### Thesis Proposal: Two-Sample Kernel Based Tests

Nelson Ray (joint work with Susan Holmes)

Stanford University

February 26, 2013

• Motivation: breast cancer study with heterogeneous data

- Motivation: breast cancer study with heterogeneous data
- Friedman's two-sample test [1]: leverage regression and classification techniques

- Motivation: breast cancer study with heterogeneous data
- Friedman's two-sample test [1]: leverage regression and classification techniques
- Univariate data and linear scoring functions: permutation *t*-test

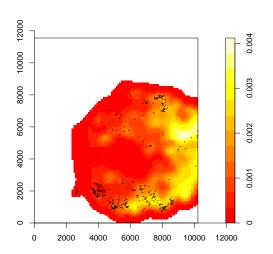
- Motivation: breast cancer study with heterogeneous data
- Friedman's two-sample test [1]: leverage regression and classification techniques
- Univariate data and linear scoring functions: permutation t-test
- Permutation dependence: Stein's method for rates of convergence

- Motivation: breast cancer study with heterogeneous data
- Friedman's two-sample test [1]: leverage regression and classification techniques
- Univariate data and linear scoring functions: permutation t-test
- Permutation dependence: Stein's method for rates of convergence
- Simulations to inform bounds in proof (experimental mathematics)

- Motivation: breast cancer study with heterogeneous data
- Friedman's two-sample test [1]: leverage regression and classification techniques
- Univariate data and linear scoring functions: permutation t-test
- Permutation dependence: Stein's method for rates of convergence
- Simulations to inform bounds in proof (experimental mathematics)
- Twitter example for text data

- Motivation: breast cancer study with heterogeneous data
- Friedman's two-sample test [1]: leverage regression and classification techniques
- Univariate data and linear scoring functions: permutation t-test
- Permutation dependence: Stein's method for rates of convergence
- Simulations to inform bounds in proof (experimental mathematics)
- Twitter example for text data
- Future work: theory for general case, heterogeneous data and combining kernels

# Breast Cancer Data: Spatial



### Breast Cancer Data: Survival

| Pathology no. | Initial<br>Diagnosis<br>Date | Relapse or Disease Free  | RDF<br>(R=relapsed;<br>F=DF) | Recurrence Date | Las |
|---------------|------------------------------|--|------------------------------|-----------------|-----|
| 98_17969D     | 1997-08-25                   | Disease Free   | F                            | Disease Free    |     |
| 97_24046C8    | 1997-08-25                   | Disease Free   | F                            | Disease Free    |     |
| 98_8501C1     | 1998-04-03                   | Disease Free   | F                            | Disease Free    |     |
| 98_8501A1     | 1998-04-03                   | Disease Free   | F                            | Disease Free    |     |
| 98_9134D4     | 1998-04-09                   | Left in-situ BrCa in 1999 (2nd primary cancer, not a metastasis from the right BrCa in 1997)       | F                            | Disease Free    |     |
| 98_9134B      | 1998-04-09                   | Left in-situ BrCa in 1999 (2nd<br>primary cancer, not a metastasis<br>from the right BrCa in 1997) | F                            | Disease Free    |     |
| 98_14783B1    | 1998-06-10                   | bone, brain, lymph nodes, pericardium,<br>liver metastasis   | R                            | 2004-07-30      |     |
| 98_14783A     | 1998-06-10                   | bone, brain, lymph nodes, pericardium,<br>liver metastasis   | R                            | 2004-07-30      |     |
| 98_16169C2    | 1998-06-24                   | Disease Free   | F                            | Disease Free    |     |
| 98_16169A     | 1998-06-24                   | Disease Free   | F                            | Disease Free    |     |
| 98_16169B     | 1998-06-24                   | Disease Free   | F                            | Disease Free    |     |
| 98_16253C1    | 1998-06-25                   | Disease Free   | F                            | Disease Free    |     |
| 60C1          | 1998-07-10                   | Disease Free   | F                            | Disease Free    |     |

### Breast Cancer Data: Medical

| Pathology no.         | Age at time of diagnosis | Gender | SLN tumor status              | Diagnosis                       | ER<br>status | PR<br>status | Her-2 overexpression |
|-----------------------|--------------------------|--------|-------------------------------|---------------------------------|--------------|--------------|----------------------|
| 98 17969D             | 68                       | F      | +                             | Invasive ductal carcinoma (IDC) | _            | _            | _                    |
| 97 24046C8            | 68                       | F      | +                             | Invasive ductal carcinoma (IDC) | _            | _            | _                    |
| 98 8501C1             | 51                       | F      | +                             | IDC & DCIS                      | +            | +            | ?                    |
| 98_8501A1             | 51                       | F      | +                             | IDC & DCIS                      | +            | +            | ?                    |
| 98_9134D4<br>98_9134B | 70<br>70                 | F      | +                             | IDC                             | +            | +            | n/a<br>n/a           |
| 98 14783B1            | 67                       | F      | +                             | IDC & DCIS                      | +            | +            | +                    |
| 98_14783A             | 67                       | F      | +                             | IDC & DCIS                      | +            | +            | +                    |
| 98_16169C2            | 79                       | F      | +mic                          | IDC                             | +            | +            | +                    |
| 98_16169A             | 79                       | F      | +mic                          | IDC                             | +            | +            | +                    |
| 98_16169B             | 79                       | F      | +mic                          | IDC                             | +            | +            | +                    |
| 98_16253C1            | 70                       | F      | +mic                          | IDC & DCIS                      | +            | -            | -                    |
| 60C1                  | 51                       | F      | - (rare<br>keratin+<br>cells) | IDC & DCIS                      | +            | +            | +                    |

• How do you deal with the data integration problem?

- How do you deal with the data integration problem?
- Kernel methods

- How do you deal with the data integration problem?
- Kernel methods
- Are there any differences (spatial, medical) between women who relapse and those who remain disease free?

- How do you deal with the data integration problem?
- Kernel methods
- Are there any differences (spatial, medical) between women who relapse and those who remain disease free?
- Two-sample tests

```
\{\mathbf{x}_i\}_1^N from p(\mathbf{x}) and \{\mathbf{z}_i\}_1^M from q(\mathbf{z}) testing \mathcal{H}_A: p \neq q against \mathcal{H}_0: p = q
```

```
\{\mathbf{x}_i\}_1^N from p(\mathbf{x}) and \{\mathbf{z}_i\}_1^M from q(\mathbf{z}) testing \mathcal{H}_A: p \neq q against \mathcal{H}_0: p = q
```

 $\textbf{0} \ \ \mathsf{Pool the two samples} \ \{\mathbf{u}_i\}_1^{N+M} = \{\mathbf{x}_i\}_1^N \cup \{\mathbf{z}_i\}_1^M.$ 

```
\{\mathbf{x}_i\}_1^N from p(\mathbf{x}) and \{\mathbf{z}_i\}_1^M from q(\mathbf{z}) testing \mathcal{H}_A: p \neq q against \mathcal{H}_0: p = q
```

- $\textbf{ 0} \ \ \mathsf{Pool the two samples} \ \{\mathbf{u}_i\}_1^{N+M} = \{\mathbf{x}_i\}_1^N \cup \{\mathbf{z}_i\}_1^M.$
- ② Assign label  $y_i = 1$  to the first group and  $y_i = -1$  to the second group.

```
\{\mathbf{x}_i\}_1^N from p(\mathbf{x}) and \{\mathbf{z}_i\}_1^M from q(\mathbf{z}) testing \mathcal{H}_A: p \neq q against \mathcal{H}_0: p = q
```

- ② Assign label  $y_i = 1$  to the first group and  $y_i = -1$  to the second group.
- **3** Apply a binary classification learning machine f to the training data to score the observations  $\{s_i = f(\mathbf{u}_i)\}_1^{N+M}$ .

 $\{\mathbf{x}_i\}_1^N$  from  $p(\mathbf{x})$  and  $\{\mathbf{z}_i\}_1^M$  from  $q(\mathbf{z})$  testing  $\mathcal{H}_A$ :  $p \neq q$  against  $\mathcal{H}_0$ : p = q

- ② Assign label  $y_i = 1$  to the first group and  $y_i = -1$  to the second group.
- **3** Apply a binary classification learning machine f to the training data to score the observations  $\{s_i = f(\mathbf{u}_i)\}_1^{N+M}$ .
- **3** Calculate a univariate two-sample test statistic  $T = T(\{s_i\}_1^N, \{s_i\}_{N+1}^{N+M})$ .

 $\{\mathbf{x}_i\}_1^N$  from  $p(\mathbf{x})$  and  $\{\mathbf{z}_i\}_1^M$  from  $q(\mathbf{z})$  testing  $\mathcal{H}_A$ :  $p \neq q$  against  $\mathcal{H}_0$ : p = q

- ② Assign label  $y_i = 1$  to the first group and  $y_i = -1$  to the second group.
- **3** Apply a binary classification learning machine f to the training data to score the observations  $\{s_i = f(\mathbf{u}_i)\}_1^{N+M}$ .
- Calculate a univariate two-sample test statistic  $T = T(\{s_i\}_{1}^{N}, \{s_i\}_{N+1}^{N+M})$ .
- Determine the permutation null distribution of the above statistic to yield a p-value.

#### Permutation T-test Connection

With univariate data and linear scoring functions, Friedman's test reduces to the permutation *t*-test.

#### Permutation T-test Connection

With univariate data and linear scoring functions, Friedman's test reduces to the permutation *t*-test.

With multivariate data, the test is close to Hotelling's  $T^2$ -test.

#### Permutation T-test Connection

With univariate data and linear scoring functions, Friedman's test reduces to the permutation *t*-test.

With multivariate data, the test is close to Hotelling's  $T^2$ -test.

Strategy: Analyze the simple case (univariate/linear) and attempt to generalize.

### Other Work

• Fisher (1935) [2] proposed distribution free randomization test.

### Other Work

- Fisher (1935) [2] proposed distribution free randomization test.
- Lehmann [3] proved a normal convergence result for the randomization distribution.

### Other Work

- Fisher (1935) [2] proposed distribution free randomization test.
- Lehmann [3] proved a normal convergence result for the randomization distribution.
- Bentkus et al. [4], Shao [5] proved Berry-Esseen bounds for Student's *t*-statistic in independent (but not i.d.) case.

### Stein's Method and the Randomization Distribution

Let  $\Phi(t)$  denote the standard normal CDF and T be a random variable that is distributed according to our permutation t null distribution. Can we get a bound on

$$\sup_{t\in\mathbb{R}}|P(T\leq t)-\Phi(t)|?$$

### Stein's Method and the Randomization Distribution

Let  $\Phi(t)$  denote the standard normal CDF and T be a random variable that is distributed according to our permutation t null distribution. Can we get a bound on

$$\sup_{t\in\mathbb{R}}|P(T\leq t)-\Phi(t)|?$$

We are finishing up a proof using the method of exchangeable pairs where our bound is  $O(N^{-1/4})$ .

Chen et al. [6]:

#### **Theorem**

If T, T' are mean 0, variance 1 exchangeable random variables satisfying

$$\mathbb{E}[T - T'|T] = \lambda(T - R)$$

for some  $\lambda \in (0,1)$  and some random variable R, then

$$\sup_{t\in\mathbb{R}}|P(T\leq t)-\Phi(t)|\leq B+(2\pi)^{-1/4}\sqrt{\frac{\mathbb{E}|T'-T|^3}{\lambda}}+\mathbb{E}|R|,$$

where  $B \leq \frac{\Theta}{2\lambda}$  and  $\Theta = \sqrt{\operatorname{var}(\mathbb{E}[(T'-T)^2|T])}$ .



 Attempts to follow Stein's [7] proof of the Hoeffding combinatorial central limit theorem

- Attempts to follow Stein's [7] proof of the Hoeffding combinatorial central limit theorem
- General contraction property, or "approximate case," from Stein et al.
   [8] and Holmes [9]

- Attempts to follow Stein's [7] proof of the Hoeffding combinatorial central limit theorem
- General contraction property, or "approximate case," from Stein et al.
   [8] and Holmes [9]
- Simulation aided proof (Borwein [10]) with efficient *t*-statistic updates similar to Diaconis et al. [11]

# Exchangeable Pair

For simplicity, assume M=N. We have data  $\{u_1,\ldots,u_N,u_{N+1},\ldots,u_{2N}\}$ . Take a uniformly random permutation  $\pi$ , and let

$$T = T\left(\{u_{\pi(i)}\}_{i=1}^{N}, \{u_{\pi(i)}\}_{i=N+1}^{2N}\right).$$

# Exchangeable Pair

For simplicity, assume M=N. We have data  $\{u_1,\ldots,u_N,u_{N+1},\ldots,u_{2N}\}$ . Take a uniformly random permutation  $\pi$ , and let

$$T = T\left(\{u_{\pi(i)}\}_{i=1}^{N}, \{u_{\pi(i)}\}_{i=N+1}^{2N}\right).$$

Let (I, J) be a uniformly random transposition between groups: over the  $N^2$  cases where  $1 \le I \le N$  and  $N+1 \le J \le 2N$ . Then

$$T' = T\left(\{u_{\pi\circ(I,J)(i)}\}_{i=1}^N, \{u_{\pi\circ(I,J)(i)}\}_{i=N+1}^{2N}\right).$$

T and T' form an exchangeable pair.



#### **Bound Calculations**

$$\sup_{t \in \mathbb{R}} |P(T \le t) - \Phi(t)| \le \underbrace{\frac{\sqrt{\operatorname{var}(\mathbb{E}[(T'-T)^2|T])}}{2\lambda}}_{1} + \underbrace{(2\pi)^{-1/4}\sqrt{\frac{\mathbb{E}|T'-T|^3}{\lambda}}}_{2} + \underbrace{\mathbb{E}[-\frac{1}{\lambda}\mathbb{E}[T-T'|T] + T]}_{3}$$

① Draw samples  $\{\mathbf{x}_i\}_1^N$  and  $\{\mathbf{z}_i\}_1^N$ .

- **1** Draw samples  $\{\mathbf{x}_i\}_1^N$  and  $\{\mathbf{z}_i\}_1^N$ .
- $\textbf{ 2} \ \, \mathsf{Pick} \,\, \mathsf{a} \,\, \mathsf{permutation} \,\, \pi \,\, \mathsf{uniformly} \,\, \mathsf{at} \,\, \mathsf{random}.$

- **1** Draw samples  $\{\mathbf{x}_i\}_1^N$  and  $\{\mathbf{z}_i\}_1^N$ .
- ② Pick a permutation  $\pi$  uniformly at random.
- **3** Calculate the two-sample t-statistic, T, on the permuted data.

- Draw samples  $\{\mathbf{x}_i\}_1^N$  and  $\{\mathbf{z}_i\}_1^N$ .
- 2 Pick a permutation  $\pi$  uniformly at random.
- **3** Calculate the two-sample t-statistic, T, on the permuted data.
- Calculate the  $N^2$  values of T' resulting from all allowable transpositions (I, J) that swap an x for a z.

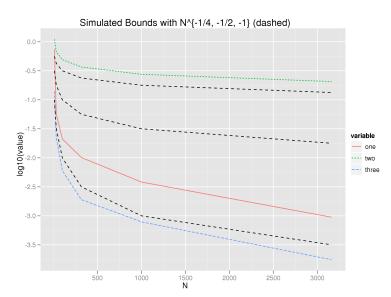
- Draw samples  $\{\mathbf{x}_i\}_1^N$  and  $\{\mathbf{z}_i\}_1^N$ .
- 2 Pick a permutation  $\pi$  uniformly at random.
- **3** Calculate the two-sample t-statistic, T, on the permuted data.
- Calculate the  $N^2$  values of T' resulting from all allowable transpositions (I, J) that swap an x for a z.
- Calculate conditional expectations with respect to T.

- Draw samples  $\{\mathbf{x}_i\}_1^N$  and  $\{\mathbf{z}_i\}_1^N$ .
- 2 Pick a permutation  $\pi$  uniformly at random.
- **3** Calculate the two-sample t-statistic, T, on the permuted data.
- Calculate the  $N^2$  values of T' resulting from all allowable transpositions (I, J) that swap an x for a z.
- **5** Calculate conditional expectations with respect to T.
- **O** Average over many values of T, and repeat for a sequence of N's.

### Simulated Data

```
Tprime
                                           lambda
         -1.6646969 -1.4150824
                                  10 0.2000000000
2
                                  10 0.2000000000
         -1.6646969 -2.8302749
3
         -1.6646969 -1.5975851
                                  10 0.2000000000
4
                                     0.2000000000
         -1.6646969 -2.1813520
5
                                  10 0.2000000000
         -1.6646969 -2.5914846
6
         -1.6646969 -1.9817233
                                  10 0.2000000000
88873283
          0.2425782
                     0.3088987 3162 0.0006325111
88873284
          0.2425782
                     0.2740881 3162 0.0006325111
88873285
          0.2425782
                     0.2816923 3162 0.0006325111
88873286
          0.2425782
                     0.2992468 3162 0.0006325111
88873287
          0.2425782
                     0.2931195 3162 0.0006325111
88873288
          0.2425782
                     0.2677967 3162 0.0006325111
```

# **Bounds Comparison**



# Twitter Example



# Barack Obama

@BarackObama Washington, DC 44th President of the United States http://www.barackobama.com



C Follow

#### Sarah Palin o

@SarahPalinUSA Alaska

Former Governor of Alaska and GOP Vice Presidential Nominee http://www.facebook.com/sarahpalin



Speaking today about the United States' policy in the Middle East and North Africa. Watch live: http://wh.gov/live #MEspeech

19 May



Delivering the commencement address at the United States Coast Guard Academy. Watch live at 11:30am ET:

www.wh.gov/live 18 May

Favorites Following Followers Lists

Sarah Palin USA Sarah Palin

You betcha!! MT "@AlaskaAces: Alaska Aces are 2011 Kelly Oup Champs w/ 5-3 win over Kalamazoo Wings! Aces win ECHL Championship series 4-1" 21 May

Sarah Palin USA Sarah Palin

Yes, they did & we couldn't be any more blessed! RT" @C4Palin: Track Palin and Britta Hanson Married http://bit.lv/iCkT3i #tcot #palin" 19 May

Sarah Palin USA Sarah Palin

I'm jealous! RT"@secupp: At the Wasilla Sportsman's Warehouse w/Joe the Plumber, Colorado Buck, Ken Onion and Sarah's parents. Good people." 19 May

4 D > 4 B > 4 B > 4 B >

### Twitter Data

#### Raw:

"BarackObama: We need to reward education reforms that are driven not by Washington, but by principals and teachers and parents. http://OFA.BO/6p2EMy"

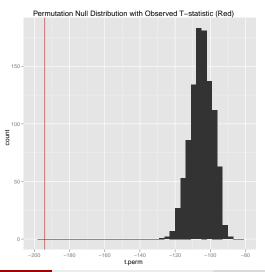
"SarahPalinUSA: You betcha!! MT \"@AlaskaAces: Alaska Aces are 2011 Kelly Cup Champs w/ 5-3 win over Kalamazoo Wings! Aces win ECHL Championship series 4-1\""

### After pre-processing:

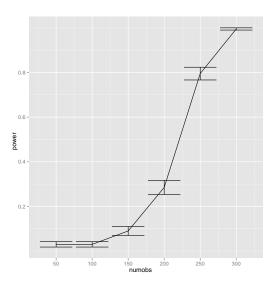
"we need to reward education reforms that are driven not by washington but by principals and teachers and parents "
"you betcha mt alaskaaces alaska aces are kelly cup champs w win over kalamazoo wings aces win echl championship series "

# Twitter Example

p < .001:



# Power Simulations at .05 Level



 Generalize theory for higher dimensional settings and/or non-linear scoring functions

- Generalize theory for higher dimensional settings and/or non-linear scoring functions
- Develop similarities with Hotelling's  $T^2$ -test

- Generalize theory for higher dimensional settings and/or non-linear scoring functions
- Develop similarities with Hotelling's  $T^2$ -test
- Explore performance on different types of data, in particular, unstructured data such as images

- Generalize theory for higher dimensional settings and/or non-linear scoring functions
- Develop similarities with Hotelling's  $T^2$ -test
- Explore performance on different types of data, in particular, unstructured data such as images
- Heterogeneous data: optimal combinations of kernels via SDPs, KL divergence

- Generalize theory for higher dimensional settings and/or non-linear scoring functions
- Develop similarities with Hotelling's  $T^2$ -test
- Explore performance on different types of data, in particular, unstructured data such as images
- Heterogeneous data: optimal combinations of kernels via SDPs, KL divergence

# References I

- J. Friedman, "On Multivariate Goodness-of-Fit and Two-Sample Testing," *Proceedings of Phystat2003*, http://www.slac.stanford.edu/econf/C, vol. 30908, 2003.
- R. Fisher, "The design of experiments.," 1935.
- E. Lehmann, *Elements of large-sample theory*. Springer Verlag, 1999.
- V. Bentkus and F. Götze, "The berry-esseen bound for student's statistic," *The Annals of Probability*, vol. 24, no. 1, pp. 491–503, 1996.
- Q. Shao, "An explicit berry-esseen bound for students t-statistic via steins method," *Steins Method and Applications (AD Barbour and LHY Chen eds)*. Lecture Notes Series, Institute for Mathematical Sciences, NUS, vol. 5, pp. 143–155, 2005.

# References II

- L. Chen, L. Goldstein, and Q. Shao, *Normal Approximation by Stein's Method*.

  Springer Verlag, 2010.
- C. Stein, "Approximate computation of expectations," *Lecture Notes-Monograph Series*, vol. 7, 1986.
- C. Stein, P. Diaconis, S. Holmes, and G. Reinert, "Use of exchangeable pairs in the analysis of simulations," *Lecture Notes-Monograph Series*, pp. 1–26, 2004.
- S. Holmes, "Stein's method for birth and death chains," *Lecture Notes-Monograph Series*, pp. 45–67, 2004.
  - J. Borwein and D. Bailey, *Mathematics by Experiment: Plausible reasoning in the 21st century*.

    AK Peters, 2004.

# References III



P. Diaconis and S. Holmes, "Gray codes for randomization procedures," *Statistics and Computing*, vol. 4, no. 4, pp. 287–302, 1994.