Cost effective population screening and testing for Covid-19

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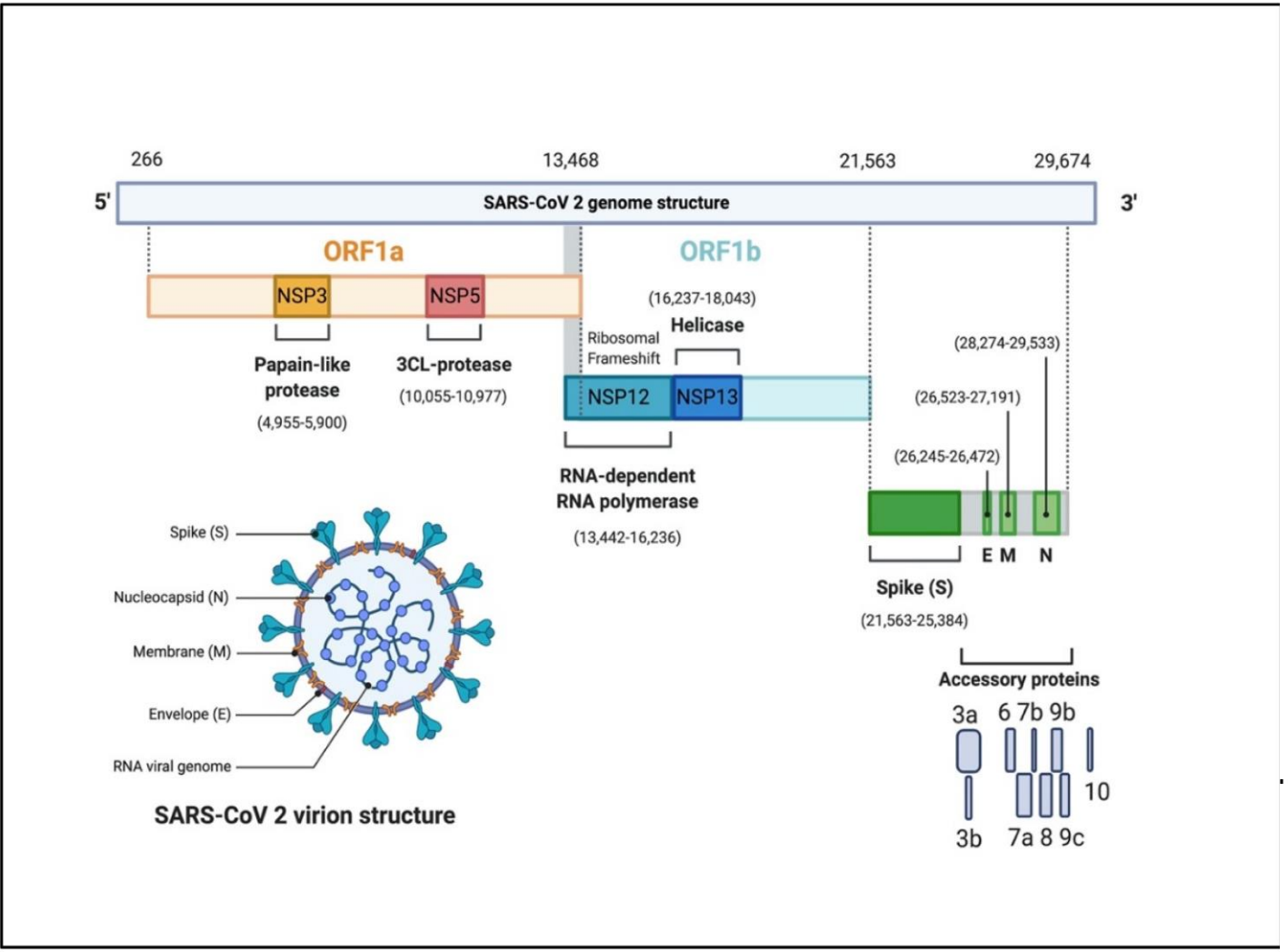
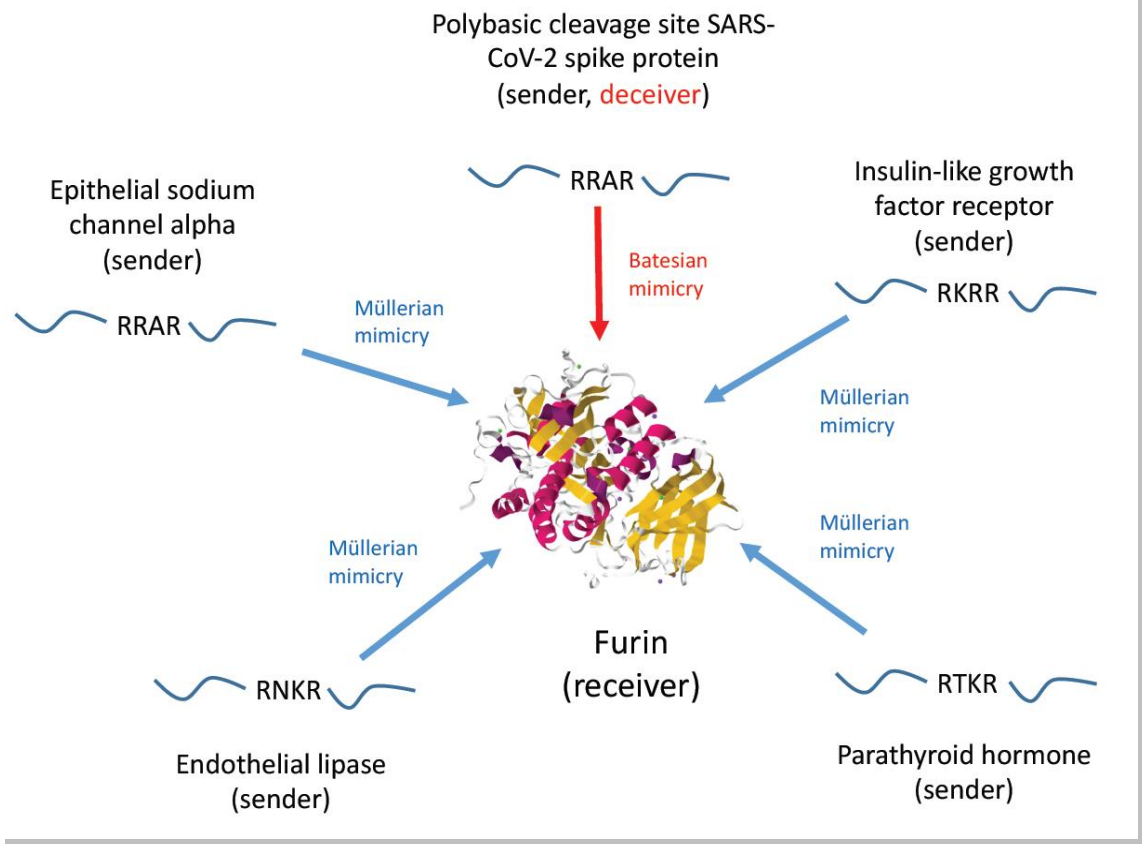
Collaborators: **Charles Cantor**, Manoj Gopalakrishnan, Anurag Agrawal, Bud Mishra, Lee Chou, Foy Sayas, Vamsi Veeramachaneni

The Beast





Stephen Massey and Bhubaneswar Mishra

BioMimicry and Signalling Games

J of Royal Society Interface 2018

COVID-19 is a wicked social problem! [Rittel & Webber 1973]

1. There is no definitive formulation of a wicked problem
2. Wicked problems have no stopping rule
3. Solutions to wicked problems are not true or false, but good or bad
4. There is no immediate or no ultimate test of a solution to a wicked problem
5. Every solution to a wicked problem is a “one shot” operation; because there is no opportunity to learn by trial and error , every attempt counts
6. Wicked problems do not have an exhaustive describable set of potential solutions, nor a set of permissible operations that can be used in a plan.
7. Every wicked problem is essentially unique
8. Every wicked problem can be considered to be a symptom of another problem
9. The existence of a discrepancy in representing a wicked problem can be explained in numerous ways
10. The planner has no right to be wrong

Approaches: **Authoritative, Competitive, Collaborative**

Maximum decrease in mortality & morbidity per rupee spent

- **Campus:** “people, buildings, and grounds affiliated to a given institution”
- Site of productive activity
- People in close proximity through the working day
- Keep people safe
- Help people feel safe
- Regulatory compliance

Uncompromisables:

- Reflex to State Health and ICMR guidelines for all clinical actions
- Respect personal liberties
- Maintain highest ethical standards of consent, information, fairness
- Equity in access for all services

Assumptions:

A. We will need the ability to test ***campus populations*** (industry/colony/research park/academic campus) repeatedly for SARS-Cov2 RNA, Antigen, Antibodies until vaccination and inexpensive therapies become available

B. High Speed, Low Cost, Accessible Testing Platforms will soon be available

C. The cost of doing thorough testing at population scale "*one individual at a time*" is untenable. Will need to prioritize using *intelligent systems*:

- Smart Contact Tracing
- Modeling
- Pooling Strategies

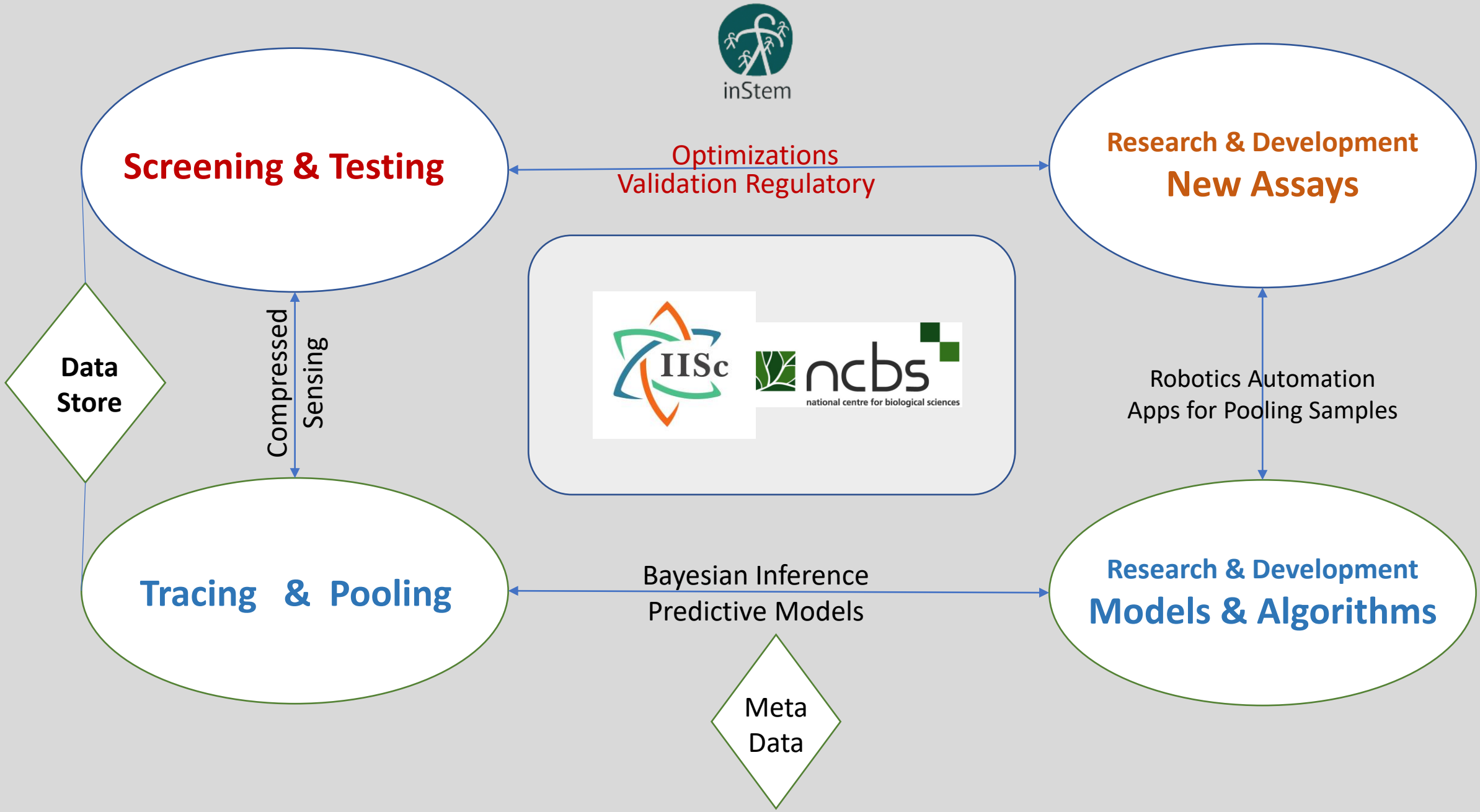
D. "**Testing alone** has proved no match for SARS-CoV2 **once it overwhelms** local governments' abilities to trace an infected person's contacts and forces those who were exposed to self-quarantine." *US Experience reported in NY Times – Cf. Bangalore as of 20-07-2020*

Screening and Testing a Campus Population

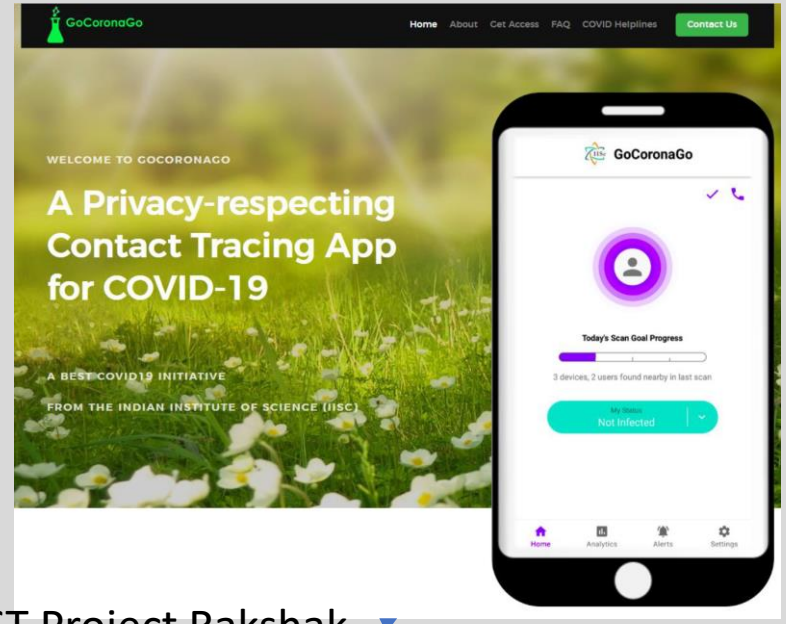
- A **test** has high accuracy meaning **high sensitivity** (few false negatives) and **high specificity** (few false positives). Usually a diagnostic test protocol requires **regulatory approval**, and the results are reported to the subject (patient).

- A **screen** can have less sensitivity and less specificity than a test. Typically a screen is used to decide whether or not to test a subject. The results of the screen are sometimes **not reported to individual patients**.

- For example **antibody screens (sero-surveillance)** for infection or **contact tracing** based on mobile apps - may not be accurate enough to inform individual patients but may be useful for campus health monitoring purposes

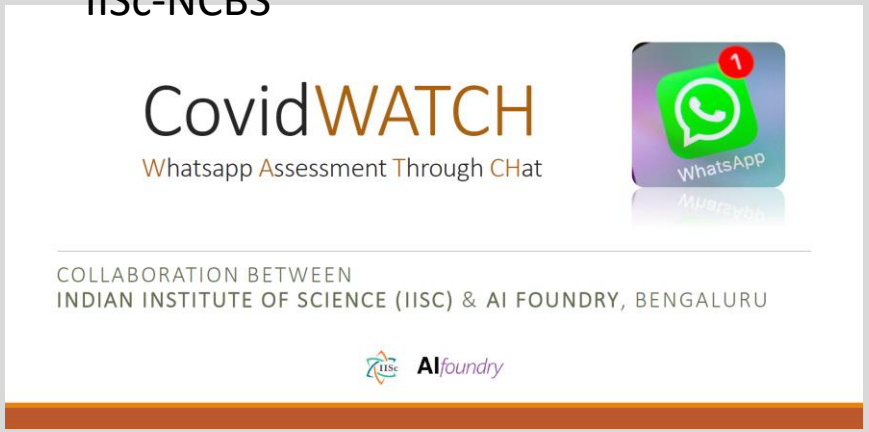

inStem
Screening & Testing
Optimizations
Validation Regulatory
Research & Development
New Assays
Data
Store
Compressed
Sensing
IISc
ncbs
national centre for biological sciences
Robotics Automation
Apps for Pooling Samples
Tracing & Pooling
Bayesian Inference
Predictive Models
Research & Development
Models & Algorithms
Meta
Data

Models and Algorithms



DST Project Rakshak
IISc-NCBS

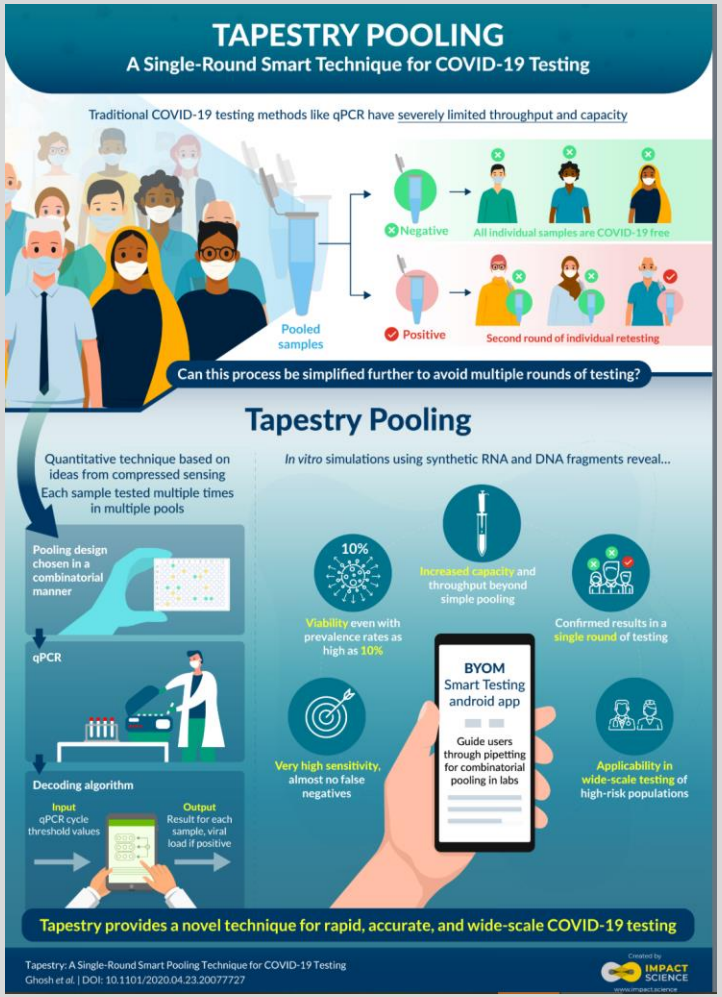
Contact Tracing



ChatBot Self-Assessment (Aarogya Setu)

Compressed Sensing

IITB-NCBS-Wyss(Harvard)



Models and Algorithms - 2

How Reliable are Test Numbers for Revealing the COVID-19 Ground Truth and Applying Interventions?

Aditya Gopalan Himanshu Tyagi

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COVID-19 Epidemic:

Unlocking the Lockdown in India

(Working Paper)

IISc-TIFR Covid-19 City-Scale Simulation Team

*Indian Institute of Science, Bengaluru

†TIFR, Mumbai

19 April 2020

Suppress, and not just flatten:Strategies for Rapid Suppression of COVID19 transmission in Small World Communities

CHIRANJIB BHATTACHARYYA, Indian Institute of Science
V VINAY, Ati Motors and Chennai Mathematical Institute

Badges and Pool testing with exponential backup: Aloha Protocol

Inavamsi Enaganti, Bud Mishra, Jantine Broek, Shirshendu Chatterji, …

Screening and Testing

RNA Testing:

Open RT-PCR systems (Bio Rad, ABI,…)
Reagents/Kits (Atma nirbhar)
Closed Systems (Roche, Cepheid, MICO BioMed/ MediSys, TrueNat – BigTecMolBio*)
Mass Array Platforms: Agena, Star Array (NTU)
Next generation Genome Sequencing: Illumina, Nanopore, M
CRISPR POC

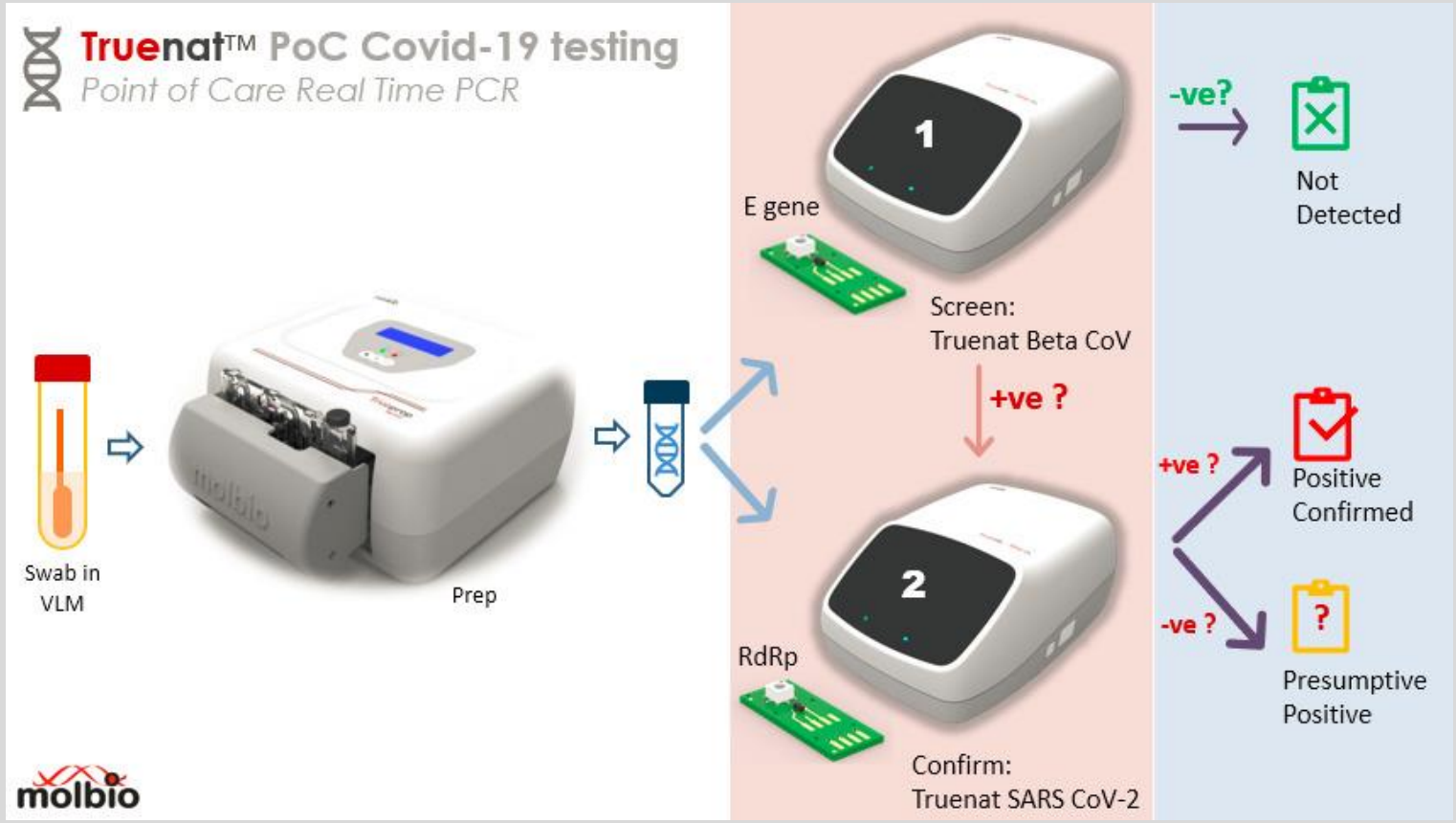
AntiBody (IgM) IgG Testing:

ELISA Tests (ICMR-Zydus Cadilla, Syngene-HiMedia, …)
ABBOTT (chemiluminescent microparticle immunoassay (CMIA))

Antigen Testing:

Truenat™ Beta CoV & Truenat™ SARS CoV 2

- Based on WHO recommended screening target in covid-19 genome (E gene & RdRp)
- Highly sensitive test – uses advanced enzyme chemistry.
- Semi quantitative results – indicate viral load & severity of infection
- Every run has internal control (RNAseP) to validate swab collection adequacy and run status



Research & Development Projects (Informatics)

1. Campus mobility graph as a ground zero project.

2. Digital Health Initiatives. How does this project relate to the Blueprint for digital health proposed by the Ministry of Health and WHO.

3. Adaptive Covid Testing – a game theoretic approach. Behavioural experiments on Campuses. [collaboration with B Mishra et al – Courant]

4. IHEC/Internal Review Board – data privacy, consent and research with human subjects in the context of contact tracing, screening and testing in a campus. A technology and society research project

Research & Development (Assay Development)

- Saliva as a Sample: Viral titer is high in most saliva samples; Patient can self test without discomfort; Repeated testing is practical. (CSIR, Strand/UChicago, Rutgers/Lee Chou)
- RNA Extraction can be optimized 1-5 minute heat treatment (CSIR, Strand)
- Antibody tests can be done on a drop of blood - they can be self tested or tested by pairs of people helping each other
- Including *viral clade identification* as a part of the nucleic testing should be tried because it has great potential to make contact tracing much more definitive

FDA U.S. FOOD & DRUG ADMINISTRATION

May 7, 2020

Christian Bixby
Assistant Director, Research and Clinical Lab Services, RUCDR
Rutgers Clinical Genomics Laboratory-Rutgers University
604 Allison Road,
Piscataway, NJ 08854

Device:	Rutgers Clinical Genomics Laboratory TaqPath SARS-CoV-2 Assay
Company:	Rutgers Clinical Genomics Laboratory at RUCDR Infinite Biologics – Rutgers University ("Rutgers Clinical Genomics Laboratory").
Indication:	Qualitative detection of nucleic acid from Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in oropharyngeal (throat) swab, nasopharyngeal swab, anterior nasal swab, mid-turbinate nasal swab, and bronchoalveolar lavage (BAL) fluid from individuals suspected of COVID-19 by their healthcare provider. This test is also for use with saliva specimens that are self-collected at home or in a healthcare setting by individuals using the Spectrum Solutions LLC SDNA-1000 Saliva Collection Device when determined to be appropriate by a healthcare provider.
Authorized Laboratories:	Testing is limited to Rutgers Clinical Genomics Laboratory (RCGL) at RUCDR Infinite Biologics – Rutgers University, Piscataway, NJ, that is a Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a certified high-complexity laboratory.

Electrical Stimulation of Salivary Flow in Patients with Sjögren's Syndrome

M. STELLER, L. CHOU, and T.E. DANIELS

Department of Stomatology, School of Dentistry, University of California at San Francisco, San Francisco, California 94143-0512

FDA U.S. FOOD & DRUG ADMINISTRATION

July 8, 2020

Niall J. Lennon, Ph.D.
Institute Scientist and Sr. Director
Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard
320 Charles Street
Cambridge, MA 02141

Device:	CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay
Laboratory:	Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard
Indication:	Qualitative detection of nucleic acid from SARS-CoV-2 in upper respiratory specimens (such as nasopharyngeal, oropharyngeal, nasal, and mid-turbinate swabs, nasopharyngeal wash/aspirate or nasal aspirate specimens) and bronchoalveolar lavage specimens from individuals suspected of COVID-19 by their healthcare provider. Testing is limited to the Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard located at 320 Charles Street, Cambridge, MA 02141 which is certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

Global Options

Organization

- **Campus Rakshak Task Force**
  - Senior Leadership – Making recommendations on the return of students and staff to campus
- **Campus Safety Implementation Team**
  - Will develop the policies, procedures, guidelines, strategies and tactics that will enable the Campus to further its discovery and learning missions in the safest possible ways. Assisted by many subcommittees.
- **Advised by Science**
  - Subject matter experts and external medical experts in a variety of areas and disciplines, including infectious disease, epidemiology, clinical science, human and animal sciences, pharmacy, public safety and risk assessment, privacy and employee benefits.

Principles to Protect our Campus

1. Expect each Campus Member to assume personal responsibility to Protect Campus — myself, others, our community.
2. Implement personal health safety practices and protocols.
3. Enact health safety changes in physical spaces.
4. Offer a range of instructional options for students, staff and faculty.
5. Identify and protect the most vulnerable members of the community.
6. Engage our stakeholders with consistent, compelling and timely communication and clear guidance.
7. Advance our research mission in a safe and responsible way.
8. Anticipate and plan for contingencies.

Next Steps:

- Proposal for a “Secured Campus” technology platform that includes screening, testing and tracing which can be utilized nation wide.
- Scope the testing technologies that can be deployed effectively in our campuses with cost effective repeated testing of “at risk” campus residents and visitors.
- A business model that would attract a commercial operator (could be a campus startup) in the clinical diagnostics space to manage the facility at campuses that may not want to develop institutional lab operations.