

Adaptive Information

Goal: Estimate an unknown object $x \in \mathcal{X}$ from scalar samples

Information: samples of the form $y_1(x), \ldots, y_n(x)$, the values of certain functionals of x

Non-Adaptive Information: $y_1, y_2, \dots \in \mathcal{Y}$ non-adaptively chosen (deterministically or randomly) independent of x

Adaptive Information: $y_1, y_2, \dots \in \mathcal{Y}$ are selected sequentially and y_i can depend on previously gathered information, i.e., $y_1(x), \dots, y_{i-1}(x)$

Does adaptivity help?



































False Discovery RateFWER control: $\mathbb{P}(\text{one or more false discoveries}) \leq \alpha$ too conservativeAlternative: # false discoveries $\sim \alpha |\widehat{S}|$ number of false discoveries
should be a small fraction of
number of total discoveriesDefinition 3 Let $S := \{i : x_i \neq 0\}$ and let $\widehat{S}(y)$ denote an estimator of S.
The false-discovery proportion is $FDP(\widehat{S}) := \frac{|\widehat{S} \setminus S|}{|\widehat{S}|} = \frac{\#$ falsely discovered components
total # discovered componentsDefinition 4 The false-discovery rate is the expected value of the false-discovery
proportion $FDR(\widehat{S}) := \mathbb{E} \left[\frac{|\widehat{S} \setminus S|}{|\widehat{S}|} \right] = \mathbb{E} \left[\frac{\#$ falsely discovered components
total # discovered components



Theoretical Performance in High-Dimensional Limit

 $FDP(\widehat{S}) := \frac{|\widehat{S} \setminus S|}{|\widehat{S}|} = \frac{\# \text{ falsely discovered components}}{\text{total } \# \text{ discovered components}}$

Definition 5 The non-discovery proportion is

$$NDP(\widehat{S}) := \frac{|S \setminus \widehat{S}|}{|S|} = \frac{\# missed \ components}{\# \ true \ non-zero \ component}$$

Theorem 1 Assume x has $n^{1-\beta}$, $\beta \in (0,1)$, non-zero components of amplitude $\sqrt{2r \log n}$, r > 0. There exists a threshold test that yields an estimator $\widehat{S} = \widehat{S}(y)$ such that if $r > \beta$, then as $n \to \infty$,

$$\operatorname{FDP}(\widehat{\mathcal{S}}) \xrightarrow{P} 0$$
, $\operatorname{NDP}(\widehat{\mathcal{S}}) \xrightarrow{P} 0$,

where \xrightarrow{P} denotes convergence in probability. Moreover, if $r < \beta$, then there does not exist a coordinate-wise thresholding procedure that can guarantee that both quantities above tend to 0 as $n \to \infty$.





Science and Data Analysis

Often there are no components that exceed $\sqrt{\log n}$ in magnitude!

Nothing is statistically significant at FWER=5% or FDR=5%.

What's a scientist to do?

Take a closer look at the most significant components.

What do scientists need?

perhaps **not** an FWER/FDR certification

Principled guidance on how to design the next experiment (and the next, and the next...)

- * how many components should be re-tested
- * guarantees that important effects will not be overlooked or discarded prematurely

Sequential Experimental Design

Instead of the usual non-adaptive observation model

$$y_i = x_i + z_i, \ i = 1, \dots, n$$

suppose we are able to sequentially collect multiple noisy measurements of each component of x, according to

$$y_{i,j} = x_i + \gamma_{i,j}^{-1/2} z_{i,j}, \quad i = 1, \dots, n, \quad j = 1, \dots, k$$

where

j indexes the measurement steps

k denotes the total number of steps

$$z_{i,j} \stackrel{\text{iid}}{\sim} \mathcal{N}(0,1)$$

 $\gamma_{i,j} \geq 0$ controls the precision of each measurement

Total precision budget is constrained, but the choice of $\gamma_{i,j}$ can depend on past observations $\{y_{i,\ell}\}_{\ell < j}$.

Experimental (Precision) Budget

sequential measurement model

$$y_{i,j} = x_i + \gamma_{i,j}^{-1/2} z_{i,j}, \quad i = 1, \dots, n, \quad j = 1, \dots, k$$

The precision parameters $\{\gamma_{i,j}\}$ are required to satisfy

$$\sum_{j=1}^k \sum_{i=1}^n \gamma_{i,j} \leq n$$

For example, the usual non-adaptive, single measurement model corresponds to taking k = 1, and $\gamma_{i,1} = 1, i = 1, ..., n$. This baseline can be compared with adaptive procedures by allowing k > 1 and variable $\{\gamma_{i,j}\}$ satisfying budget.

Precision parameters control the SNR per component.

SNR is increased/decreased by

— more/fewer repeated samples or

— longer/shorter observation times

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total number of measurements $\approx 2n$







Distilled Sensing Theorem

Theorem 2 Assume $x \ge 0$ with $n^{1-\beta}$, $\beta \in (0,1)$, non-zero components of amplitude $\mu(n)$, and sequential measurement model DS with $k = \lceil \log_2 \log n \rceil + 2$, and precision budget distributed over the measurement steps so that $\sum_{j=1}^{k} R_j \le n$, $R_{j+1}/R_j \ge \delta > 1/2$, and $R_1 = c_1n$ and $R_k = c_k n$ for some $c_1, c_k \in (0,1)$. Consider the thresholding estimator based on the output of the DS procedure:

$$\widehat{\mathcal{S}}_{\mathrm{DS}} := \{ i \in I_k : y_{i,k} > \sqrt{2/c_k} \}$$

If $\mu(n)$ is any positive diverging sequence in n, then as $n \to \infty$

$$\operatorname{FDP}(\widehat{\mathcal{S}}_{\mathrm{DS}}) \xrightarrow{P} 0, \operatorname{NDP}(\widehat{\mathcal{S}}_{\mathrm{DS}}) \xrightarrow{P} 0$$

- Take $k \sim \log \log n$ steps, with geometric (decreasing) allocation of budget
- Discard the weakest half of measured components at each step
- Re-measure only surviving components

With very high probability will detect almost all components with amplitude \geq than some constant, independent of n







Experimental Budgets

Distilled Sensing acquires approximately 2n measurements: n in the first stage, $\sim n/2$ in the second, $\sim n/4$ in the third, etc.

But there are far fewer, $|S| \ll n$, relevant components to detect.

Can we find these components with less than n measurements? Yes, if we measure randomized combinations of the components.





The fluorescence data are very noisy, and so biologists employ a multistage adaptive experimental procedure to home-in on the important genes. The results of the first stage inform the design of the second stage. This is an example of feedback from data analysis to data collection. This is what scientists are doing all the time. The figure above shows the inferred network pathway exploited by the virus for the purposes of replication. Unfortunately, single gene deletions may not tell the whole story, since certain genes act together in concert. Such effects can only be detected through multiple gene deletions. Multiple deletion studies become daunting or impossible quite rapidly; e.g., there are 85 million pairwise deletions that can be considered in the case of Drosophila. Biologists have the technology (gene knockdowns) to study multiple deletions, but it is difficult to decide where to start and how to proceed.





stage 1: random combinations of all components stage 2: random combos top 1/2 components stage 3: random combos top 1/4 components stage 4: random combos top 1/8 components stage 5: random combos top 1/16 components stage 6: random combos top 1/32 components

support of random sensing matrix

Theorem 4 Assume $x \ge 0$ with $|\mathcal{S}|$ non-zero components of amplitude μ , and take $O(|\mathcal{S}| \log n)$ randomized DS measurements. If $\mu \succeq \log \log \log n$, then there is a threshold test guaranteeing that

$$\mathrm{FDP}(\widehat{\mathcal{S}}_{\mathrm{RDS}}) \xrightarrow{P} 0, \mathrm{NDP}(\widehat{\mathcal{S}}_{\mathrm{RDS}}) \xrightarrow{P} 0$$

In essence, this implies that we can identify most of the |S| relevant components using only slightly more than |S| measurements.



Key Elements of DS Theorem: Remove 1/2 the Noise





Key Elements of DS Theorem: Iteration

At each step of DS, $j = 1, \ldots, k$, define

- $s_i :=$ number of non-zero components
- $z_j :=$ number of zero components

Lemma 3 Let $0 < \varepsilon < 1/6$ and assume that $R_j > \frac{8(s_1+z_1)}{\mu^2}(1/2+\varepsilon)^{j-1}, j = 1, \dots, k-1$. Then $(1-\varepsilon)^{j-1}s_1 \le s_j \le s_1$

and

$$\left(\frac{1}{2}-\varepsilon\right)^{j-1}z_1 \le z_j \le \left(\frac{1}{2}+\varepsilon\right)^{j-1}z_1$$

for j = 2, ..., k with probability at least

$$1 - \sum_{j=1}^{k-1} \exp\left(\frac{-s_1(1-\varepsilon)^{j-1}}{2\sqrt{2\pi}}\right) - 2\sum_{j=1}^{k-1} \exp\left(-2z_1(1/2-\varepsilon)^{j-1}\varepsilon^2\right) \,,$$

With high probability each distillation keeps almost all the non-zero components and rejects about half of the non-signal components.

SNR increases at each step