Group Testing for Efficient SARS-CoV-2 Assessment

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Thanks to: ONR N00014-15-1-2550, NSF CNS-1213128, NSF CCF-1410009,
ARO W911NF1910269, NSF CPS-1446901
Design of Experiments

Sir Ronald Fisher
1890-1962
More Broadly

Herman Chernoff
1923-

David Blackwell
1890-1962

Abraham Wald
1902-1950
Classical SPRT

- Sequential probability ratio test
  - Samples: $y_m = [y_1, y_2, \ldots, y_m]$

- Likelihood ratio: $L_m(y_m) = \frac{p_{y_m|s_1}}{p_{y_m|s_0}}$

- Detection rule: $\delta(L_m(y_m)) = \begin{cases} s_0, & L_m(y_m) \leq A \\ s_1, & L_m(y_m) \geq B \\ \text{sample}, & \text{else} \end{cases}$
Controlling Observations

observation = state, control

\[ y = f(x, u) \rightarrow \hat{x} \]

active hypothesis testing

Jovanov et al. Journal of NeuroEngineering and Rehabilitation 2005
Different sensors are good at discriminating different states

True state influences best experiment/observations
The quality of observations

- How to quantify informativeness?

- Choice of control makes hypotheses easier to distinguish

\[ u^\alpha \] control = choice of experiment

likelihood of a particular hypothesis

- Choice of control makes hypotheses easier to distinguish
Metrics for distributions

- Relative entropy (Kullback-Leibler distance)

\[ D(p\|q) = \sum_{x \in \mathcal{X}} p(x) \log \frac{p(x)}{q(x)} \geq 0 \]

\[ D(p\|q) \neq D(q\|p) \]

- Not a true distance – does not satisfy triangle inequality, asymmetry...

Active Hypothesis Testing

**EXPLORATION**

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**EXPLOITATION**

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policies/experiments
The quality of observations

- The most informative experiment depends on the true hypothesis.

- $u^\alpha$ control = choice of experiment
- likelihood of a particular hypothesis

- $u^\beta$

- $u^\gamma$

- $h_0$
- $h_1$
- $h_2$
- $h_3$
System Model

M people

\[ X = \begin{cases} 
0 & \text{if no anomaly} \\
1 & \text{if component } j \text{ anomalous} 
\end{cases} \]

controller decides who to test at each time

one test for each person

\[ X \in \{0, 1, \ldots, M\} \]

\[ M = 7, X = 3 \]
System Evolution

We assume these are known

We will need to learn these

conditional density

Person $u$

Observation $y$

$U_1 = 1, Y_1$
$U_2 = 5, Y_2$
$U_3 = 2, Y_3$
$U_4 = 3, Y_4$

$p_0(y)$
$p_1(y)$
Goals

- Experiment Selection Strategy:

\[
(U_1, Y_1) \quad (U_2, Y_2) \quad \ldots \quad (U_n, Y_n) \quad \ldots \quad (U_N, Y_N) \quad \hat{X}_N
\]

\[
U_n \sim g_n(I_n)
\]

experiment choice – which person to test?

- Inference Strategy: decide infected or not infected

\[
\hat{X}_N \sim f(I_{N+1})
\]

not infected \( X = 0 \)

infected \( X \neq 0 \)
Define

\[ D^* = \max_{\alpha \in \Delta \mathcal{U}} \min_{j \in \mathcal{U}} \sum_{u \in \mathcal{U}} \alpha(u) D^u_j \]

\[ = \min_{\beta \in \Delta \mathcal{U}} \max_{u \in \mathcal{U}} \sum_{j \in \mathcal{U}} \beta(j) D^u_j \]

Lemma: we can compute \( D^* \)

\[ D^* = \left( \sum_{u \in \mathcal{U}} \frac{1}{D^u_u} \right)^{-1} \]

\( \alpha, \beta \) distributions

argmax: \( \alpha^* \)

argmin: \( \beta^* \)
Theorem:

**Strong converse:** from decomposition and strong converse in Polyanskiy, Poor and Verdu Trans IT 2010

\[ -\log \phi_N^* \leq \text{INV}_N \left( \epsilon_N + \frac{\epsilon_N}{\eta} \right) + \log \frac{\eta}{\epsilon_N} \]

\[ -\log \phi_N^* \geq \text{INV}_N \left( \epsilon_N - \frac{\epsilon_N}{\eta} \right) - O \left( \log \frac{\eta}{\epsilon_N} \right) \]

function of \( D^* \)

- Bounds enable the design of strategies

\( \text{INV}_N \): quantile function of \( \bar{Z}_N + D(\beta^* \parallel \bar{\rho}_1) \)
Comparisons

- Open-loop randomized (OPE): asymptotically optimal
  randomly select component from distribution $\alpha^*$
  uniform in symmetric case

- Deterministic adaptive (DAS): also asymptotically optimal
  at each time $n$, select the component $j$ that minimizes $Z_{n-1}(j) - \log \tilde{\rho}_1(j)$
  function of previous observations and experiment choices

- Example setting: two-people and binary observations
Numerical Results

Open-loop:
Not second-order optimal

Need to be adaptive for second-order optimality
Practical SARS-CoV-2 Testing

1. What are good testing strategies?
2. What is the role of cheap tests?
3. Can we pool tests?
Practical SARS-CoV-2 Testing

1. What are good testing strategies?
2. What is the role of cheap tests?
3. Can we pool tests?
Group Testing – pooling samples

- Used in WW2 to test soldiers for syphilis

- N tests $\rightarrow$ log (N) tests
Prior Belief: At Most One Anomaly

- Single anomaly at index 3
- No anomaly

Eventually anomaly is localized and sampled for confirmation

- All components grouped together to confirm there is no anomaly
- Initial groups aimed at searching

- No anomaly
Two Anomalies

Confirmation: normal components are pooled and anomalies are tested individually.

Initial tests are individual - known to be optimal with uniform prior - but groups are formed as belief improves.

Groups formed initially due to prior info.

Anomalies at 1 and 4.

Prior: Any number anomalous

Prior: At most two anomalous
A single type of test retesting enables achieving accuracy of 99.9%
Fully-adaptive Tests

- Perform a cheap test first on each individual – we consider tests with 80% and 90% accuracy
- Use the prior for group testing subsequently
- Can reduce number of group tests by 20%
- Performing cheap tests first better when the cost of cheap test is about 10-15 times smaller

Fully adaptive tests can take a lot of time – need to parallelize
Optimal test design is computationally expensive

We can exploit machine learning/neural network tools to compute optimal solution

- Have to do this carefully
  - recursive neural networks did not work
  - Need the output of experiment sequences
- Exploit structural properties of optimal solution to design NN

Challenges
Deep Q Network

- Evolution of expected confidence under hypothesis $h_0$ over time
  - DQN learns the best policy
- DAS close to optimal rate
- OPE asymptotically optimal but very slow convergence
- EJS not optimal
Other Strategies

**A x = b**

- **random**
- **coding theory: LDPC**
- **fixed pooling**
- **compressed sensing (lasso, AMP)**
- **optimization box**
- **LDPC decoder**

**NON-ADAPTIVE**, but can be parallelized
Contrasts

- Our method is data adaptive
  - More challenging to parallelize

- The test matters
  - Serological tests are blood based – easy to pool?

- Gold standard: PCR (polymerase chain reaction)
  - For SARS-CoV-2 test on RNA
  - Can parallelize

Wuhan tested millions of people for COVID-19 in just days. Could US cities do the same?

The city of Wuhan, China, where the COVID-19 outbreak first emerged, recently launched a campaign to test every one of its 11 million residents for the virus.

Mayo Clinic explainer
Contrasts

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June 10, 2020 — In a new study, Johns Hopkins researchers found that testing people for SARS-CoV-2 (COVID-19) too early in the course of infection is likely to result in a false negative test, even though they may eventually test positive for the virus.[1] This is important to understand since many hospitals are using these COVID tests to screen patients before imaging exams, diagnostic testing or procedures.
Conclusions

- Optimized solutions for a finite number of observations/tests
  - Not asymptotics as in traditional methods
- We can design for both the exploration and the exploitation phases
- We can accommodate different kinds of information
  - Prior medical history, outcomes of other measurements (temperature, symptoms)
  - We can accommodate different kinds of SARS-CoV-2 tests, each with different efficacies
- Optimal testing for hot spots?
- Challenges
  - Complexity
  - Unknown onset
  - Parallelization
References