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ATLANTA 2019

PANACEA: A Cyber-Physical System for Early Detection and Mitigation of Infections

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REFERENCES

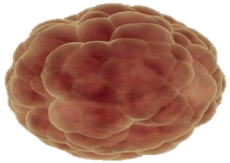
- I.F. Akyildiz, M. Pierobon, S. Balasubramaniam, Y. Koucheryavy, "The Internet of Bio-NanoThings", IEEE Communications Magazine, March 2015.

- I. F. Akyildiz, U. Guler, T. Ozkaya-Ahmedov, A. F. Sarioglu, B. D. Unluturk, "PANACEA: An Internet of Bio-NanoThings Application for Early Detection and Mitigation of Infectious Diseases", submitted to IEEE Access Journal, 2019.

BIO-NANOTHINGS

I.F. Akyildiz, F. Brunetti, F., and C. Blazquez,
"Nanonetworks: A New Communication Paradigm," Computer Networks (Elsevier) Journal, June 2008.

- Cells are nanoscale-precise biological machines

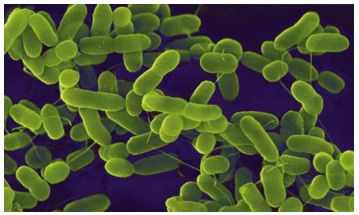


Eukaryotic Cell

Prokaryotic Cell

- They communicate and interact/cooperate

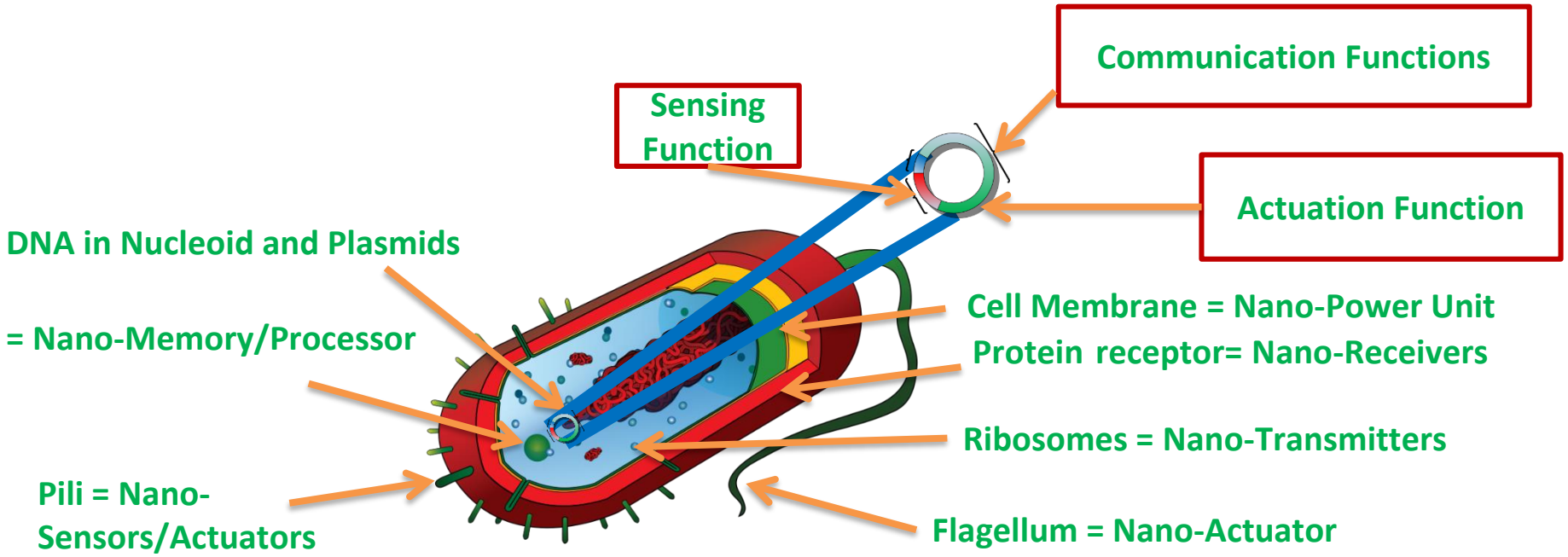
Eukaryotic Cell Tissue



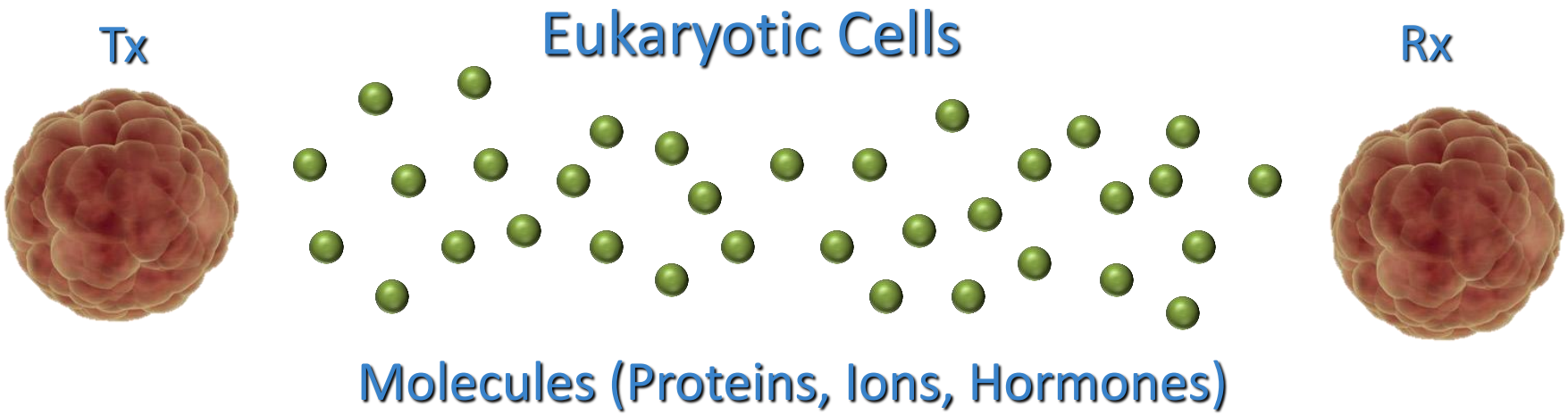
Bacteria Population

BACTERIA-BASED NANOMACHINES

- Reuse of entire biological cells
  - Through genetic programming of bacteria plasmids (Synthetic Biology)



BIOLOGICAL NANOMACHINES:
COMMUNICATION THROUGH MOLECULES



BIOLOGICAL NANOMACHINES:
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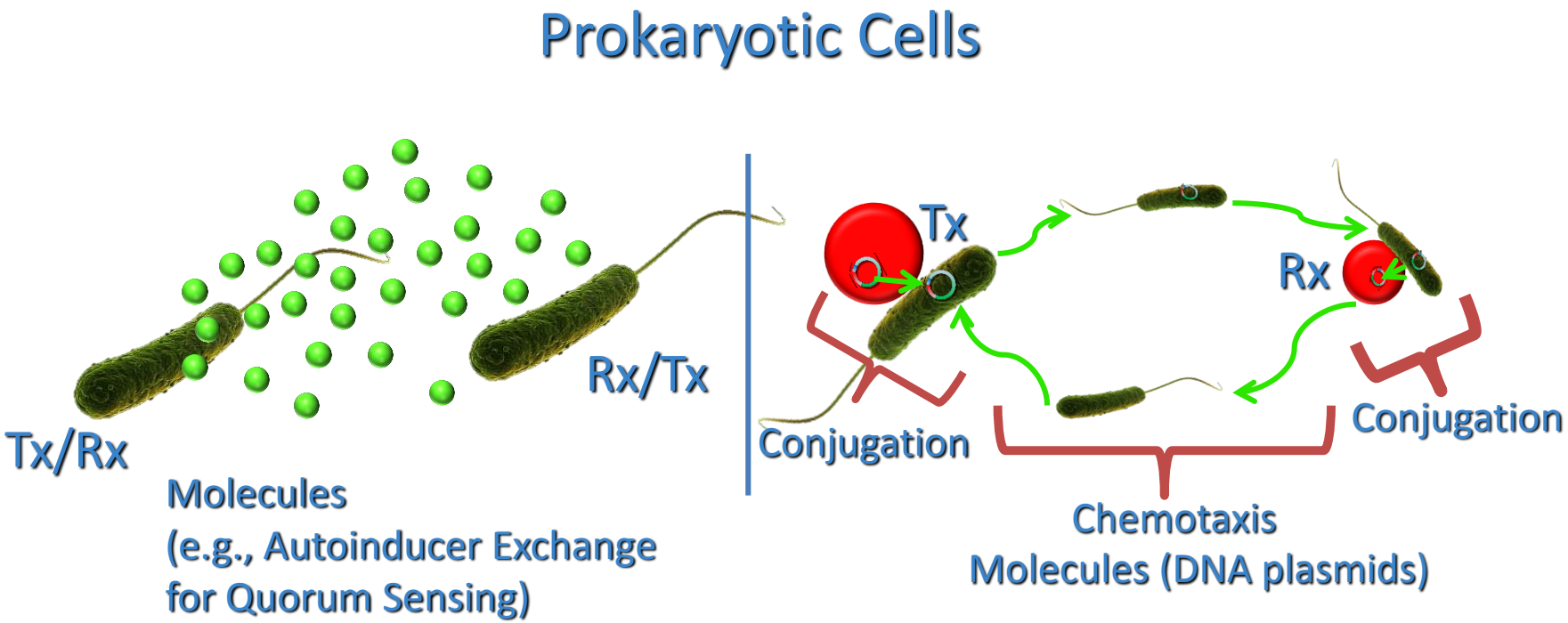
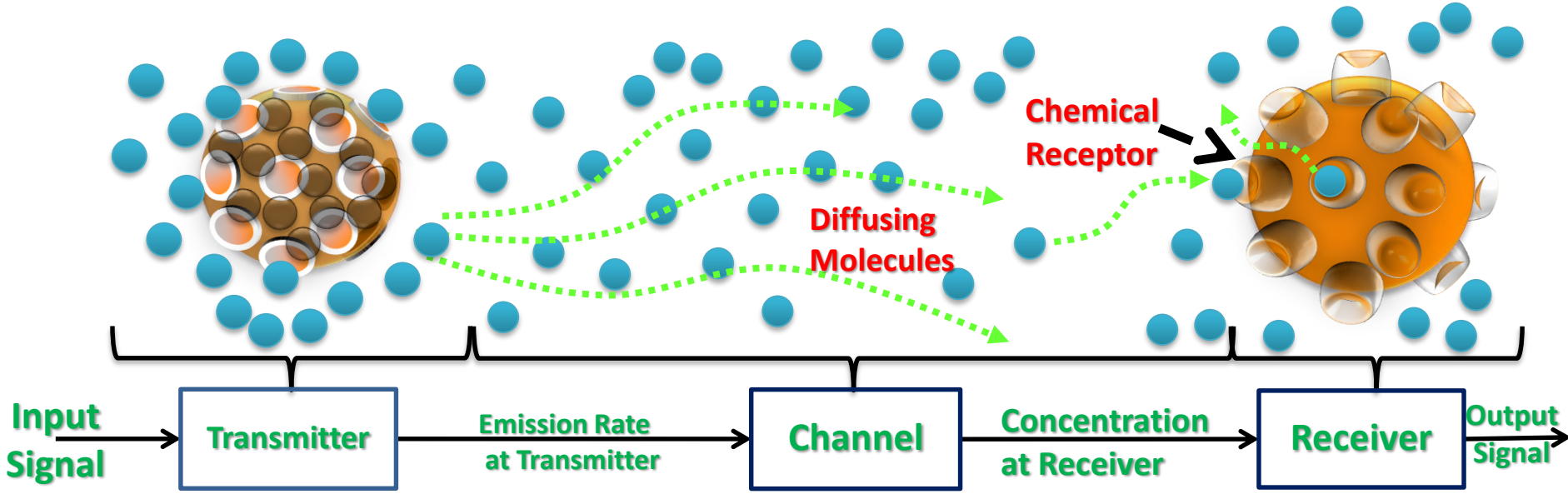


WHAT IS MOLECULAR COMMUNICATION?

M. Pierobon and I.F.. Akyildiz,
"A Physical End-to-End Model for Molecular Communication in Nanonetworks,"
IEEE JSAC (Journal of Selected Areas in Communications), vol. 28, no. 4, pp. 602-611, May 2010.

- Transmission and reception of information encoded in molecules
- Interdisciplinary field spanning Nanotechnology, ECE, CS, Bio, Physics, Chemistry, Medicine and Information Technologies

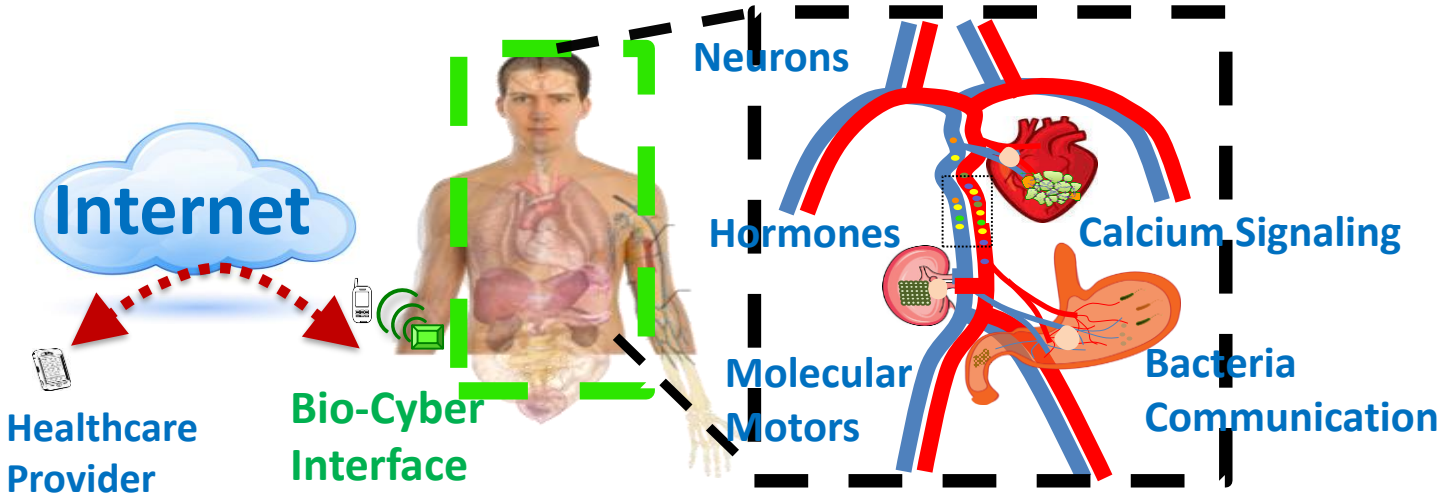


INTERNET OF BIO-NANOTHINGS

I.F. Akyildiz, M. Pierobon, S. Balasubramaniam, Y. Koucheryavy,
"The Internet of Bio-NanoThings",
IEEE Communications Magazine, vol. 53, no. 3, pp. 32-40, March 2015.

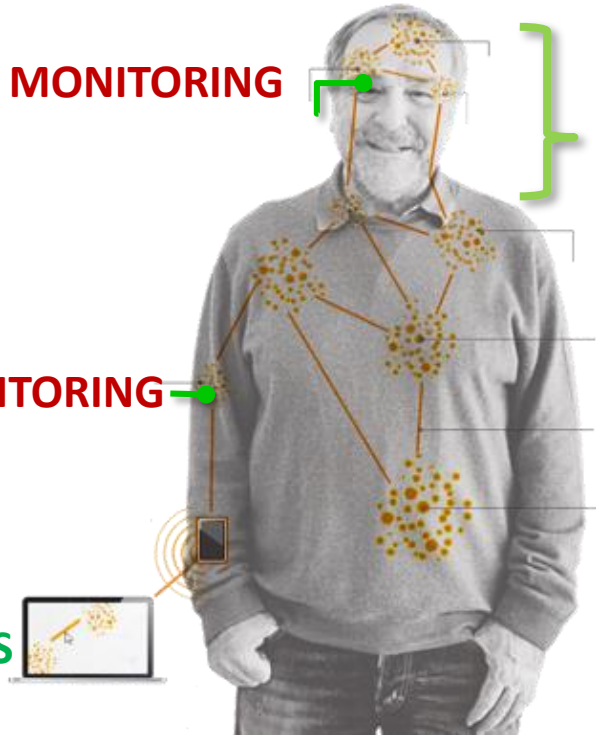
Objective:

To interconnect the heterogeneous Bio-NanoThing Networks to the Internet



BIO-NANOTHINGS APPLICATIONS: ADVANCED HEALTH SYSTEMS

INTERCONNECTED INTRABODY NANONETWORKS



BRAIN CELLS MONITORING

Alzheimer, Epilepsy,
Depression Monitoring

Heart problems & cardiac function

GLUCOSE MONITORING

BLOOD SUGAR MONITORING NETWORK

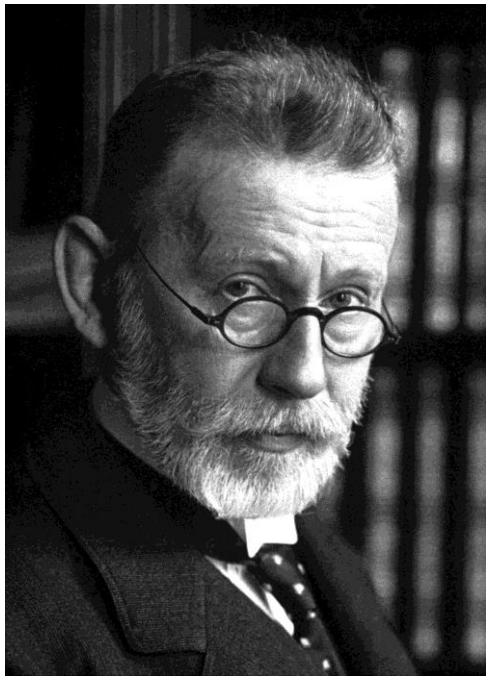
CROHN's DISEASE

INTERFACE WITH
EXTERNAL NETWORKS

CANCER MONITORING NETWORK

ORIGINS

- Paul Ehrlich (1854-1915):
  - He imagined the concept of "magic bullets" (Magische Kugeln) which are the ideal therapeutic agent killing the targeted diseases without affecting the other healthy parts of the body.



Paul Ehrlich
Nobel prize in Medicine (1908)

PANACEA: IoBNT FOR EARLY DETECTION AND MITIGATION OF INFECTIONS

I. F. Akyildiz, U. Guler, T. Ozkaya-Ahmedov, A. F. Sarioglu, B. D., Unluturk,
"PANACEA: An Internet of Bio-NanoThings Application for Early Detection and Mitigation of Infectious Diseases", submitted to IEEE Access, 2019.

- Problem: **Early Detection of Infections**
  - **Cancer:** Chemo patients are very vulnerable to infections.
  - **Cystic fibrosis:** Infections come wave by wave especially for young children

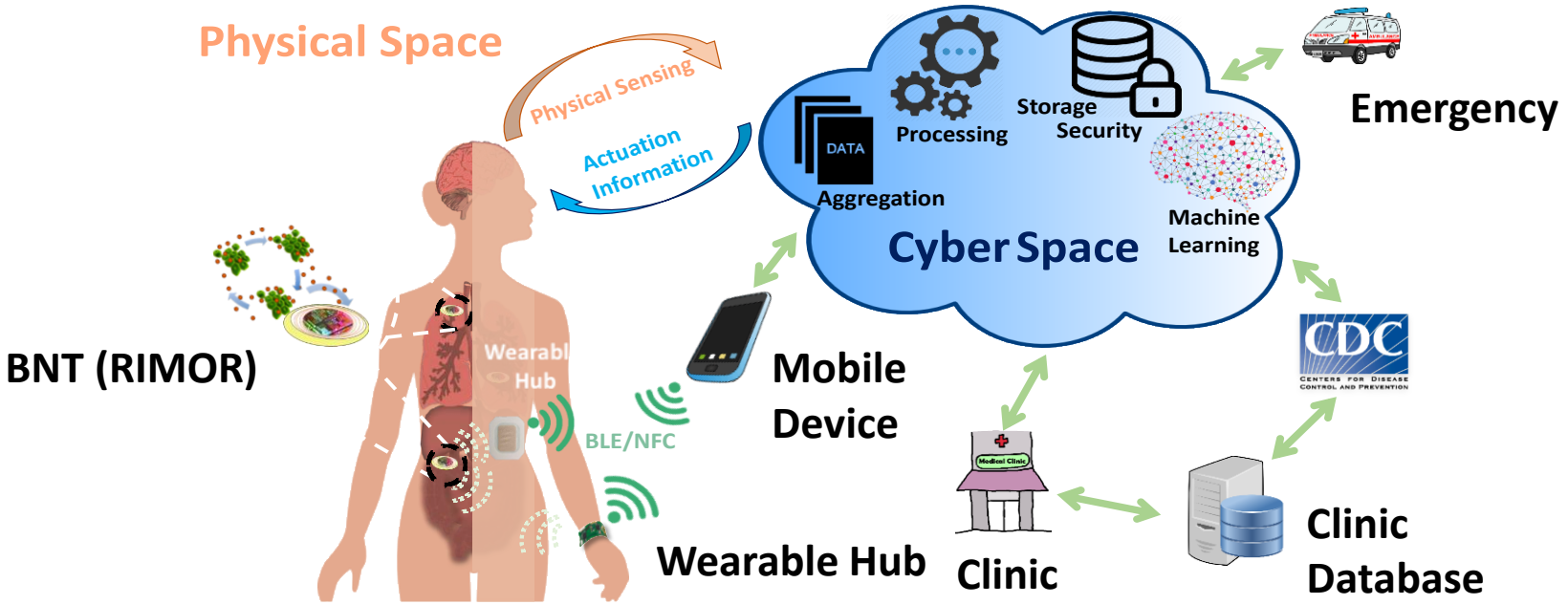
- Solution: **Project PANACEA**

  Continuous monitoring of bacterial infections with IoBNT
  - Early detection of infections
  - Timely administration of antibiotics
  - Tracking efficiency of antibiotics

  } **Reducing mortality and hospital costs !**

PANACEA: ARCHITECTURE

Approach: Develop and integrate a novel cyber-physical system

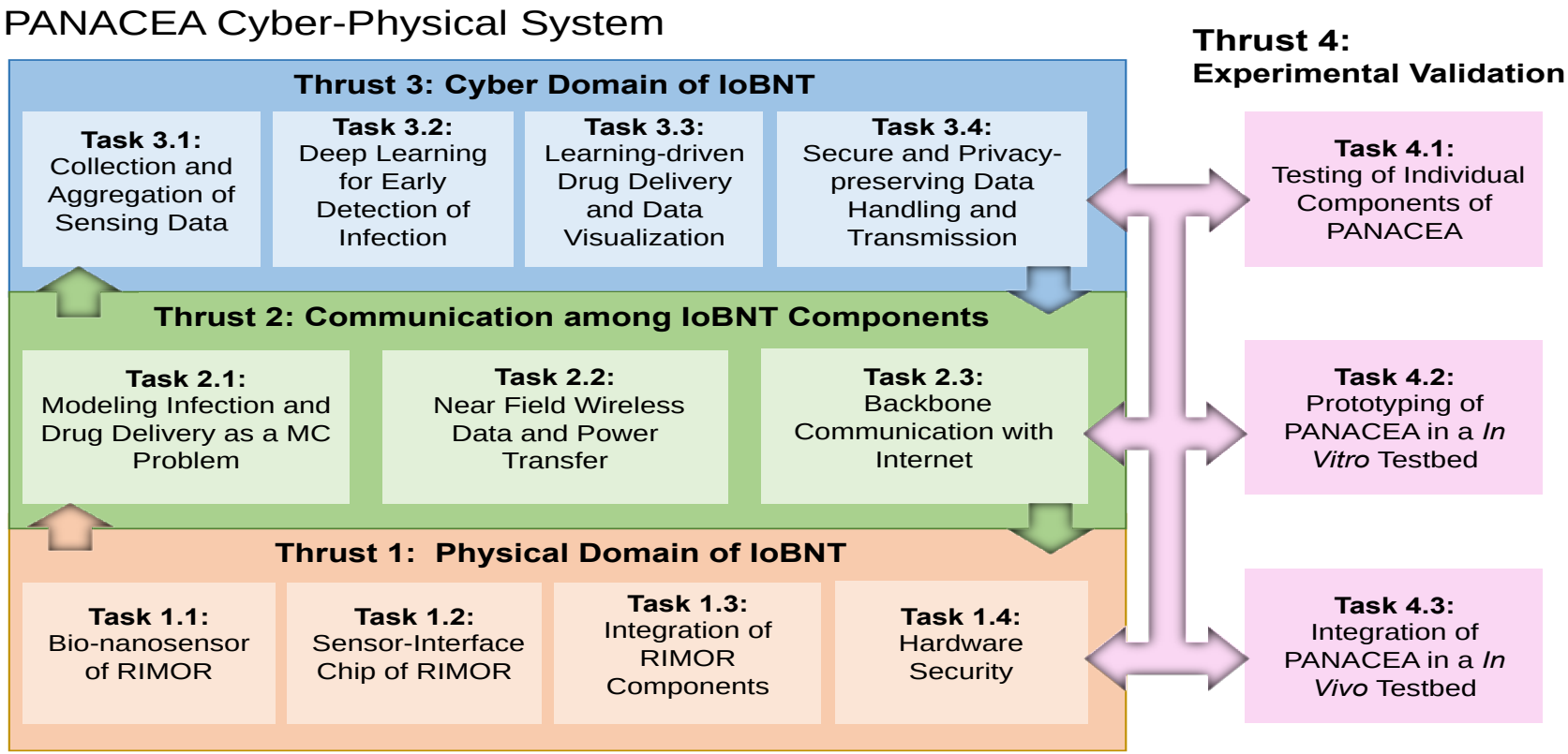


APPLICATION

BIO-NANOTHING NETWORKS FOR EARLY DETECTION OF PNEUMONIA IN IMMUNOCOMPROMISED PATIENTS

- Problem: Infections in Immunocompromised Patients
- Pseudomonas aeruginosa infections are very problematic
- Responsible for infections of
  - Hospital acquired infections
  - Cystic fibrosis and burn patients
  - Chemo Patients
- Resistant to a large spectrum of antibiotics
- Can infect various organs such as lungs, urinary tract, kidney, and skin.

FRAMEWORK OF THE PROJECT



THRUST 1: CYBER SPACE OF IoBNT

Challenges:

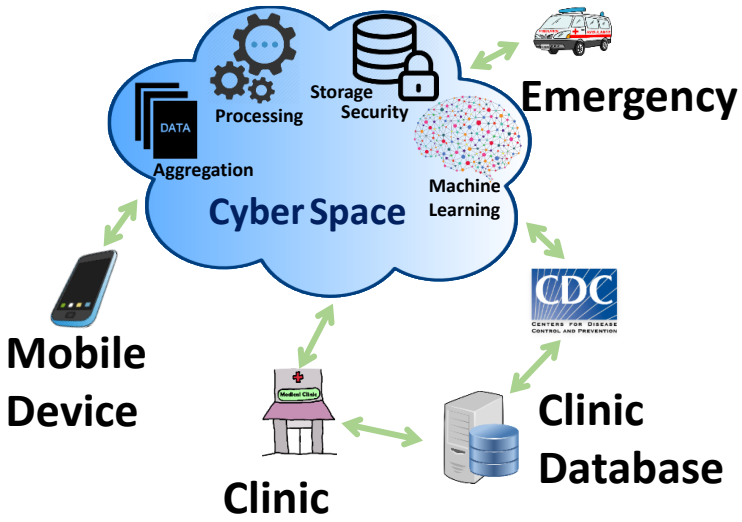
- How to effectively sense date by RIMOR and deliver to the cloud ?
  (Energy and transmission constraints)

* How to early detect forthcoming infections with high accuracy ?

- Patient health data is very sensitive
  - How to relay personal data to clinic securely and privately ?

THRUST 1: CYBER SPACE OF IoBNT

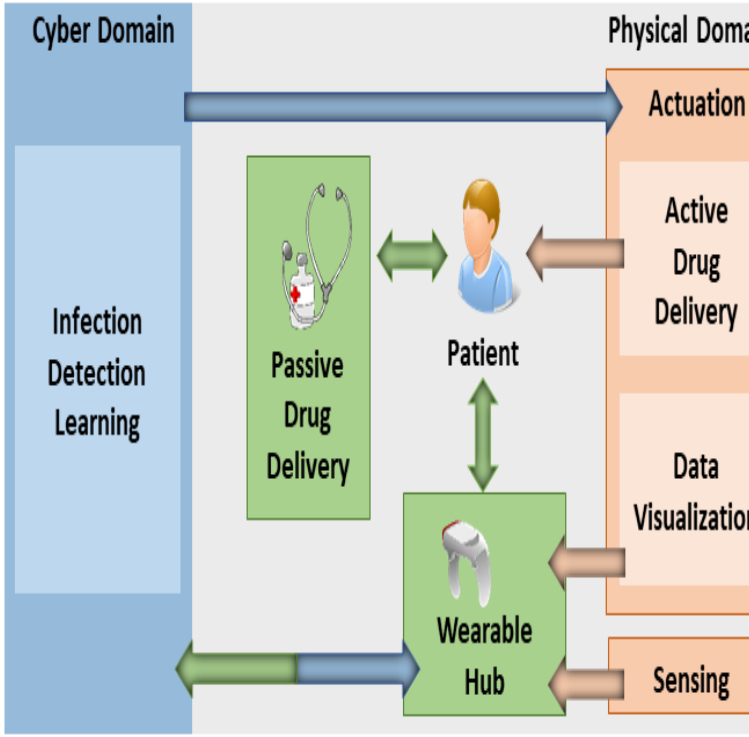
- **Research Efforts Pillars:**
  - Sophisticated data aggregation and visualization algorithms
  - Cutting-edge DL techniques
  - Learning-based actuation technologies
  - Secure and Privacy-preserving Information Handling



THRUST 1: CYBER SPACE OF IoBNT

Collection and Aggregation of Sensing Data

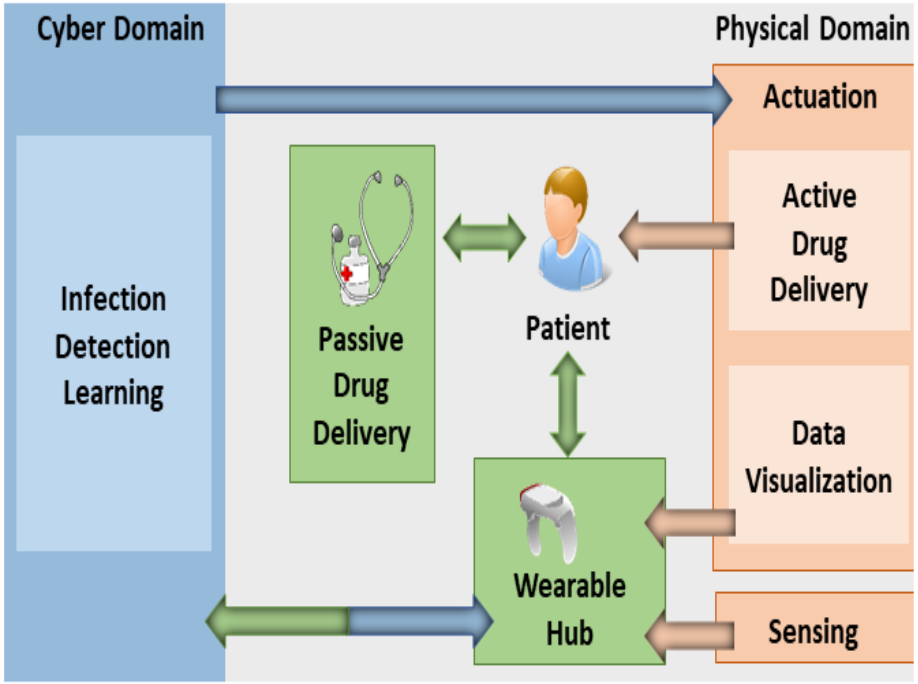
- Large number of RIMORs → Tremendous Amount of Sensing and Monitoring Data
- How much of this info can be effectively transmitted to Cyber domain?
- Investigate trade-offs between data redundancy, power consumption and detection accuracy



THRUST 1: CYBER SPACE OF IoBNT

DL for Early Infection Detection

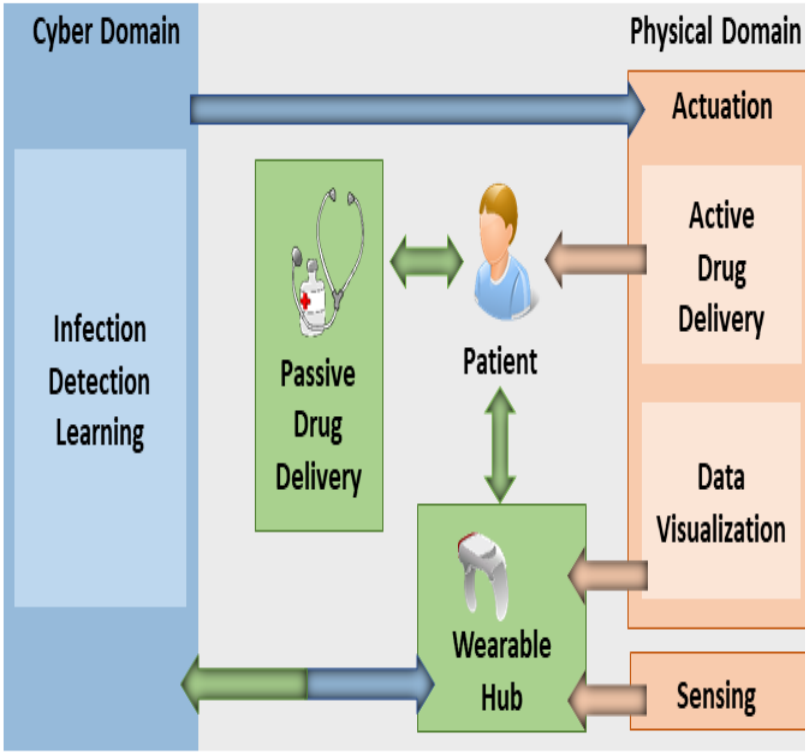
- **ML will be used for analysis of high-dimensional and multimodal biomedical data generated by the RIMORs**
- **DL enables feature learning directly on raw sensor data based on high-level supervised objectives**
- **Design DL algorithms for complex and non-deterministic infection detection**



THRUST 1: CYBER SPACE OF IoBNT

Learning-driven Drug Delivery and Data Visualization

- Stop/alleviate infection from spreading by
  - Active Drug Delivery:
    - Automated antibotic and enzyme delivery by implanted or dressing devices
  - Passive Drug Delivery:
    - Alerted patient takes antibiotics orally by the suggestion of PANACEA/ doctor
- Provide a reliable data visualization platform to access and analyze collected data
- Enable human-machine interactions between patients, caregivers and the PANACEA.



THRUST 1: CYBER SPACE OF IoBNT

Secure and Privacy-preserving Data Handling and Transmission

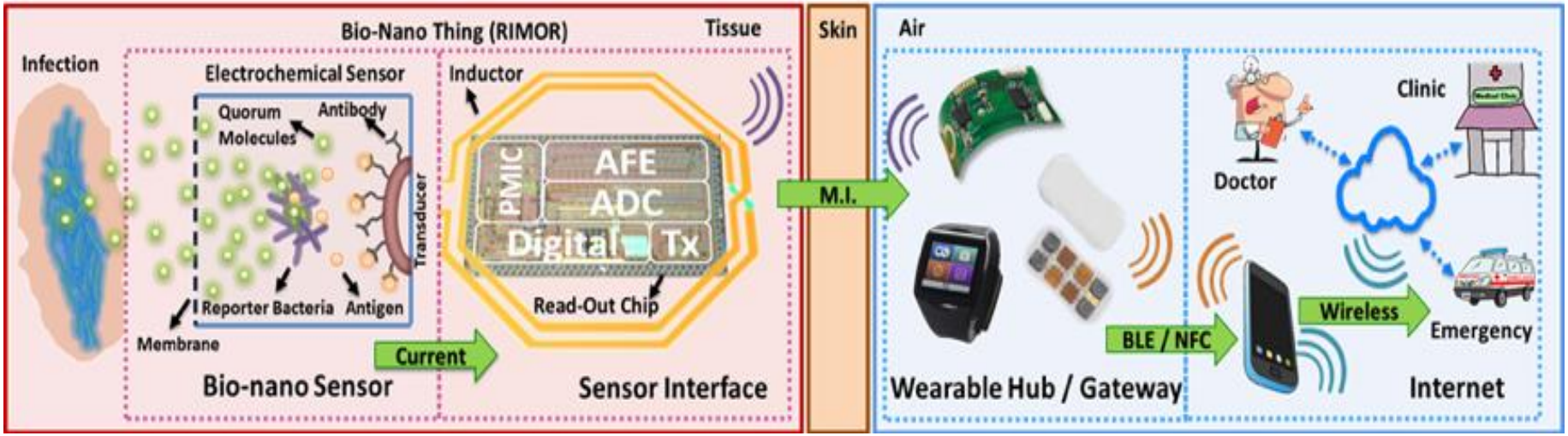
- **Design a secure and low-complexity HW and cyber platform**
  - **HW Embedded Security:**
    RIMOR and wearable hub designed against hardware and side channel attacks
  - **Authentication, Confidentiality, Integrity, and Availability:**
    Design lightweight asymmetric authentication protocols

- **Develop privacy-preserving data storage and processing protocols**
  - **Homomorphic Encryption Techniques:**
    Efficient computation over encrypted data
  - **Trusted Execution Environments:**
    Such as Intel SGX to decrypt and compute over patient-specific data within secure enclaves (preventing unauthorized access by the cloud provider/OS)

THRUST 2: PHYSICAL DOMAIN OF IoBNT

Bio-Nanothing called RIMOR

- **Hardware**: Design and Fabrication
- **Bio-nanosensor**→measures QS communication representing infection
- **Sensor Interface Electronics**→processes sensor data
- **Inductor**→wireless power and data transfer over magnetic-induction



THRUST 2: PHYSICAL DOMAIN OF IoBNT

Challenge 1: Designing Bio-Nanosensor

a) **Electrochemical Sensor**

Functionalized electrodes directly bind with QS molecules

b) **Bacterial Sensor 1**

An engineered reporter bacteria produces an electroactive product upon reception of QS molecules

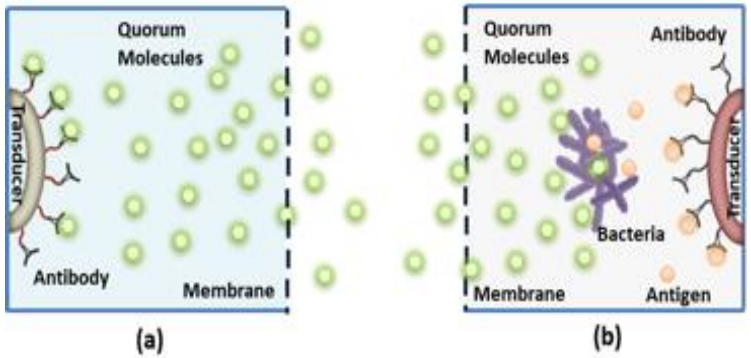
An electrochemical sensor generates current corresponding to the concentration of QS received

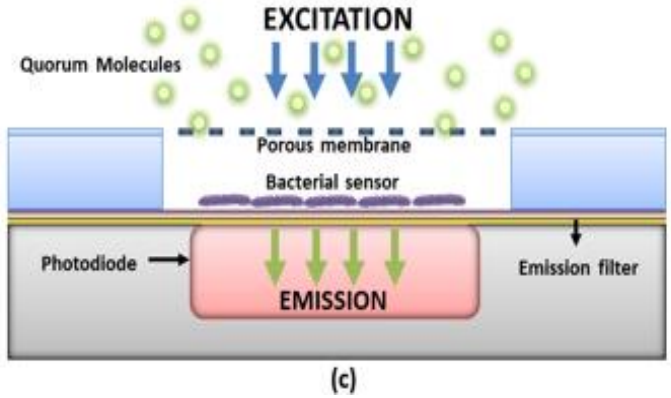
c) **Bacterial Sensor 2**

An engineered reporter bacteria produces bioluminescence upon reception of QS molecules

A light sensor generates current corresponding to the **concentration of QS received**

Maintaining live bacteria inside the sensor is difficult and the sensing process is noisy.

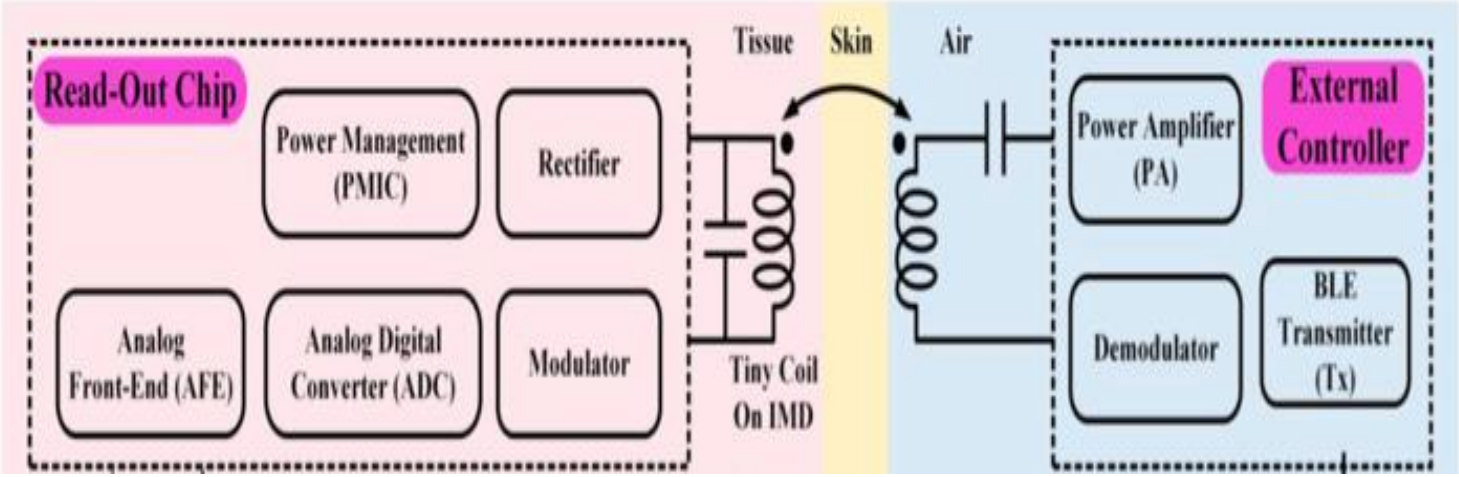




THRUST 2: PHYSICAL DOMAIN OF IoBNT

Challenge 2: Designing Sensor Interface Electronics

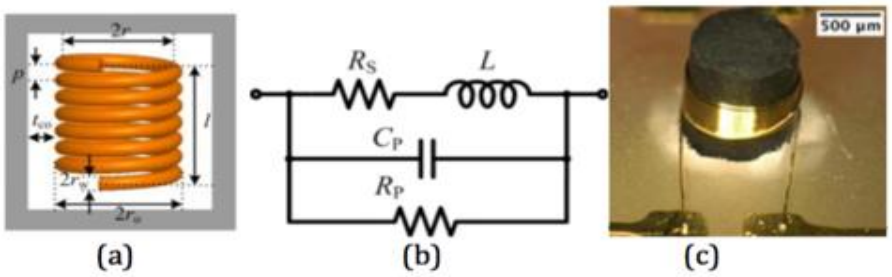
- Electronics to process biosensor signal
  - Deep-submicron ASIC technology application-specific design
  - Ultra-low power design since energy is limited by harvesting
  - Ultra-low noise since biosensor outputs are very low voltage/current



THRUST 2: PHYSICAL DOMAIN OF IoBNT

Challenge 3: Inductor for MI Communication & Power Transfer

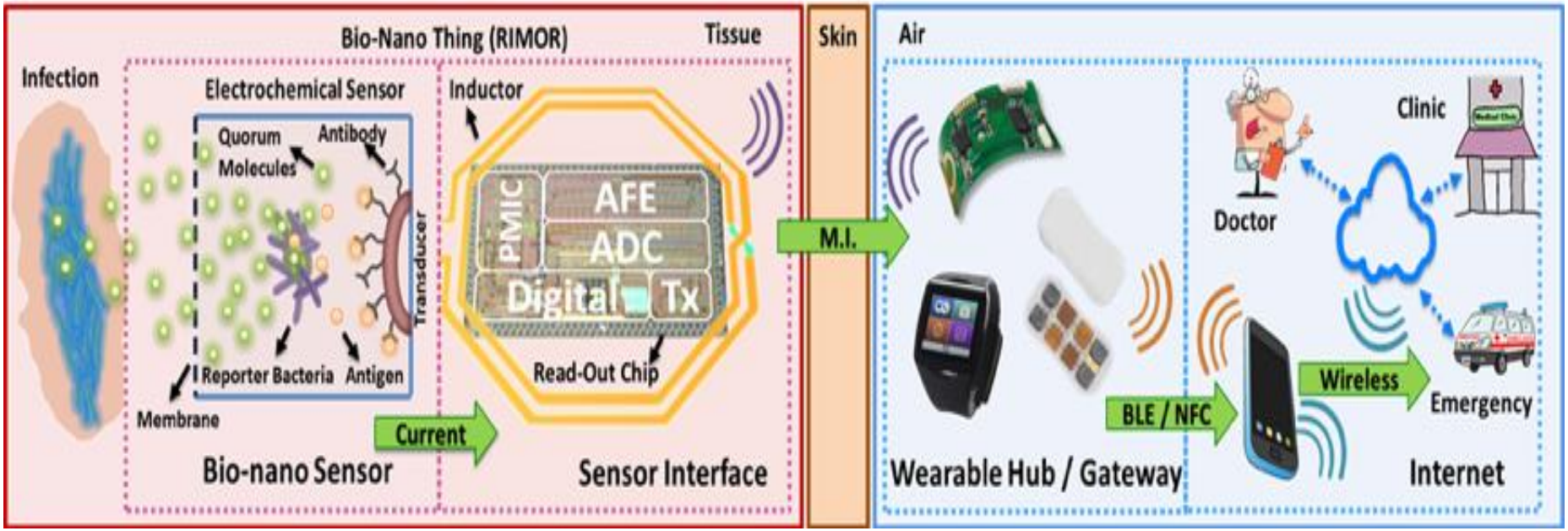
- Wireless Simultaneous Power and Data Transfer (WPT)
  - **Efficient and reliable designs of coils to connect RIMOR to wearable hub**



a) 3D rendering of a solenoid coil, showing its key geometrical parameters
b) Lumped RLC model of a solenoid coil, showing its parasitic resistance and capacitance
c) An example bonding wire coil.

THRUST 3: COMMUNICATION AMONG IoBNT COMPONENTS

- **Developing novel communication techniques and networking protocols to transfer information from the body to the cyber world**

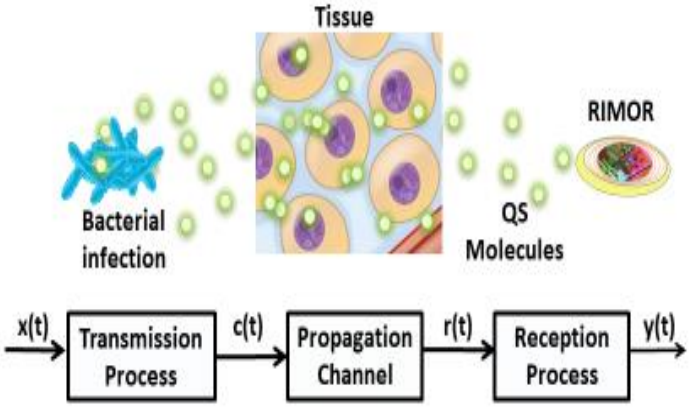


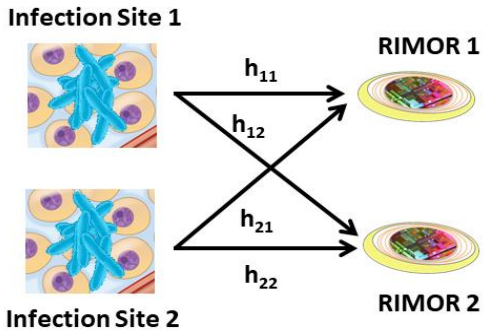
THRUST 3: COMMUNICATION AMONG IoBNT COMPONENTS

Challenge 1: Modeling Infection as a Molecular Communication Problem

Solution: MIMO Molecular Communication Channels

- Infectious bacteria communicate with each other using QS
- Spatio-temporal distribution of concentration of QS molecules provides info about infection
- RIMOR's will sense QS molecule concentration to detect infection
- Develop MC channel models for the propagation of QS molecules within tissues
  - Time-varying channels based on diffusion in interstitial fluid, within cells and among cells
  - Shadowing by tissue structures
  - Multipath effects



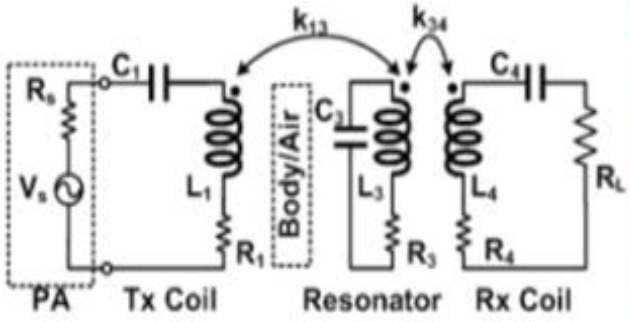


THRUST 3: COMMUNICATION AMONG IoBNT COMPONENTS

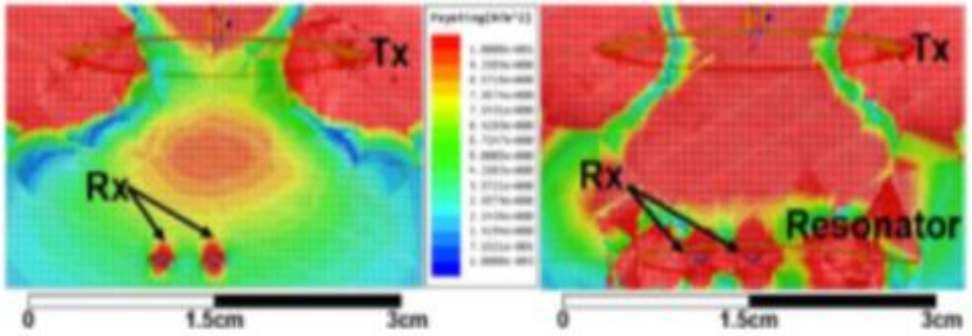
Challenge 2: Wireless Data Transfer from RIMORs to Wearable Hub

SOLUTION: Wireless Power and Data Transmission via MI

- Design EM coupled Tx/Rx for MI communication
  - Deliver enough power with very small mm-sized inductor coils
  - Keep temperature and body exposure to EM field remain within safe limits
- Use IR-UWB with low frequency such as 13.56 MHz
- Design novel energy harvesting systems



Equivalent Circuit Model for TX/RX



Poynting vectors for 2-coil and 3-coil links [Poynting vector represents the directional energy flux (the energy transfer per unit area per unit time)]

THRUST 4: EXPERIMENTAL VALIDATION

TASK 1. TESTING OF INDIVIDUAL COMPONENTS OF PANACEA

- **Testing of RIMOR Components**
  - Bio-Nanosensor
  - Sensor-Interface Chip
- **Testing of Wearable Hub**
- **Testing of Communication Protocols**
  - MC Models for Infection Detection and Mitigation
  - Magnetic-Induction Link between RIMOR and Wearable Hub
  - Backbone Internet Connectivity and Networking Protocols

THRUST 4: EXPERIMENTAL VALIDATION

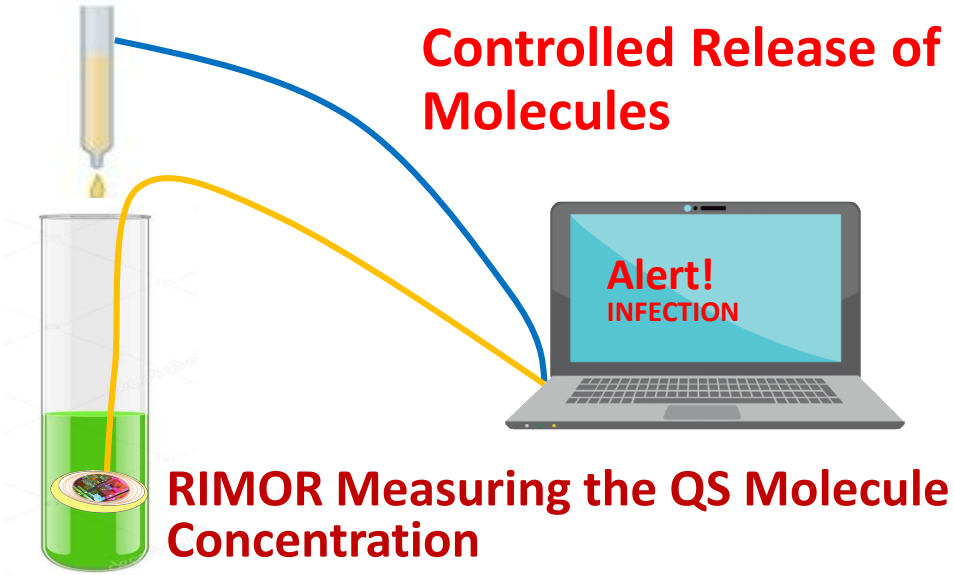
TASK 1. TESTING OF INDIVIDUAL COMPONENTS OF PANACEA

- **Testing of CPS Algorithms**
  - Data Aggregation Algorithms
  - Learning Engine
  - Closed loop with Passive Delivery
  - Security Protocols and Hardware Counter Measures

THRUST 4: EXPERIMENTAL VALIDATION

TASK 2. PROTOTYPING OF PANACEA IN AN "IN VITRO" TESTBED

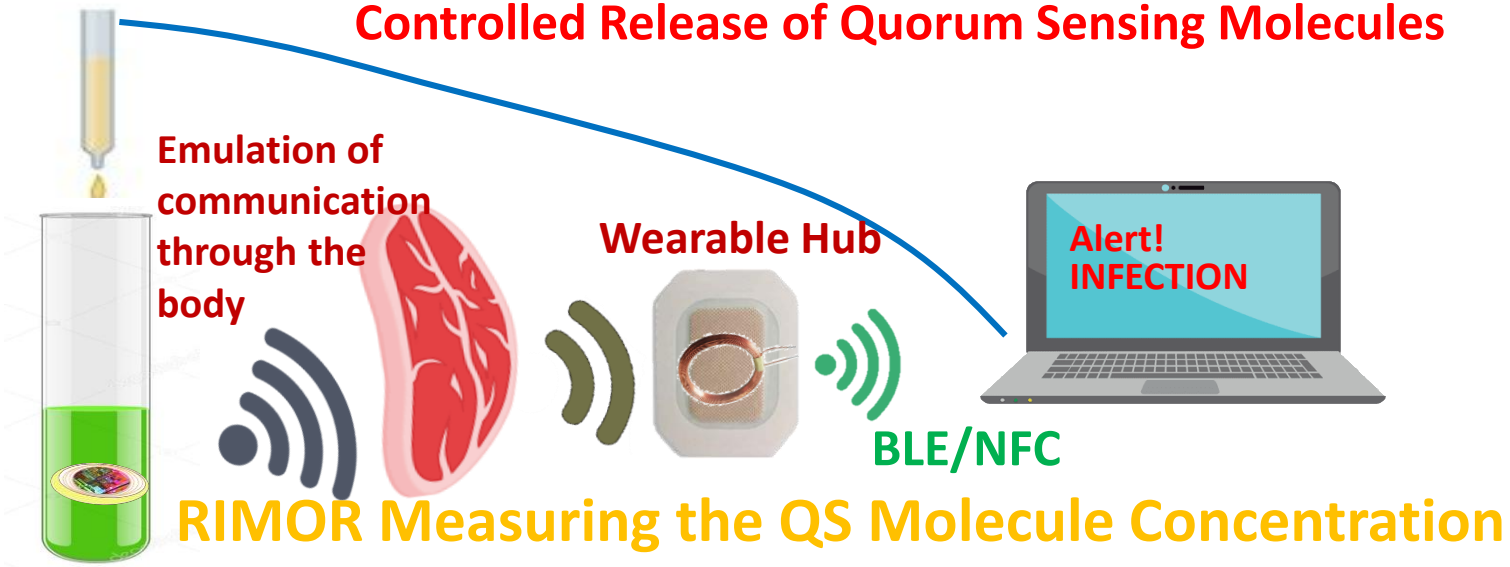
- Experimental Verification of RIMOR



THRUST 4: EXPERIMENTAL VALIDATION

TASK 2. PROTOTYPING OF PANACEA IN AN "IN VITRO" TESTBED

- Experimental verification of Communication between RIMOR and Wearable Hub



THRUST 4: EXPERIMENTAL VALIDATION

TASK 3. INTEGRATION OF PANACEA IN AN "IN VIVO" TESTBED

- Monitor infection on individual rodent models
- Outcome of infection is quantified by the time to morbidity and/or colony-forming units of bacteria

STANDARDIZATION EFFORTS IN MC

- IEEE P1906.1.1 - Standard Data Model for Nanoscale Communication Systems
  - IEEE 1906.1-2015 - IEEE Recommended Practice for Nanoscale and Molecular Communication Framework 2015

- Very basic

- Nano-communication umbrella with MC and THz

- Overlooks challenges arising from the biological nature of MC

→ A Unified Framework for MC is needed!

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Thank you