Adaptive Sensing and Sparse Interactions



BIRS Workshop on Sparse Statistics Optimization and Machine Learning January 16-21 2011 Rob Nowak www.ece.wisc.edu/~nowak

Joint work with R. Castro, J. Haupt, M. Malloy and B. Nazer

Motivation: Inferring Biological Pathways



Motivation: Inferring Biological Pathways



microwell array

Challenges:

- 1. very low SNR data and huge number of experiments and tests
- 2. non-linear interactions

Challenge 1: High-Dimensionality and Low SNR

nature

Vol 454|14 August 2008|doi:10.1038/nature07151

Drosophila RNAi screen identifies host genes important for influenza virus replication

Linhui Hao^{1,2}*, Akira Sakurai³*†, Tokiko Watanabe³, Ericka Sorensen¹, Chairul A. Nidom^{5,6}, Michael A. Newton⁴, Paul Ahlquist^{1,2} & Yoshihiro Kawaoka^{3,7,8,9}

How do they confidently determine the ~100 out of 13K genes hijacked for virus replication from extremely noisy data?

Sequential Experimental Design:

- **Stage 1**: assay all 13K strains, twice; keep all with significant fluorescence in one or both assays for 2nd stage $(13K \rightarrow 1K)$
- **Stage 2**: assay remaining 1K strains, 6-12 times; retain only those with statistically significant fluorescence $(1K \rightarrow 100)$

vastly more efficient that replicating all 13K experiments many times

Feedback from Data Analysis to Data Collection



Challenge 2: Sparsity & Nonlinear Effects



Outline of Talk

I. Sequential Experimental Designs for High-Dimensional Testing

thresholds for recovery in high-dimensional limit:

non-adaptive designsSNR $\sim \log n$ sequential designsSNR \sim arbitrarily slowly growing function of n

2. Compressed Sensing of Sparse Multilinear Functions

number of compressed sensing measurements for sparse recovery:

linear sparsity $K \sim S \log n$ multilinear sparsity $K \sim \min\{S^2 \log n, S \log^3(S) \log n, S^\alpha \log^\alpha n\}$

where $\alpha \geq 1$ depends on pattern of sparsity

Sparse Signal Model

Let $x = (x_1, \ldots, x_n) \in \mathbb{R}^n$ be an unknown sparse vector; most (or all) of its components x_i are equal to zero.



Noisy Observation Model

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

 $z_i \stackrel{\text{iid}}{\sim} \mathcal{N}(0, 1)$



Suppose we want to locate just one signal component: $\hat{i} = \arg \max_i y_i$

Even if no signal is present, $\max_i y_i \sim \sqrt{2 \log n}$

It is *impossible* to reliably detect signal components weaker than $O(\sqrt{\log n})$

Threshold Tests

Our goal is to estimate the set of non-zero components: $S := \{i : x_i \neq 0\}$



Bonferroni Correction: To keep the error level small (e.g., less than 5%) the threshold must be on the order of $\sqrt{\log n}$.

False Discovery Rate Control (Ingster '97, Jin & Donoho '03)

Assume sublinear sparsity level: $|\mathcal{S}| = n^{1-\beta}$, $\beta \in (0,1)$



reliable detection iff $\mu \sim \sqrt{\log n}$!

Is there really a problem ?





Scanning Dead Salmon in fMRI Machine Highlights Risk of Red Herrings

By <u>Alexis Madrigal</u> September 18, 2009 | 5:37 pm | Categories: <u>Brains and Behavior</u>



An Alternative: 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 several independent 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

 \boldsymbol{j} indexes the measurement steps

 \boldsymbol{k} denotes the total number of steps

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

 $\gamma_{i,j} \ge 0$ 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

Fruit Fly Example

virus



How to find genes involved in virus replication ?

Sequential Design Idea

Budget: **k** assays, n tests/assay

Assay I: measure fluorescence of all n genes; discard n/2 genes with weakest fluorescence.

Assay 2: measure fluorescence for remaining n/2 genes, each tested twice (double SNR); discard n/4 genes with weakest fluorescence.

Assay 3: measure fluorescence for remaining n/4 genes, each tested four times (quadruple SNR); discard n/8 genes with weakest fluorescence. continue distilling....

Idealized Example



Distilled Sensing

$$\begin{array}{l} \hline \textbf{Simple Distilled Sensing} \\ \text{initialize: } \mathcal{S}_{0} = \{1, \dots, n\}, \ \gamma_{i,j}^{-1} = 2 + \epsilon, \ \epsilon > 0 \\ \text{for } j = 1, \dots, k \\ 1) \text{ measure: } y_{i,j} \sim \mathcal{N}(x_{i}, 2 + \epsilon) \ , \ i \in \mathcal{S}_{j-1} \\ 2) \text{ threshold: } \mathcal{S}_{j} = \{i : y_{i,j} \ge 0\} \\ \text{end} \\ \text{output: } \mathcal{S}_{k} = \{i : y_{i,k} > 0\} \end{array}$$

$$\begin{array}{l} \text{total precision budget: } \mathbb{E}\left[\sum_{i,j} \gamma_{i,j}\right] \\ = \frac{1}{2 + \epsilon} \sum_{j=1}^{k} \mathbb{E}|\mathcal{S}_{j-1}| \\ \leq \frac{1}{2 + \epsilon} \sum_{j=1}^{k} \left(\frac{n - |\mathcal{S}|}{2^{j-1}} + |\mathcal{S}|\right) \\ \leq \frac{2(n - |\mathcal{S}|)}{2 + \epsilon} + k|\mathcal{S}| \le n \end{array}$$

(for n large)

n

probability of error: $\mathbb{P}(\mathcal{S}_k \neq \mathcal{S}) = \mathbb{P}(\{\mathcal{S}^c \cap \mathcal{S}_k \neq \emptyset\} \cup \{\mathcal{S} \cap \mathcal{S}_k^c \neq \emptyset\})$ $\leq \mathbb{P}\left(\mathcal{S}^c \cap \mathcal{S}_k \neq \emptyset\right) + \mathbb{P}\left(\mathcal{S} \cap \mathcal{S}_k^c \neq \emptyset\right)$

False Positives

 $\mathbb{P}(\mathcal{S}_k \neq \mathcal{S}) \leq \mathbb{P}\left(\mathcal{S}^c \cap \mathcal{S}_k \neq \emptyset\right) + \mathbb{P}\left(\mathcal{S} \cap \mathcal{S}_k^c \neq \emptyset\right)$

$$\mathbb{P}\left(\mathcal{S}^{c} \cap \mathcal{S}_{k} \neq \emptyset\right) = \mathbb{P}\left(\bigcup_{i \notin \mathcal{S}} \bigcap_{j=1}^{k} y_{i,j} > 0\right)$$
$$\leq \sum_{i \notin \mathcal{S}} \mathbb{P}\left(\bigcap_{j=1}^{k} y_{i,j} > 0\right)$$
$$= \sum_{i \notin \mathcal{S}} 2^{-k} = \frac{n-s}{2^{k}}$$

False Negatives

$$\mathbb{P}(\mathcal{S}_k \neq \mathcal{S}) \leq \mathbb{P}\left(\mathcal{S}^c \cap \mathcal{S}_k \neq \emptyset\right) + \mathbb{P}\left(\mathcal{S} \cap \mathcal{S}_k^c \neq \emptyset\right)$$

$$\mathbb{P}\left(\mathcal{S} \cap \mathcal{S}_{k}^{c} \neq \emptyset\right) = \mathbb{P}\left(\bigcup_{j=1}^{k} \bigcup_{i \in \mathcal{S}} y_{i,j} < 0\right)$$
$$\leq \frac{k|\mathcal{S}|}{2} \exp\left(-\frac{\mu^{2}}{2(2+\epsilon)}\right)$$

Probability of Error Bound

$$\mathbb{P}(\mathcal{S}_{k} \neq \mathcal{S}) \leq \mathbb{P}\left(\mathcal{S}^{c} \cap \mathcal{S}_{k} \neq \emptyset\right) + \mathbb{P}\left(\mathcal{S} \cap \mathcal{S}_{k}^{c} \neq \emptyset\right) \\
\leq \frac{n-s}{2^{k}} + \frac{k|\mathcal{S}|}{2} \exp\left(-\frac{\mu^{2}}{2(2+\epsilon)}\right) \\
= \frac{n-s}{2^{k}} + \frac{1}{2} \exp\left(-\frac{(\mu^{2}-2(2+\epsilon)\log(k|\mathcal{S}|))}{2(2+\epsilon)}\right)$$

Consider high-dimensional limit as $n \to \infty$ and take $k = \log_2 n^{1+\epsilon}$

$$\mathbb{P}(\mathcal{S}_k \neq \mathcal{S}) \leq \frac{n-s}{2^k} + \frac{1}{2} \exp\left(-\frac{(\mu^2 - 2(2+\epsilon)\log(|\mathcal{S}|(1+\epsilon)\log_2 n))}{2(2+\epsilon)}\right)$$

Second term tends to zero if

$$\mu \geq \sqrt{2(2+\epsilon)\log(|\mathcal{S}|(1+\epsilon)\log_2 n)}$$

Gains of Sequential Design

non-adaptive threshold:

$$\mu \geq \sqrt{2\log n}$$

DS threshold:

$$\mu \geq \sqrt{2(2+\epsilon)\log(|\mathcal{S}|(1+\epsilon)\log_2 n)}$$

We get a gain whenever $|\mathcal{S}| \leq n^{1/2}$

Punchline: In ultra-sparse setting, say $|\mathcal{S}| = C \log n$, DS drives error to zero if $\mu \ge \sqrt{(8 + \epsilon)} \log \log n$, compared to the non-adaptive requirement $\mu \ge \sqrt{2 \log n}$.

False Discovery Rate Control (Ingster '97, Jin & Donoho '03)

Assume sublinear sparsity level: $|\mathcal{S}| = n^{1-\beta}$, $\beta \in (0,1)$



non-sequential methods require $\mu \sim \sqrt{\log n}$

FDR-type Control using DS

FDR Distilled Sensing
initialize: $S_0 = \{1, \ldots, n\}$, $k = \lceil \log \log n \rceil$
 $\gamma_{i,j} = (\frac{3}{4})^j \frac{n}{8} / |S_{j-1}|, j = 1, \ldots, k-1$
 $\gamma_{i,k} = \frac{n}{2|S_{k-1}|}$ sublinear sparsity:
 $|S| = n^{1-\beta}, \beta \in (0, 1)$ for $j = 1, \ldots, k$
1) measure: $y_{i,j} \sim \mathcal{N}(x_i, \gamma_{i,j}^{-1}), i \in S_{j-1}$ $|S| = n^{1-\beta}, \beta \in (0, 1)$ 2) threshold: $S_j = \{i : y_{i,j} \ge 0\}$
end
output: $S_k = \{i : y_{i,k} \ge 4\}$

To guarantee that the proportions of FDP and NDP to zero as $n \to \infty$

Distilled Sensing $\mu \sim \text{arbitrarily slowly growing function of } n$ **non-adaptive** $\mu \sim \sqrt{\log n}$

Adaptivity effectively eliminates the fundamental statistical challenge in high-dimensional multiple testing.

Example $n = 2^{14}, ||x||_0 = \sqrt{n} = 128$



Challenge 2: Nonlinearities



 $\binom{13000}{2} \approx 85,000,000$ possible two-fold gene deletion strains !

Sparse Interaction Models



Approximate output (virus reproduction) with a sparse bilinear system.

$$x_i^{(1)}$$
 non-zero iff gene is critical to pathway sparsity = $x_{ij}^{(2)}$ non-zero iff gene pair is critical to pathway

 a_i 1 if gene is knocked down; 0 otherwise

Sensing Sparse Interactions

Linear model: $y(x) = \sum_{i} x_{i} a_{i}$ Bilinear model: $y(x) = \sum_{i} x_{i}^{(1)} a_{i} + \sum_{i < j} x_{i,j}^{(2)} a_{i} a_{j}$

 $\binom{13000}{2} \approx 85,000,000$ possible pairwise interactions !

Since most coefficients, $\{x_i\}$ or $\{x_i^{(1)}, x_{ij}^{(2)}\}$, are zero our goal is to identify critical components and interactions from using very few measurements



collect $K \ll \text{size}(\mathbf{x})$ measurements y_1, y_2, \ldots, y_K using K random inputs

(Linear) Compressed Sensing

This is the conventional compressed sensing problem for the linear model.

$$y_k = \sum_i a_{ki} x_i, \quad k = 1, \dots, K \qquad \qquad \mathbf{x} \in \mathbb{R}^n, \quad \mathbf{a} \in \{-1, +1\}^n$$

sparse \mathbf{x} : $\|\mathbf{x}\|_0 = S \ll n$

find sparse solution to $\mathbf{y} = \mathbf{A}\mathbf{x}$

If the measurement matrix satisfies the restricted isometry property (RIP) with $\delta_{2S} < \sqrt{2} - 1$ for all S-sparse vectors:

 $(1 - \delta_S) \|\mathbf{x}\|_2^2 \le \|\mathbf{A}\mathbf{x}\|_2^2 \le (1 + \delta_S) \|\mathbf{x}\|_2^2$

then x can be recovered from y by convex optimization:

 $\min \|\mathbf{z}\|_1$ subject to $\mathbf{A}\mathbf{z} = \mathbf{y}$

RIP holds with high probability if $K \ge c S \log(n/S)$

Multilinear Compressed Sensing

Multilinear model:

 $y = \sum_{i_1 < i_2 < \dots < i_D} a_{i_1} a_{i_2} \cdots a_{i_D} x_{i_1 i_2 \cdots i_D} \qquad \mathbf{x} \in \mathbb{R}^N, \ \mathbf{a} \in \{-1, 1\}^n$

$$\|x\|_0 = S \ll N \qquad N = \binom{n}{D}$$

y is called a **Rademacher chaos** of order D

Compressed sensing problem for multilinear model

K measurements of this form: $\mathbf{y} = [y_1 \cdots y_K]^T$ find sparse solution to $\mathbf{y} = \mathbf{A} \mathbf{x}$

matrix **A** now composed of monomials in $a_{i,j}$

Does it satisfy the RIP property?

On Average, Things Look Good

RIP: $(1 - \delta_S) \|\mathbf{x}\|_2^2 \le \|\mathbf{A}\mathbf{x}\|_2^2 \le (1 + \delta_S) \|\mathbf{x}\|_2^2$

isotropic measurements: $\mathbb{E}\left[\|\mathbf{A}\mathbf{x}\|^2\right] = \|\mathbf{x}\|_2^2$

symmetric binary random inputs: $\mathbb{P}(a_{i,j} = +1) = \mathbb{P}(a_{i,j} = -1) = 1/2$

Linear CS: n = 3 inputs, K = 2 measurements and D = 1,

$$\mathbf{A} = \frac{1}{\sqrt{2}} \begin{bmatrix} a_{1,1} & a_{1,2} & a_{1,3} \\ a_{2,1} & a_{2,2} & a_{2,3} \end{bmatrix} \implies \mathbb{E}[\mathbf{A}^T \mathbf{A}] = \text{Identity}$$

Bilinear CS: n = 3 inputs, K = 2 measurements and D = 2,

$$\mathbf{A} = \frac{1}{\sqrt{2}} \begin{bmatrix} a_{1,1}a_{1,2} & a_{1,1}a_{1,3} & a_{1,2}a_{1,3} \\ a_{2,1}a_{2,2} & a_{2,1}a_{2,3} & a_{2,2}a_{2,3} \end{bmatrix} \Rightarrow \mathbb{E}[\mathbf{A}^T \mathbf{A}] = \text{Identity}$$

What about the distributions?

$$\mathbf{y} = \mathbf{A}\mathbf{x}, \ \mathbb{E}\|\mathbf{y}\|_{2}^{2} = \|\mathbf{x}\|_{2}^{2}$$

$$\mathbb{P}(|\|\mathbf{y}\|^{2} - \|\mathbf{x}\|_{2}^{2}| > t) \sim \exp(-\operatorname{poly}(t))$$

$$\stackrel{\uparrow}{=} \stackrel{\uparrow}{=} \stackrel{\downarrow}{=} \stackrel{\downarrow}{=}$$

Tail Behavior

Best case: decoupled chaos

$$y = a_1 a_2 x_{1,2} + a_3 a_4 x_{3,4} + \dots + a_{2k-1} a_{2k} x_{2k-1,2k}$$

$$\equiv \tilde{a}_1 x_{1,2} + \tilde{a}_2 x_{3,4} + \dots + \tilde{a}_k x_{2k-1,2k}$$

equivalent to iid binary symmetric sensing

 \Rightarrow subgaussian tails independent of D: $\mathbb{P}(y^2 - ||x||_2^2 > t) \leq \exp(-ct)$

Worst case: strongly coupled chaos

$$y = \sum_{1 \le i < j \le \ell} a_i a_j x_{i,j} , \quad k := \binom{\ell}{2}$$

significant probability of large deviations from mean:

if
$$x_{i,j} = 1/\sqrt{k}$$
, then $\mathbb{P}(y^2 \ge k) = 2^{-\ell} = 2^{-c k^{1/2}}$

 \Rightarrow heavy tails depending on D: $\mathbb{P}(y^2 - ||x||_2^2 > t) \ge \exp(-ct^{1/D})$

Combinatorial Dimension of Rademacher Chaos

The combinatorial dimension $1 \le \alpha \le D$ measures the level of dependence introduced by a particular pattern of sparsity.

$$y = \sum_{i_1 < i_2 < \dots < i_D} a_{i_1} a_{i_2} \cdots a_{i_D} x_{i_1 i_2 \cdots i_D}$$

Blei-Janson '04: A Rademacher chaos with combinatorial dimensional α satisfies

$$\exp\left(-c_1 t^{1/\alpha}\right) \le \mathbb{P}\left(|y|^2 > t\right) \le \exp\left(-c_2 t^{1/\alpha}\right)$$

tails are light to heavy, depending on $1 \le \alpha \le D$

Dependencies Matter (in practice)

RIP: $(1 - \delta_S) \|\mathbf{x}\|_2^2 \le \|\mathbf{A}\mathbf{x}\|_2^2 \le (1 + \delta_S) \|\mathbf{x}\|_2^2$



Dependencies Matter (in theory)

K = number of measurements needed to recovery S-sparse multilinear forms

	C .	, 1		•	
proof	[1	tec	hn	10	lue
T					

bound on K

ingredients

Gershgorin	$S^2 \log N$	empirical 2nd moment bounds, union bound
Rudelson- Vershynin	$S(\log^3 S)(\log N)$	empirical 2nd moment bounds, no union bound
Rademacher chaos	$S^{\alpha} \log^{\alpha} (N/S)$ $1 \le \alpha \le D$	tail bounds union bound

compare with linear CS bound: $K \ge S \log(N/S)$

Gershgorin Bound

i) Control each element of (partial) Gram matrix $\mathbf{G}_{\mathcal{T}} = \mathbf{A}_{\mathcal{T}}^T \mathbf{A}_{\mathcal{T}}$ using Hoeffding's inequality and bound probability that $\mathbf{G}_{\mathcal{T}}$ is approximately diagonal.

$$\mathbf{G}_{\mathcal{T}} = \begin{bmatrix} 1 & \frac{\delta_S}{S} & \cdots & \frac{\delta_S}{S} \\ \frac{\delta_S}{S} & 1 & \cdots & \frac{\delta_S}{S} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{\delta_S}{S} & \frac{\delta_S}{S} & \cdots & 1 \end{bmatrix}$$

ii) Gershgorin's Disc Theorem guarantees that eigenvalues lie in the range

$$g_{ii} - \sum_{j \neq i} |g_{ij}| \leq \lambda_i(\mathbf{G}_T) \leq g_{ii} + \sum_{j \neq i} |g_{ij}|$$

iii) union bound over all $\binom{N}{S}$ sparsity patterns. RIP holds if

 $K \ge c S^2 \log N$

Heavy-Tailed Restricted Isometries

Theorem 1 (Vershynin) Let $\widetilde{\mathbf{A}}$ be a $K \times N$ measurement matrix whose rows \mathbf{a}_i^T are independent isotropic random vectors in \mathbb{R}^N . Let B be a number such that all entries $|a_{ij}| \leq B$ almost surely. Then the normalized matrix $\mathbf{A} = \frac{1}{\sqrt{K}} \widetilde{\mathbf{A}}$ satisfies the following for $K \leq N$, for every sparsity level $S \leq N$ and $0 < \epsilon < 1$:

if the number of measurements satisfies

 $K \ge C \ \epsilon^{-2} S \log N \log^3 \left(S\right)$

then the RIP constant δ_S of **A** satisfies $\mathbb{E}[\delta_S] \leq \epsilon$.

Check conditions:

- isotropy: $\mathbf{G} := \mathbf{A}^T \mathbf{A}$, $\mathbb{E}[\mathbf{G}]$ = Identity
- elements of $\widetilde{\mathbf{A}}$ bounded by 1.

Chaos Tail Bound

Lemma 1 Assume that y_k , $k = 1, \ldots, K$, are i.i.d. Rademacher variables of order D with combinatorial dimension $1 \le \alpha \le D$ and $\mathbb{E}y_k^2 = 1$. There exist constants c, C > 0 such that

$$\mathbb{P}\left(\left|\frac{1}{K}\sum_{k=1}^{K}y_{k}^{2}-1\right| > t\right) \le C\exp(-c\min(Kt^{2},K^{1/\alpha}t^{1/\alpha}))$$

proof technique:

- Blei-Jansen chaos tail bounds
- moment bound for sums of symmetric i.i.d. variables due to R. Latala
- apply lemma and union bound over ϵ -net for sparse vectors (technique from Baraniuk-Devore-Davenport-Wakin '08)

RIP holds if $K \ge C S^{\alpha} \log^{\alpha}(N/S)$

Conclusions

I. Sequential Experimental Designs for High-Dimensional Testing thresholds for recovery in high-dimensional limit:

non-adaptive designsSNR $\sim \log n$ sequential designsSNR \sim arbitrarily slowly growing function of n

Distilled Sensing: Adaptive Sampling for Sparse Detection and Estimation J. Haupt, R. Castro, and RN, arXiv:1001.5311v2

2. Compressed Sensing of Sparse Multilinear Functions

number of compressed sensing measurements for sparse recovery:

linear sparsity $K \sim S \log n$ multilinear sparsity $K \sim \min\{S^2 \log n, S \log^3(S) \log n, S^\alpha \log^\alpha n\}$

where $\alpha \geq 1$ depends on pattern of sparsity

Sparse Interactions: Identifying High-Dimensional. Multilinear Systems via Compressed Sensing, B. Nazer and RN, Allerton 2010