# Combining Kernels for Classification

#### **Doctoral Thesis Seminar**

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#### **Outline**

- Summary of Contribution
- Stationary kernel combination
- Nonstationary kernel combination
- Sequential minimal optimization
- Results
- Conclusion

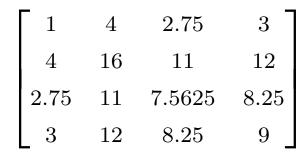
# **Summary of Contribution**

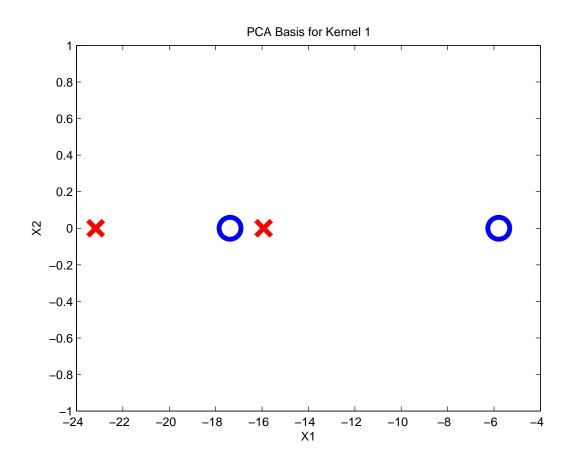
- Empirical study of kernel averaging versus SDP weighted kernel combination
- Nonstationary kernel combination
- Double Jensen bound for latent MED
- Efficient iterative optimization
- Implementation

#### **Outline**

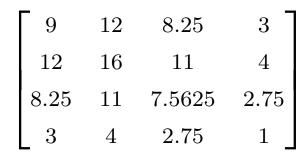
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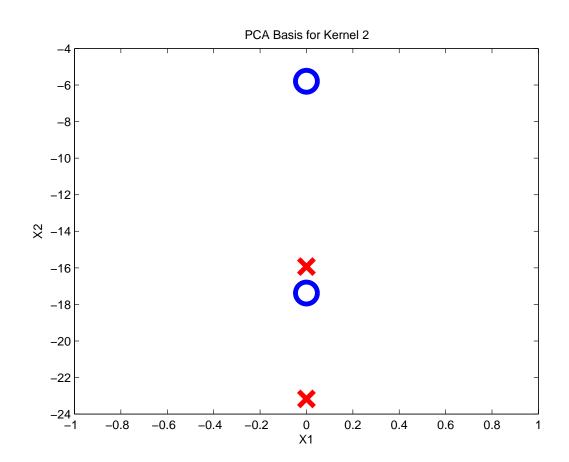
# **Example Kernel One**



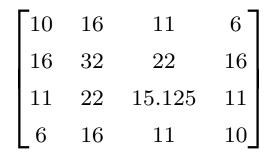


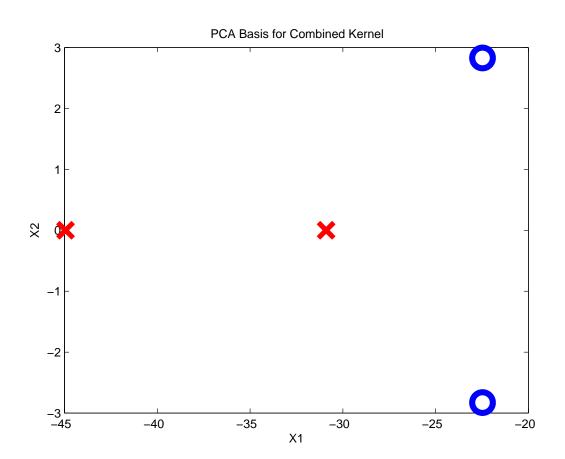
# **Example Kernel Two**





# **Example Kernel Combination**





#### **Effect of Combination**

$$K_C(x,z) = K_1(x,z) + K_2(x,z)$$

$$= \langle \phi_1(x), \phi_1(z) \rangle + \langle \phi_2(x), \phi_2(z) \rangle$$

$$= \langle \phi_1(x) : \phi_2(x), \phi_1(z) : \phi_2(z) \rangle$$

- The implicit feature space of the combined kernel is a concatenation of the feature spaces of the individual kernels.
- A basis in the combined feature space may be lower dimensional than the sum of the dimensions of the individual feature spaces.

# **Combination Weights**

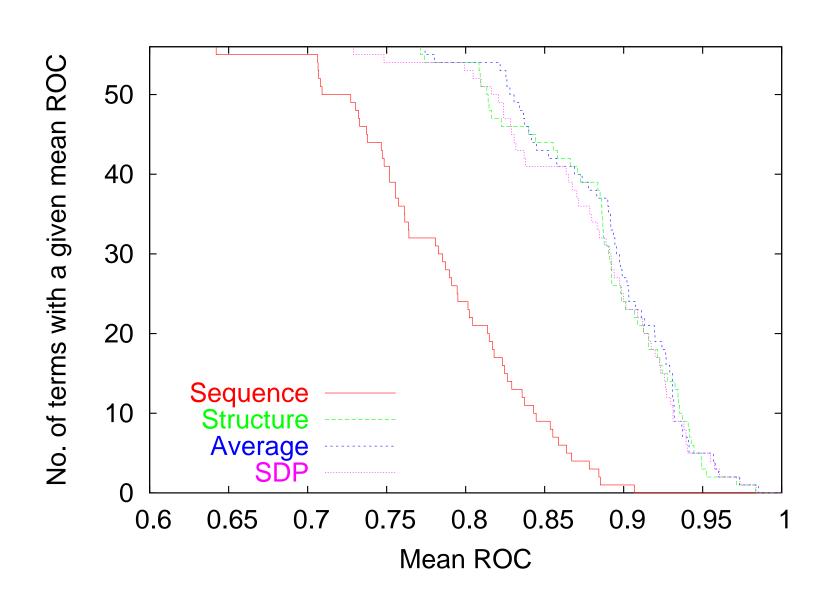
There are several ways in which the combination weights can be determined:

- equal weight: or unweighted combination. This is also essentially kernel averaging <sup>14</sup>.
- optimized weight: SDP weighted combination<sup>6</sup>. Weights and SVM Lagrange multipliers are determined in a single optimization. To regularize the kernel weights, a constraint is enforced to keep the trace of the combined kernel constant.

# Sequence/Structure

- We compare <sup>10</sup> the state-of-the-art SDP and simple averaging for conic combinations of kernels
- Drawbacks of SDP include optimization time and lack of a free implementation
- We determined the cases in which averaging is preferable and those in which SDP is required
- Our experiments predict Gene Ontology<sup>2</sup> (GO) terms using a combination of amino acid sequence and protein structural information
- We use the 4,1-Mismatch sequence kernel<sup>8</sup> and MAMMOTH (sequence-independent) structure kernel<sup>13</sup>

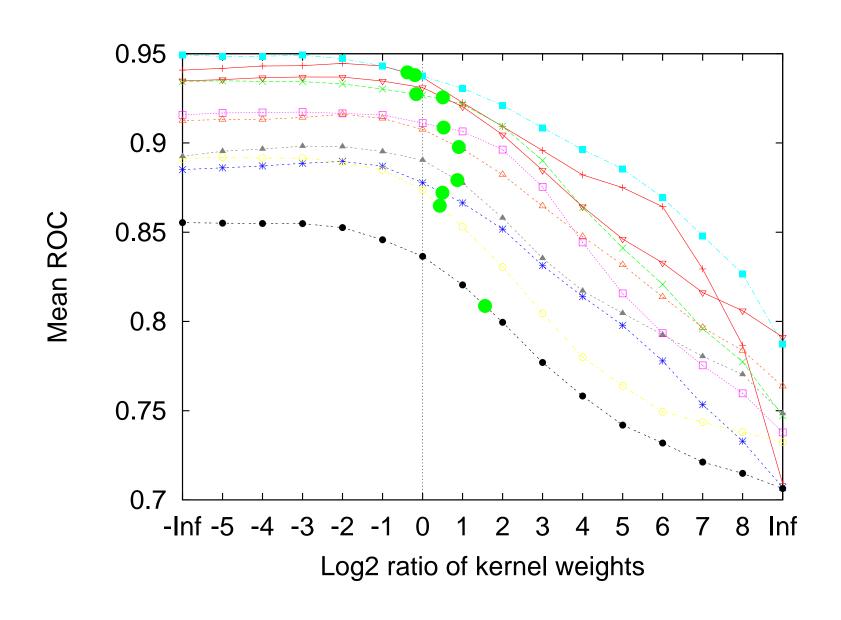
## **Cumulative ROC AUC**



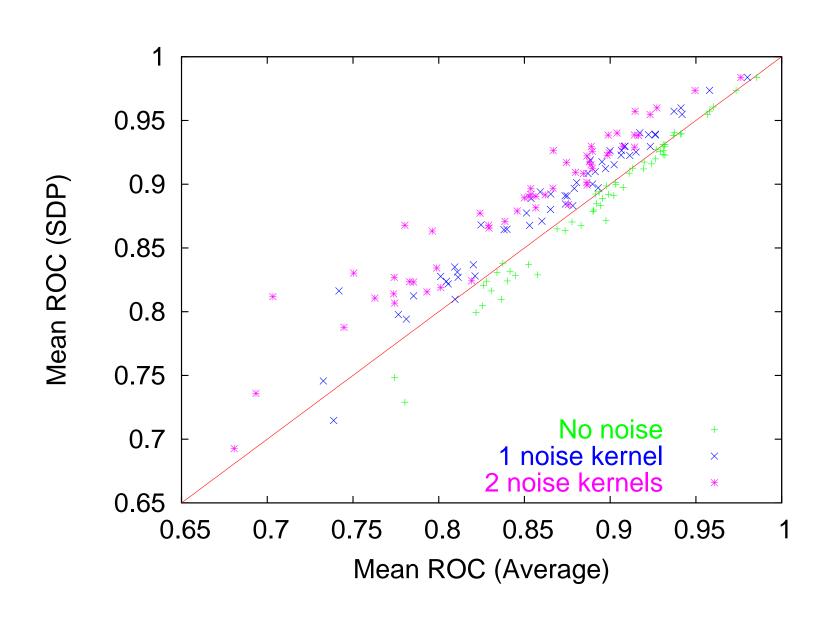
# Mean ROC AUC Top 10 GO Terms

GO term	Structure	Sequence	Average	SDP
GO:0008168	$0.941 \pm 0.014$	$0.709 \pm 0.020$	$0.937 \pm 0.016$	$0.938 \pm 0.015$
GO:0005506	$0.934 \pm 0.008$	$0.747 \pm 0.015$	$\textbf{0.927} \pm \textbf{0.012}$	$0.927 \pm 0.012$
GO:0006260	$0.885 \pm 0.014$	$0.707 \pm 0.020$	$0.878 \pm 0.016$	$0.870 \pm 0.015$
GO:0048037	$0.916 \pm 0.015$	$\textbf{0.738} \pm \textbf{0.025}$	$0.911 \pm 0.016$	$0.909 \pm 0.016$
GO:0046483	$0.949 \pm 0.007$	$0.787 \pm 0.011$	$\textbf{0.937} \pm \textbf{0.008}$	$0.940 \pm 0.008$
GO:0044255	$0.891 \pm 0.012$	$0.732 \pm 0.012$	$\textbf{0.874} \pm \textbf{0.015}$	$0.864 \pm 0.013$
GO:0016853	$0.855 \pm 0.014$	$0.706 \pm 0.029$	$\textbf{0.837} \pm \textbf{0.017}$	$0.810 \pm 0.019$
GO:0044262	$0.912 \pm 0.007$	$0.764 \pm 0.018$	$\textbf{0.908} \pm \textbf{0.006}$	$\textbf{0.897} \pm \textbf{0.006}$
GO:0009117	$0.892 \pm 0.015$	$\textbf{0.748} \pm \textbf{0.016}$	$\textbf{0.890} \pm \textbf{0.012}$	$\textbf{0.880} \pm \textbf{0.012}$
GO:0016829	$\textbf{0.935} \pm \textbf{0.006}$	$0.791 \pm 0.013$	$0.931 \pm 0.008$	$0.926 \pm 0.007$
GO:0006732	$0.823 \pm 0.011$	$0.781 \pm 0.013$	$0.845 \pm 0.011$	$0.828 \pm 0.013$
GO:0007242	$0.898 \pm 0.011$	$0.859 \pm 0.014$	$\textbf{0.903} \pm \textbf{0.010}$	$0.900 \pm 0.011$
GO:0005525	$\textbf{0.923} \pm \textbf{0.008}$	$\textbf{0.884} \pm \textbf{0.015}$	$0.931 \pm 0.009$	$0.931 \pm 0.009$
GO:0004252	$\textbf{0.937} \pm \textbf{0.011}$	$\textbf{0.907} \pm \textbf{0.012}$	$\textbf{0.932} \pm \textbf{0.012}$	$0.931 \pm 0.012$
GO:0005198	$\textbf{0.809} \pm \textbf{0.010}$	$\textbf{0.795} \pm \textbf{0.014}$	$\textbf{0.828} \pm \textbf{0.010}$	$0.824 \pm 0.011$

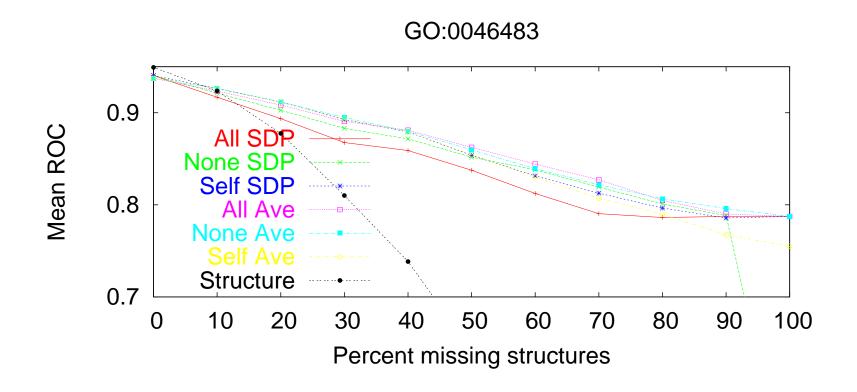
# Varying Ratio Top 10 GO Terms



## Noisy Kernels 56 GO Terms



# Missing Data Typical GO Term



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#### **Kernelized Discriminants**

Single:

$$f(x) = \sum_{t} y_t \lambda_t k(x_t, x) + b$$

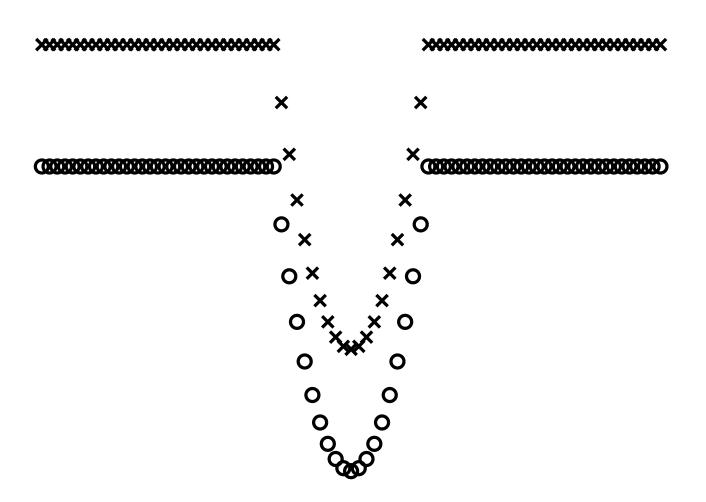
Linear combination:

$$f(x) = \sum_{t} y_t \lambda_t \sum_{m} \nu_m k_m(x_t, x) + b$$

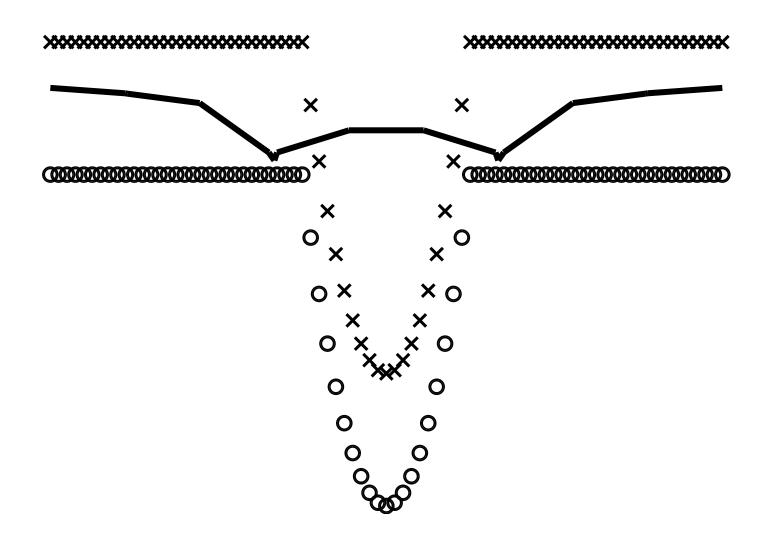
Nonstationary combination<sup>9</sup>:

$$f(x) = \sum_{t} y_t \lambda_t \sum_{m} \nu_{m,t}(x) k_m(x_t, x) + b$$

### **Parabola-Line Data**



### **Parabola-Line SDP**

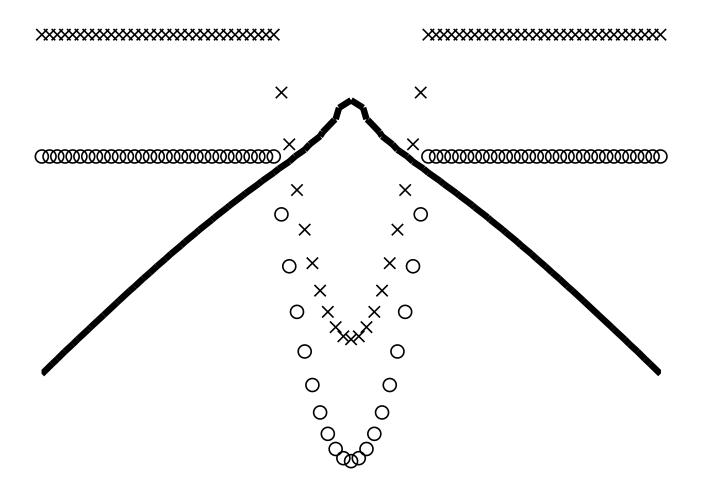


#### Ratio of Gaussian Mixtures

$$\mathcal{L}(X_t; \Theta) = \ln \frac{\sum_{m=1}^{M} \alpha_m \mathcal{N}(\phi_m^+(X_t) | \mu_m^+, I)}{\sum_{n=1}^{N} \beta_n \mathcal{N}(\phi_n^-(X_t) | \mu_n^-, I)} + b$$

- $\mu_m^+, \mu_n^-$  Gaussian means
- $\alpha, \beta$  mixing proportions
- b scalar bias
- For now, maximum likelihood parameters are estimated independently for each model.
- Note explicit feature maps,  $\phi^+, \phi^-$ .

### Parabola-Line ML



#### **Ratio of Generative Models**

$$\mathcal{L}(X_t; \Theta) = \ln \frac{\sum_{m=1}^{M} P(m, \phi_m^+(X_t) | \theta_m^+)}{\sum_{n=1}^{N} P(n, \phi_n^-(X_t) | \theta_n^-)} + b$$

- Find distribution  $P(\Theta)$  rather than specific  $\Theta^*$
- Classify using  $\hat{y} = \text{sign} \left( \int_{\Theta} P(\Theta) \mathcal{L}(X_t; \Theta) d\Theta \right)$

#### **Max Ent Parameter Estimation**

• Find  $P(\Theta)$  to satisfy "moment" constraints:

$$\int_{\Theta} P(\Theta) y_t \mathcal{L}(X_t; \Theta) d\Theta \ge \gamma_t \quad \forall t \in \mathcal{T}$$
 while assuming nothing additional.

Minimize Shannon relative entropy:

$$D(P||P^{(0)}) = \int_{\Theta} P(\Theta) \ln \frac{P(\Theta)}{P^{(0)}(\Theta)} d\Theta$$

to allow the use of a prior  $P^{(0)}(\Theta)$ .

Classic ME solution<sup>3</sup> is:

$$P(\Theta) = \frac{1}{Z(\lambda)} P^{(0)}(\Theta) e^{\sum_{t \in \mathcal{T}} \lambda_t [y_t \mathcal{L}(X_t | \Theta) - \gamma_t]}$$

- $\lambda$  fully specifies  $P(\Theta)$ .
- Maximize log-concave objective  $J(\lambda) = -\log Z(\lambda)$ .

#### **Tractable Partition**

$$\ddot{Z}(\lambda, Q|q) = \int_{\Theta} P^{(0)}(\Theta)$$

$$\exp\left(\sum_{t \in \mathcal{T}^{+}} \lambda_{t} \left(\sum_{m} q_{t}(m) \ln P(m, \phi_{m}^{+}(X_{t})|\theta_{m}^{+}) + H(q_{t})\right)\right)$$

$$-\sum_{n} Q_{t}(n) \ln P(n, \phi_{n}^{-}(X_{t})|\theta_{n}^{-}) - H(Q_{t}) + b - \gamma_{t}\right)$$

$$\exp\left(\sum_{t \in \mathcal{T}^{-}} \lambda_{t} \left(\sum_{n} q_{t}(n) \ln P(n, \phi_{n}^{-}(X_{t})|\theta_{n}^{-}) + H(q_{t})\right)\right)$$

$$-\sum_{m} Q_{t}(m) \ln P(m, \phi_{m}^{+}(X_{t})|\theta_{m}^{+}) - H(Q_{t}) - b - \gamma_{t}\right) d\Theta$$

- Introduce variational distributions  $q_t$  over the correct class log-sums and  $Q_t$  over the incorrect class log-sums to replace them with upper and lower bounds, respectively.
- Iterative optimization is required.

#### **MED Gaussian Mixtures**

$$\mathcal{L}(X_t; \Theta) = \ln \frac{\sum_{m=1}^{M} \alpha_m \mathcal{N}(\phi_m^+(X_t) | \mu_m^+, I)}{\sum_{n=1}^{N} \beta_n \mathcal{N}(\phi_n^-(X_t) | \mu_n^-, I)} + b$$

- Gaussian priors  $\mathcal{N}(0,I)$  on  $\mu_m^+,\mu_n^-$
- Non-informative Dirichlet priors on  $\alpha, \beta$
- Non-informative Gaussian  $\mathcal{N}(0,\infty)$  prior on b.

These assumptions simplify the objective and result in a set of linear equality constraints on the convex optimization.

# **Convex Objective**

$$\ddot{J}(\lambda, Q|q) = \sum_{t \in \mathcal{T}} \lambda_{t} (H(Q_{t}) - H(q_{t})) + \sum_{t \in \mathcal{T}} \lambda_{t} \gamma_{t} 
- \frac{1}{2} \sum_{t, t' \in \mathcal{T}^{+}} \lambda_{t} \lambda_{t'} \Big( \sum_{m} q_{t}(m) q_{t'}(m) k_{m}^{+}(t, t') 
+ \sum_{n} Q_{t}(n) Q_{t'}(n) k_{n}^{-}(t, t') \Big) 
- \frac{1}{2} \sum_{t, t' \in \mathcal{T}^{-}} \lambda_{t} \lambda_{t'} \Big( \sum_{m} Q_{t}(m) Q_{t'}(m) k_{m}^{+}(t, t') 
+ \sum_{n} q_{t}(n) q_{t'}(n) k_{n}^{-}(t, t') \Big) 
+ \sum_{t \in \mathcal{T}^{+}} \lambda_{t} \lambda_{t'} \Big( \sum_{m} q_{t}(m) Q_{t'}(m) k_{m}^{+}(t, t') 
+ \sum_{t' \in \mathcal{T}^{-}} \lambda_{t} \lambda_{t'} \Big( \sum_{m} q_{t}(m) Q_{t'}(m) k_{m}^{+}(t, t') \Big)$$

# **Optimization**

- For now, we discard the  $H(Q_t)$  entropy terms.
- We redefine  $\lambda \leftarrow Q\lambda$  and optimize with a quadratic program.
- Subsumes SVM (M=N=1)

The following constraints must be satisfied:

$$\sum_{t \in \mathcal{T}^{-}} \lambda_{t} Q_{t}(m) = \sum_{t \in \mathcal{T}^{+}} \lambda_{t} q_{t}(m) \ \forall m = 1 \dots M$$

$$\sum_{t \in \mathcal{T}^{+}} \lambda_{t} Q_{t}(n) = \sum_{t \in \mathcal{T}^{-}} \lambda_{t} q_{t}(n) \ \forall n = 1 \dots N$$

$$0 \leq \lambda_{t} \leq c \ \forall t = 1 \dots T$$

# **Expected Gaussian LL**

$$E\{\ln \mathcal{N}(\phi_{m}^{+}(X_{t})|\mu_{m}^{+})\} =$$

$$-\frac{D}{2}\ln(2\pi) - \frac{1}{2} - \frac{1}{2}k_{m}^{+}(X_{t}, X_{t})$$

$$+ \sum_{\tau \in \mathcal{T}^{+}} \lambda_{\tau}q_{\tau}(m)k_{m}^{+}(X_{\tau}, X_{t})$$

$$- \sum_{\tau \in \mathcal{T}^{-}} \lambda_{\tau}Q_{\tau}(m)k_{m}^{+}(X_{\tau}, X_{t})$$

$$- \frac{1}{2} \sum_{\tau, \tau' \in \mathcal{T}^{+}} \lambda_{\tau}\lambda_{\tau'}q_{\tau}(m)q_{\tau'}(m)k_{m}^{+}(X_{\tau}, X_{\tau'})$$

$$- \frac{1}{2} \sum_{\tau, \tau' \in \mathcal{T}^{-}} \lambda_{\tau}\lambda_{\tau'}Q_{\tau}(m)Q_{\tau'}(m)k_{m}^{+}(X_{\tau}, X_{\tau'})$$

$$+ \sum_{\tau \in \mathcal{T}^{+}} \lambda_{\tau}\lambda_{\tau'}q_{\tau}(m)Q_{\tau'}(m)k_{m}^{+}(X_{\tau}, X_{\tau'})$$

# **Expected Mixing/Bias LL**

$$a_m = E\{\ln \alpha_m\} + \frac{1}{2}E\{b\} \quad \forall m = 1..M$$
$$b_n = E\{\ln \beta_n\} - \frac{1}{2}E\{b\} \quad \forall n = 1..N$$

When  $\lambda_t \in (0,c)$  we must achieve the following with equality:

$$\sum_{m} q_{t}(m)(a_{m} + E\{\ln \mathcal{N}(\phi_{m}^{+}(X_{t})|\mu_{m}^{+})\}) + H(q_{t}) =$$

$$\sum_{n} Q_{t}(n)(b_{n} + E\{\ln \mathcal{N}(\phi_{n}^{-}(X_{t})|\mu_{n}^{-})\}) + H(Q_{t}) + \gamma_{t} \quad \forall t \in \mathcal{T}^{+}$$

$$\sum_{n} q_{t}(n)(b_{n} + E\{\ln \mathcal{N}(\phi_{n}^{-}(X_{t})|\mu_{n}^{-})\}) + H(q_{t}) =$$

$$\sum_{m} Q_{t}(m)(a_{m} + E\{\ln \mathcal{N}(\phi_{m}^{+}(X_{t})|\mu_{m}^{+})\}) + H(Q_{t}) + \gamma_{t} \quad \forall t \in \mathcal{T}^{-}$$

We solve for  $a_m$  for m=1..M and  $b_n$  for n=1..N in this (over-constrained) linear system, obtaining the expected bias and mixing proportions.

#### **Tractable Prediction**

$$\hat{y} = \ln \frac{\sum_{m} \exp \left( E\{\ln \mathcal{N}(\phi_{m}^{+}(X)|\mu_{m}^{+})\} + a_{m} \right)}{\sum_{n} \exp \left( E\{\ln \mathcal{N}(\phi_{n}^{-}(X)|\mu_{n}^{-})\} + b_{n} \right)}$$

# **Nonstationary Weights**

Recall the nonstationary kernelized discriminant:

$$f(x) = \sum_{t} y_t \lambda_t \sum_{m} \nu_{m,t}(x) k_m(x_t, x) + b.$$

To view a MED Gaussian mixture as nonstationary kernel combination, we choose weight functions of the form:

$$\nu_{m,t}^{+}(X) = \frac{\exp(E\{\ln \mathcal{N}(\phi_m^{+}(X)|\mu_m^{+})\} + a_m)}{\sum_{m} \exp(E\{\ln \mathcal{N}(\phi_m^{+}(X)|\mu_m^{+})\} + a_m)}.$$

Note how the kernel weight depends on the Gaussian components.

#### **NSKC Prediction**

$$\hat{y} = \sum_{\tau \in \mathcal{T}^{+}} \sum_{m} \lambda_{\tau} Q_{\tau}(m) \nu_{m}^{+}(X) k_{m}^{+}(X_{\tau}, X)$$

$$- \sum_{\tau \in \mathcal{T}^{-}} \sum_{m} \lambda_{\tau} Q_{\tau}(m) \nu_{m}^{+}(X) k_{m}^{+}(X_{\tau}, X)$$

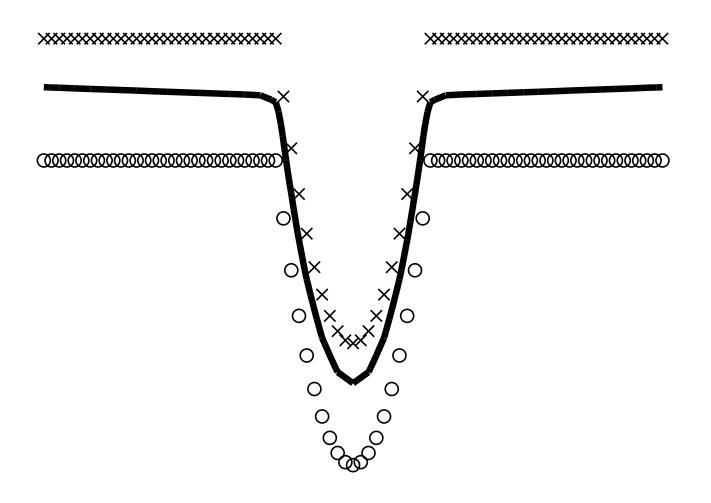
$$- \sum_{\tau \in \mathcal{T}^{-}} \sum_{n} \lambda_{\tau} Q_{\tau}(n) \nu_{n}^{-}(X) k_{n}^{-}(X_{\tau}, X)$$

$$+ \sum_{\tau \in \mathcal{T}^{+}} \sum_{n} \lambda_{\tau} Q_{\tau}(n) \nu_{n}^{-}(X) k_{n}^{-}(X_{\tau}, X)$$

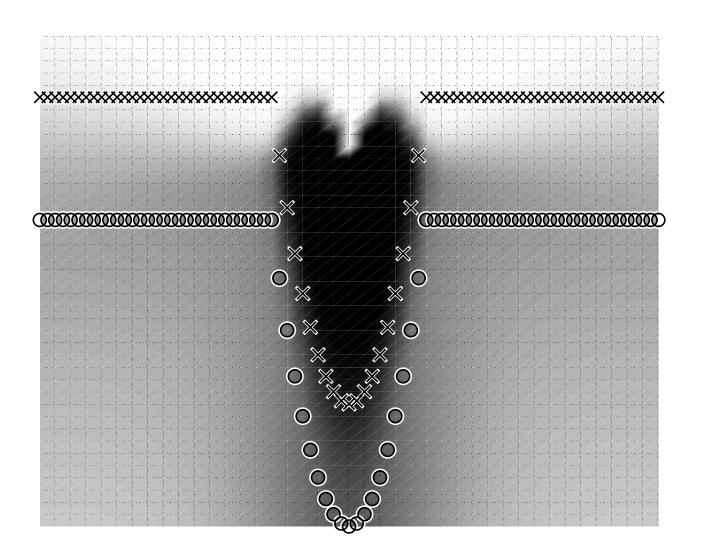
$$+ \sum_{m} \nu_{m}^{+}(X) k_{m}^{+}(X, X) - \sum_{n} \nu_{n}^{-}(X) k_{n}^{-}(X, X)$$

$$+ constant.$$

### **Parabola-Line NSKC**



# Parabola-Line NSKC Weight



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 $\operatorname{argmin}_{\lambda} J(\lambda) = c^{T} \lambda + \frac{1}{2} \lambda^{T} \mathbf{H} \lambda$  subject to:

$$\begin{bmatrix} \dots & q_{u_1} & q_{u_1} & \dots & -1 & 0 & \dots & q_{w_1} & q_{w_1} & \dots \\ \dots & q_{u_2} & q_{u_2} & \dots & 0 & -1 & \dots & q_{w_2} & q_{w_2} & \dots \\ \dots & 1 & 0 & \dots & -q_{v_1} & -q_{v_1} & \dots & 1 & 0 & \dots \\ \dots & 0 & 1 & \dots & -q_{v_2} & -q_{v_2} & \dots & 0 & 1 & \dots \end{bmatrix} \begin{bmatrix} \vdots \\ \lambda_{u_1} \\ \lambda_{v_2} \\ \vdots \\ \lambda_{w_1} \\ \lambda_{w_2} \\ \vdots \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

$$\begin{bmatrix} \vdots \\ \lambda_{u_1} \\ \lambda_{u_2} \\ \vdots \\ \lambda_{v_1} \\ \lambda_{v_2} \\ \vdots \\ \lambda_{w_1} \\ \lambda_{w_2} \\ \vdots \\ \vdots \\ \vdots \\ \lambda_{w_2} \\ \vdots \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

#### **Inter-class**

We can maintain the constraints using the following equalities in vector form:

$$q_u(\hat{\lambda_u}^T 1) - \hat{\lambda_v} = q_u(\lambda_u^T 1) - \lambda_v$$
$$\hat{\lambda_u} - q_v(\hat{\lambda_v}^T 1) = \lambda_u - q_v(\lambda_v^T 1).$$

Then, we can write

$$\Delta \lambda_v = (\Delta \lambda_u^T 1) q_u$$
  
$$\Delta \lambda_u = (\Delta \lambda_v^T 1) q_v = (((\Delta \lambda_u^T 1) q_u)^T 1) q_v = (\Delta \lambda_u^T 1) q_v.$$

## **Analytic Update**

 $(\Delta \lambda_u^T 1) = (\Delta \lambda_v^T 1) = \Delta s$ . We have  $\Delta \lambda_v = \Delta s q_u$  and  $\Delta \lambda_u = \Delta s q_v$ . The change in the quadratic objective function for the axes u and v is

$$\Delta J_{uv}(\Delta \lambda) = c_u^T \Delta \lambda_u + c_v^T \Delta \lambda_v$$

$$+ \frac{1}{2} \Delta \lambda_u^T \mathbf{H}_{uu} \Delta \lambda_u + \Delta \lambda_u^T \mathbf{H}_{uv} \Delta \lambda_v + \frac{1}{2} \Delta \lambda_v^T \mathbf{H}_{vv} \Delta \lambda_v$$

$$+ \sum_{t \neq u, v} (\Delta \lambda_t^T \mathbf{H}_{tu} \Delta \lambda_u + \Delta \lambda_t^T \mathbf{H}_{tv} \Delta \lambda_v).$$

We must express the change in the objective,  $\Delta J_{uv}(\Delta \lambda)$  as a function of  $\Delta s$ . The resulting one-dimensional quadratic objective function,  $\Delta J_{uv}(\Delta s)$ , can be analytically optimized by finding the root of the derivative under the box constraint.

### **Other Cases**

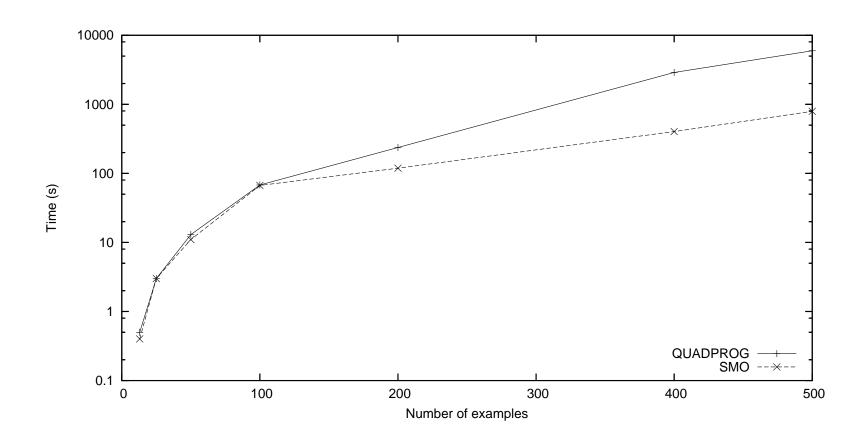
#### Intra-class:

$$q_u(\hat{\lambda_u}^T 1) + q_w(\hat{\lambda_w}^T 1) = q_u(\lambda_u^T 1) + q_w(\lambda_w^T 1)$$
$$\hat{\lambda_u} + \hat{\lambda_w} = \lambda_u + \lambda_w$$

#### Newton Step:

- Occasionally interleave a second-order step<sup>1</sup> over a larger set of axes.
- We discovered that SMO can get trapped in a local plateau in the objective function.
- Though the objective and constraints are convex, choosing a minimal set of axes to update results in slow convergence.

# **SMO Timing**



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#### Benchmark data sets

We validate NSKC on UCI<sup>11</sup> Breast Cancer, Sonar, and Heart data sets. We use a quadratic kernel  $k_1(x_1,x_2)=(1+x_1^Tx_2)^2$ , an RBF kernel  $k_2(x_1,x_2)=\exp(-0.5(x_1-x_2)^T(x_1-x_2)/\sigma)$ , and a linear kernel  $k_3(x_1,x_2)=x_1^Tx_2$ .

- All three kernels are normalized so that their features lie on the surface of a unit hypersphere.
- As in Lanckriet et al.<sup>6</sup>, we use a hard margin (c = 10,000)
- RBF width parameter  $\sigma$  is set to 0.5 (Cancer), 0.1 (Sonar) and 0.5 (Heart).

### **Breast Cancer**

<b>Algorithm</b>	Mean ROC
quadratic	$0.5486 \pm 0.091$
RBF	$0.6275 \pm 0.019$
linear	$0.5433 \pm 0.087$
SDP	$0.8155 \pm 0.015$
ML	$0.5573\pm0.03$
NSKC	0.8313 $\pm$ 0.014

## Sonar

<b>Algorithm</b>	Mean ROC
quadratic	$0.8145 \pm 0.01$
RBF	$0.8595 \pm 0.009$
linear	$0.7297 \pm 0.01$
SDP	$0.8595 \pm 0.009$
ML	$0.6817 \pm 0.022$
NSKC	$\textbf{0.8634} \pm \textbf{0.008}$

### Heart

Algorithm	Mean ROC
quadratic	0.6141 $\pm$ 0.032
RBF	$0.5556 \pm 0.01$
linear	$0.5237\pm0.02$
SDP	$0.5556 \pm 0.01$
ML	$0.5361 \pm 0.024$
NSKC	$0.6052 \pm 0.016$

## **Yeast Experiment**

We compare NSKC against three single-kernel SVMs and against an SDP combination of the three kernels. This is the data set used for the original SDP experiments<sup>7;5</sup>.

- Gene expression kernel
- Protein domain kernel
- Sequence kernel
- MIPS MYGD labels
- 500 randomly sampled genes in a 5x3cv experiment

### **Protein Function Annotation**

Class	Ехр	Dom	Seq	SDP	NSKC
1	0.630	0.717	0.750	0.745	0.747
2	0.657	0.664	0.718	0.751	0.755
3	0.668	0.706	0.729	0.768	0.774
4	0.596	0.756	0.752	0.766	0.778
5	0.810	0.773	0.789	0.834	0.836
6	0.617	0.690	0.668	0.698	0.717
7	0.554	0.715	0.740	0.720	0.738
8	0.594	0.636	0.680	0.697	0.699
9	0.535	0.564	0.603	0.582	0.576
10	0.554	0.616	0.706	0.697	0.687
11	0.506	0.470	0.480	0.524	0.526
12	0.682	0.896	0.883	0.916	0.918

## Sequence/Structure Revisited

GO term	Average	SDP	NSKC
GO:0008168	$\textbf{0.937} \pm \textbf{0.016}$	$\textbf{0.938} \pm \textbf{0.015}$	$0.944 \pm 0.014$
GO:0005506	$0.927 \pm 0.012$	$0.927 \pm 0.012$	$0.926 \pm 0.013$
GO:0006260	$0.878 \pm 0.016$	$0.870 \pm 0.015$	$\textbf{0.880} \pm \textbf{0.015}$
GO:0048037	$0.911 \pm 0.016$	$\textbf{0.909} \pm \textbf{0.016}$	$\textbf{0.918} \pm \textbf{0.015}$
GO:0046483	$\textbf{0.937} \pm \textbf{0.008}$	$0.940\pm0.008$	$0.941 \pm 0.008$
GO:0044255	$0.874 \pm 0.015$	$0.864 \pm 0.013$	$0.874 \pm 0.012$
GO:0016853	$0.837 \pm 0.017$	$0.810 \pm 0.019$	$0.823 \pm 0.018$
GO:0044262	$0.908\pm0.006$	$0.897 \pm 0.006$	$0.906 \pm 0.007$
GO:0009117	$0.890 \pm 0.012$	$0.880 \pm 0.012$	$0.887 \pm 0.012$
GO:0016829	$0.931 \pm 0.008$	$\textbf{0.926} \pm \textbf{0.007}$	$0.928 \pm 0.008$

- NSKC and averaging are in a statistical tie
- NSKC is significantly better than SDP

#### **Outline**

- Summary of Contribution
- Stationary kernel combination
- Nonstationary kernel combination
- Sequential minimal optimization
- Results
- Conclusion

### **Conclusion**

- Prior work
- Contributions
- Future directions

#### **Prior work**

To complete this research we built upon an impressive foundation of prior work in:

- Kernel methods<sup>16</sup>
- Support vector machines<sup>18</sup>
- Multi-kernel learning 14;6;12;17
- Maximum entropy discrimination<sup>3</sup>
- Protein function annotation from heterogeneous data sets<sup>7;17</sup>
- Optimization <sup>15;1</sup>

In particular, this thesis extends the work of Jebara<sup>4</sup>. William Noble and Tony Jebara are my advisors and co-authors and greatly influenced the work.

#### **Contributions**

- Empirical study of averaging versus SDP
- Nonstationary kernel combination
- Double Jensen bound for latent MED
- Efficient optimization
- Implementation

# Averaging vs. SDP

- We present a comparison of SDP and averaging for combining protein sequence and structure kernels for the prediction of function.
- We analyze the outcomes and suggest when each approach is appropriate.
- We conclude that in all practical cases, averaging is worthwhile.
- This result is significant to practitioners because it indicates that a simple, fast, free technique is also very effective.

### Nonstationary kernel combination

- We propose a novel way to combine kernels that generalizes upon the state-of-the-art.
- NSKC allows kernel combination weight to depend on the input space.
- We demonstrate our technique with a synthetic problem that existing techniques cannot solve.
- We validate NSKC with several common benchmark data sets and two real-world problems.
- NSKC usually outperforms existing techniques.

## Double Jensen, SMO, Implementation

- The new double Jensen variational bound is tight and assures that latent MED optimization will converge to a local optimum.
- Sequential minimal optimization for MED Gaussian mixtures improves optimization speed and helps to make the technique practical.
- SMO is faster than the quadprog standard QP solver and matches the speed of the highly optimized commercial Mosek optimization software.
- Our C++ SMO implementation and our Matlab classes for kernels, learning algorithms, and cross validation experiments will be freely available for academic use.

#### **Future directions**

- Saddle-point optimization of indefinite objective
- Entropy terms for Q
- Transduction
- Other latent variable models

#### References

- [1] S. Boyd and L. Vandenberghe. *Convex Optimization*. Prentice-Hall, 2003. To appear. Available at http://www.stanford.edu/~boyd/cvxbook.html.
- [2] Gene Ontology Consortium. Gene ontology: tool for the unification of biology. *Nat Genet*, 25(1):25–9, 2000.
- [3] T. Jaakkola, M. Meila, and T. Jebara. Maximum entropy discrimination. In *Advances in Neural Information Processing Systems*, volume 12, December 1999.
- [4] T. Jebara. *Machine Learning: Discriminative and Generative*. Kluwer Academic, Boston, MA, 2004.
- [5] G. R. G. Lanckriet, T. De Bie, N. Cristianini, M. I. Jordan, and W. S. Noble. A statistical framework for genomic data fusion. *Bioinformatics*, 20(16):2626–2635, 2004.
- [6] G. R. G. Lanckriet, N. Cristianini, P. Bartlett, L. El Ghaoui, and M. I. Jordan. Learning the kernel matrix with semi-definite programming. In C. Sammut and A. Hoffman, editors, *Proceedings of the 19th International Conference on Machine Learning*, Sydney, Australia, 2002. Morgan Kauffman.

- [7] G. R. G. Lanckriet, M. Deng, N. Cristianini, M. I. Jordan, and W. S. Noble. Kernel-based data fusion and its application to protein function prediction in yeast. In R. B. Altman, A. K. Dunker, L. Hunter, T. A. Jung, and T. E. Klein, editors, *Proceedings of the Pacific Symposium on Biocomputing*, pages 300–311. World Scientific, 2004.
- [8] C. Leslie, E. Eskin, J. Weston, and W. S. Noble. Mismatch string kernels for SVM protein classification. In Suzanna Becker, Sebastian Thrun, and Klaus Obermayer, editors, *Advances in Neural Information Processing Systems*, pages 1441–1448, Cambridge, MA, 2003. MIT Press.
- [9] D. Lewis, T. Jebara, and W. S. Noble. Nonstationary kernel combination. In *23rd International Conference on Machine Learning (ICML)*, 2006.
- [10] D. Lewis, T. Jebara, and W. S. Noble. Support vector machine learning from heterogeneous data: an empirical analysis using protein sequence and structure. Submitted, April 2006.
- [11] P. M. Murphy and D. W. Aha. UCI repository of machine learning databases. Dept. of Information and Computer Science, UC Irvine, 1995.

- [12] C. S. Ong, A. J. Smola, and R. C. Williamson. Learning the kernel with hyperkernels. *Journal of Machine Learning Research*, 6:1043–1071, 2005.
- [13] A. R. Ortiz, C. E. M. Strauss, and O. Olmea. MAMMOTH (Matching molecular models obtained from theory): An automated method for model comparison. *Protein Science*, 11:2606–2621, 2002.
- [14] P. Pavlidis, J. Weston, J. Cai, and W. S. Noble. Learning gene functional classifications from multiple data types. *Journal of Computational Biology*, 9(2):401–411, 2002.
- [15] J. C. Platt. Fast training of support vector machines using sequential minimal optimization. In B. Schölkopf, C. J. C. Burges, and A. J. Smola, editors, *Advances in Kernel Methods*. MIT Press, 1999.
- [16] B. Schölkopf, C. J. C. Burges, and A. J. Smola, editors. Advances in Kernel Methods: Support Vector Learning. MIT Press, Cambridge, MA, 1999.
- [17] K. Tsuda, H.J. Shin, and B. Schölkopf. Fast protein classification with multiple networks. In *ECCB*, 2005.
- [18] V. N. Vapnik. *Statistical Learning Theory*. Adaptive and learning systems for signal processing, communications, and control. Wiley, New York, 1998.