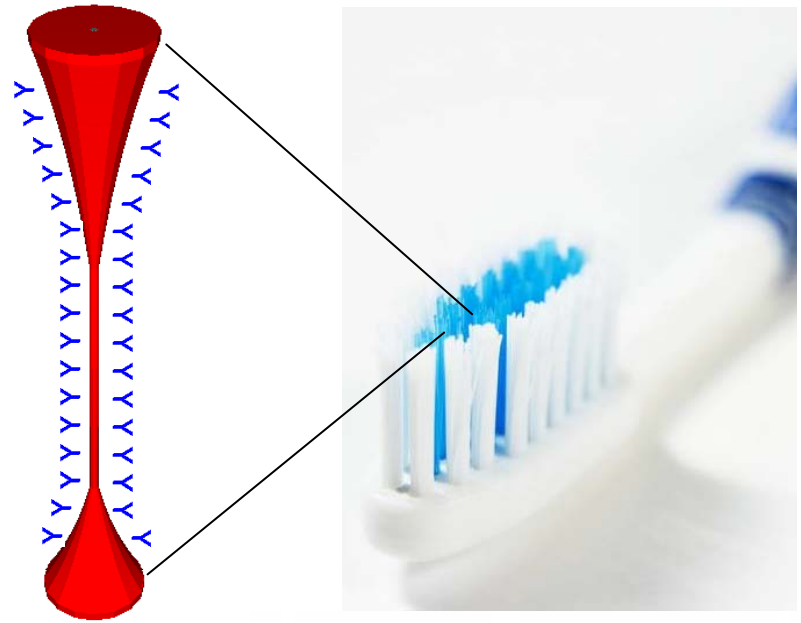
Motivation:

Traditional methods:

- Rely on labels such as dyes
- Require well-trained personnel
- Time-consuming pretreatment
- High operation cost

Potential:

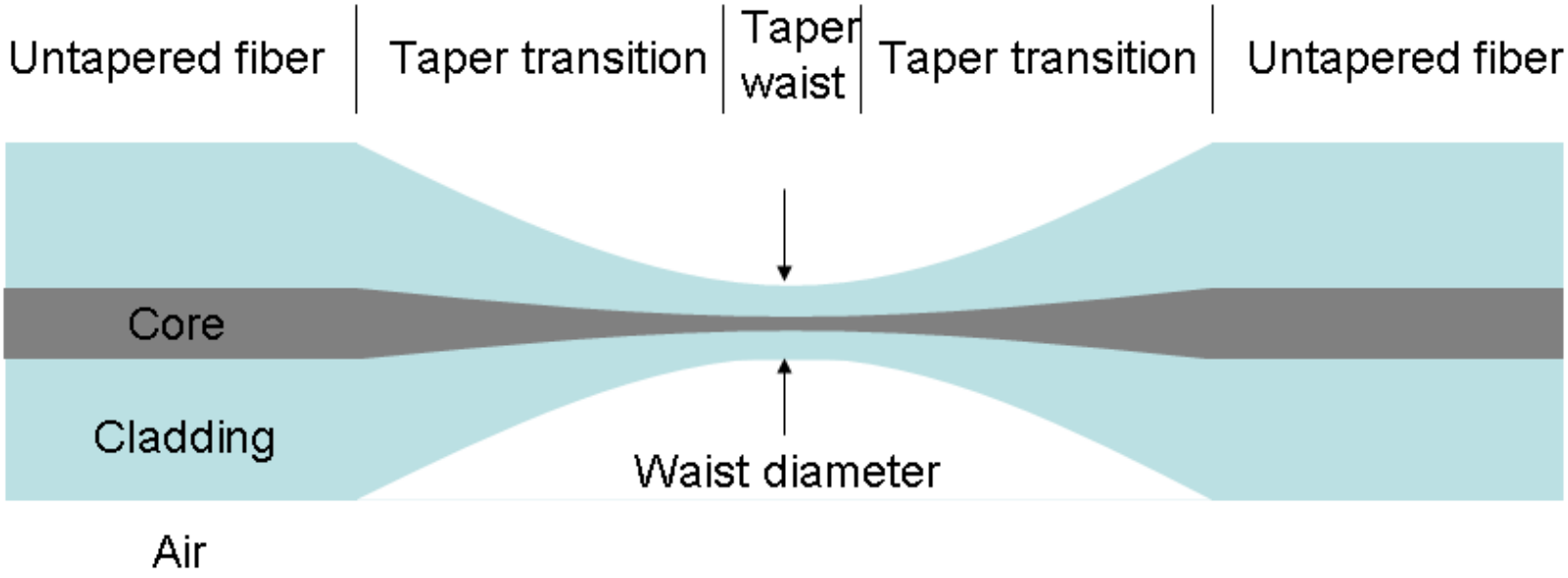
- Broad applications in detection of antigen-antibody reactions, proteins, oligonucleotides, and cells
- Extensive field in clinical, pharmaceutical, food safety, routine tests, patient home care, surgery and intensive care
- Embedded into toothbrush or kitchen utensils with intensity demodulation



Easy-to-use miniature biosensing probe embedded in a toothbrush for home care.

Fiber optic biosensor

Principle & Structure



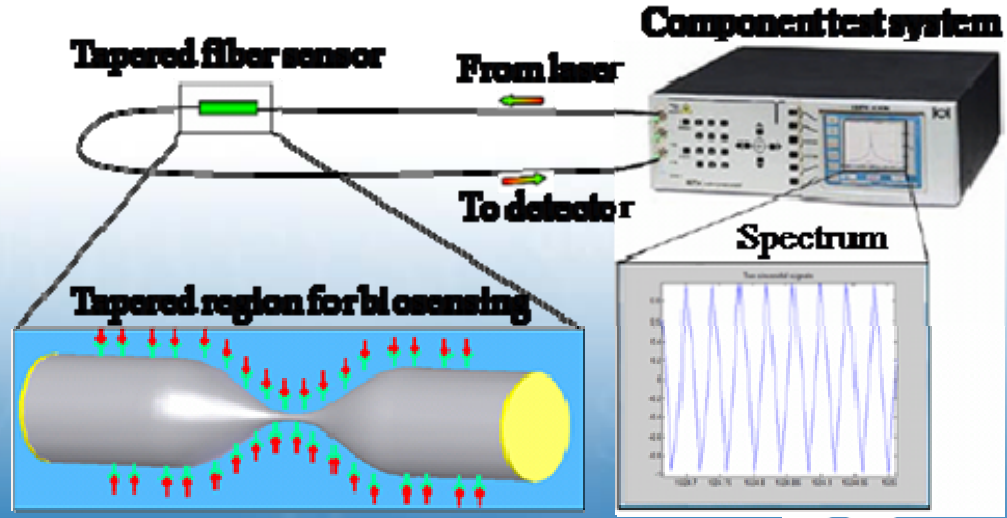
$$V = \frac{2\pi}{\lambda} r_{core} \sqrt{n_{core}^{\ 2} - n_{cladding}^{\ 2}}$$

λ : wavelength; r_{core}: core radius;
n_{core} = 1.4682; $n_{cladding}$ = 1.4629

Fundamental mode: HE_{11}

$$V = \frac{2\pi}{\lambda} r_{cladding} \sqrt{n_{cladding}^{\ 2} - n_{air}^{\ 2}}$$

$r_{cladding}$: cladding radius; n_{air} =1



High order modes excited
main: HE_{11} and HE_{12}

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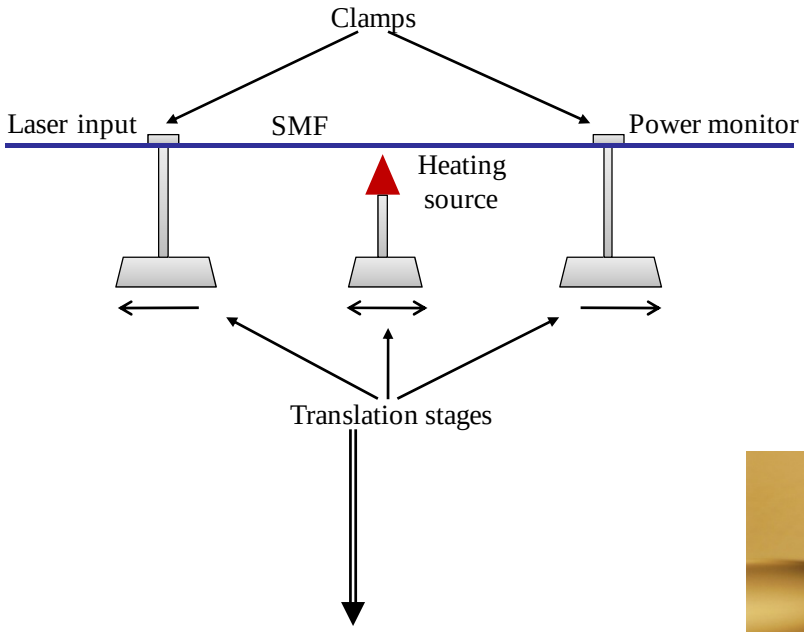
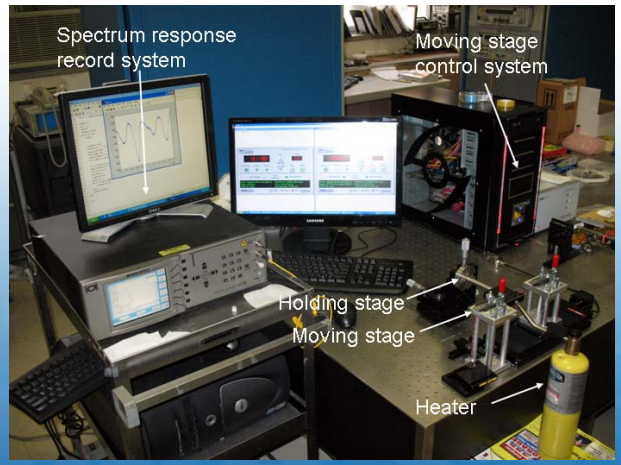
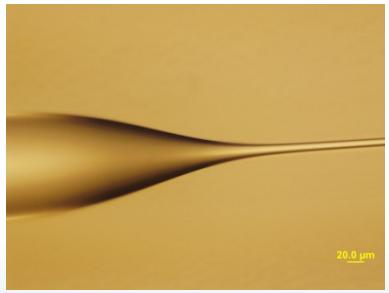
Fabrication

Traditional fabrication







Laser system

Source: www.epilogfiles.com

Fiber fusion splicer

Source: www.FurukawaAmerica.com

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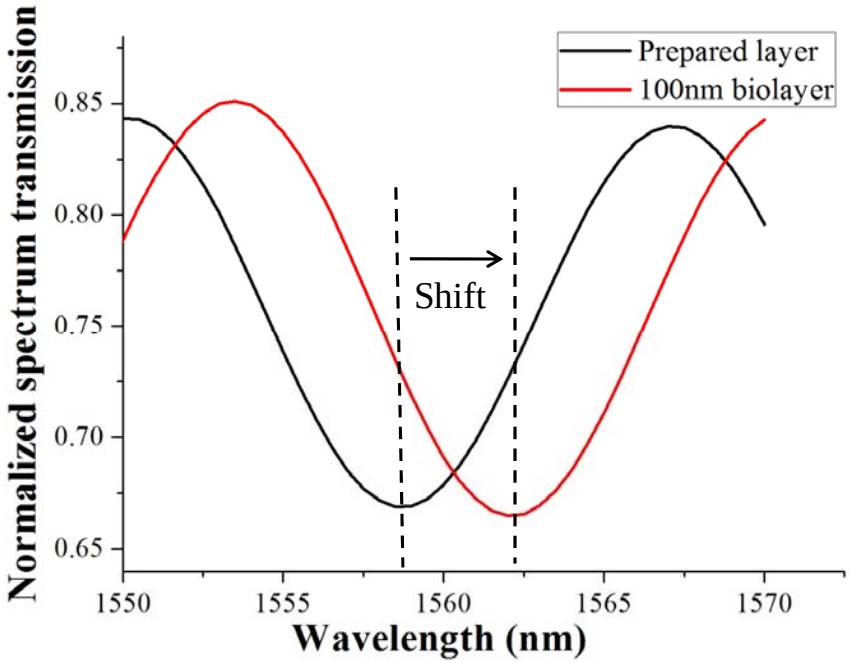
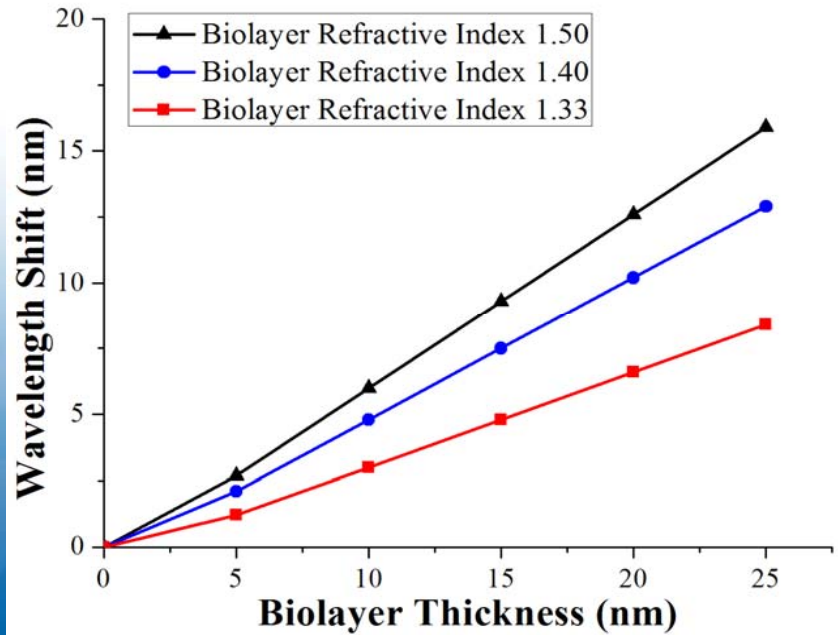
Simulation



Fringe shift under binded bio-layer. (The black curve is transmission spectrum of tapered fiber under a preparation layer with refractive index 1.33 and thickness 100 nm. After a target bio-layer with refractive index 1.33 and thickness 100 nm is binded above the preparation layer, the fringe shifts to the red curve.)



- Capability of detecting kinds of biomolecules in nanometer level
- Capability of detecting bio-layers with different refractive index
- Potential of detecting low-concentration bio-solution

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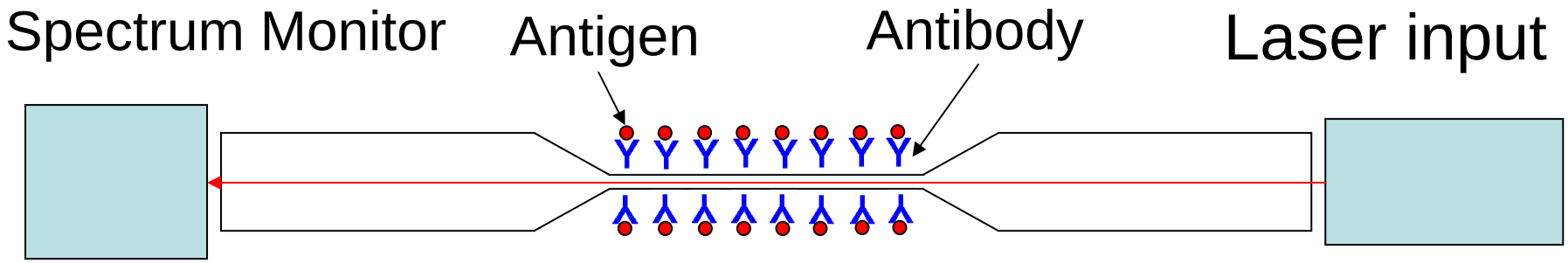
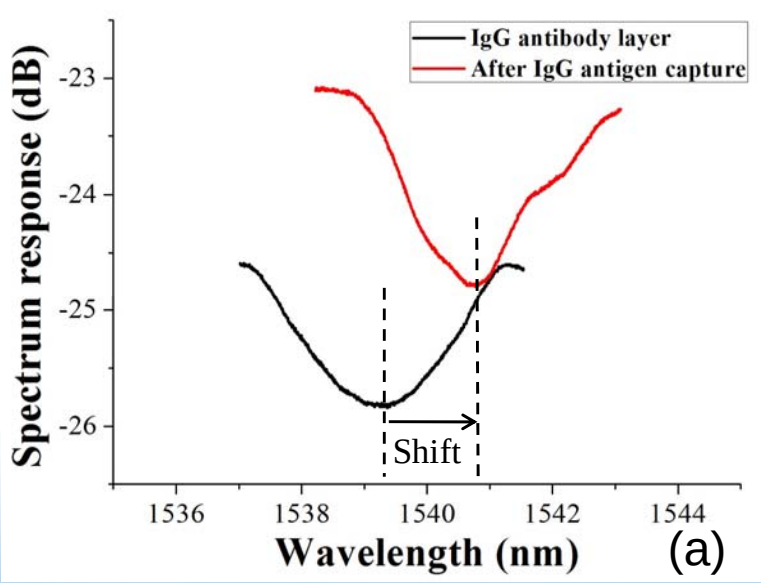
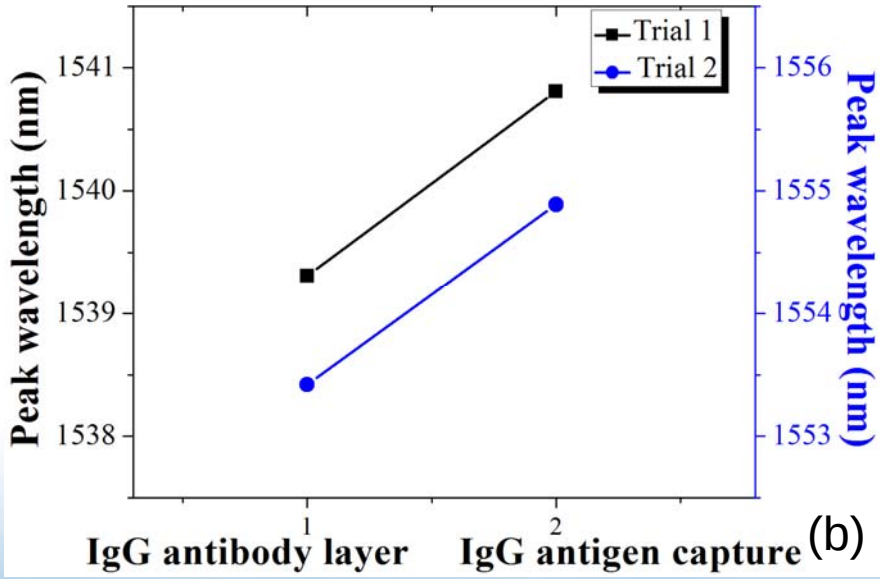
Biotest







(a) The comparison between the initial transmission spectrum (black) and IgG antibody-antigen pair layer (red). An obvious redshift of 1.50 nm after the capture of the IgG antigen was monitored. **(b)** The captures of IgG antigen were successfully detected by demodulating the peak wavelength redshift of 1.50 nm and 1.47 nm.

Summary

Completion

- Theoretical model establishment
- Numerical simulation
- Fabrication methods try-out
- Experimental validation

Further improvements

- More accurate and repeatable fabrication
- Protective Microchannel for precise bio-testing
- Elimination of cross-sensitivity
- Combination with other structures
- Intensity interrogation system