Estimating mutual information for high-dimensional sparse relationships

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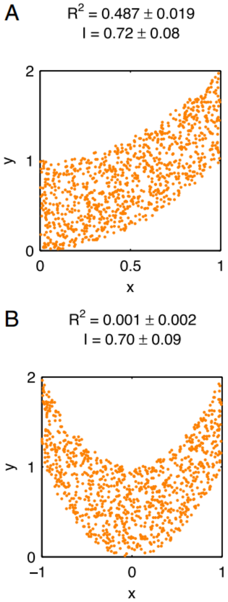
(Joint work with Yuval Benjamini.)



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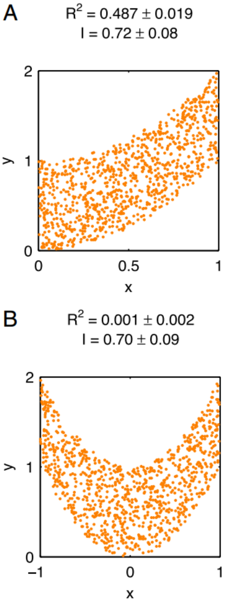
- measures dependence between two random vectors, $\vec{X}$ and $\vec{Y}$

Overview



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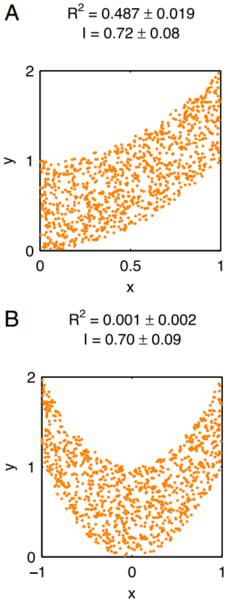

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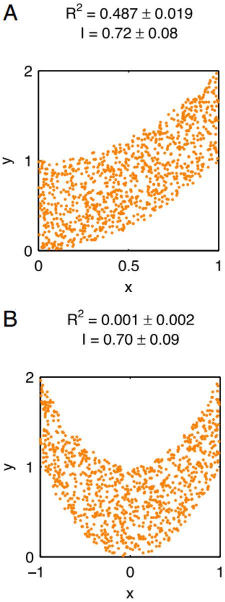

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- measures dependence between two random vectors, $\vec{X}$ and $\vec{Y}$
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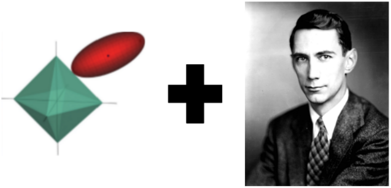
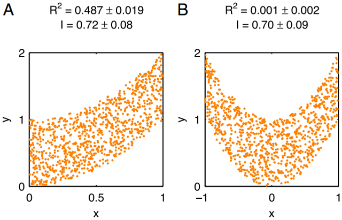
We combine *machine learning* (sparse estimation) with *information theory* to obtain better estimates of $I(\vec{X}; \vec{Y})$



Mutual information $I(X; Y)$



Introduced in Shannon's 1948 paper, "A mathematical theory of communication"

Image credit Kinney et al. 2014.

Applications of $I(X; Y)$

Mutual information has since been applied to many areas outside of information theory

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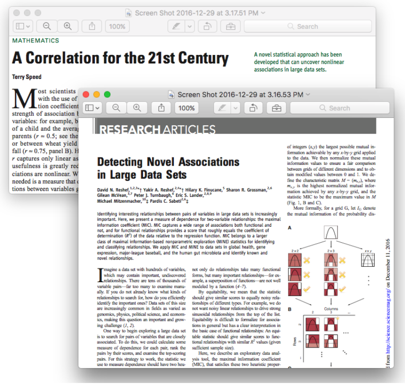
Applications [edit]

In many applications, one wants to maximize mutual information (thus

- In search engine technology, mutual information between phrases
- In telecommunications, the channel capacity is equal to the mutua
- Discriminative training procedures for hidden Markov models have
- RNA secondary structure prediction from a multiple sequence alig
- Phylogenetic profiling prediction from pairwise present and disapp
- Mutual information has been used as a criterion for feature selecti the minimum redundancy feature selection.
- Mutual information is used in determining the similarity of two diffe
- Mutual information of words is often used as a significance functio words; rather, one counts instances where 2 words occur adjacen another, goes up with N.
- Mutual information is used in medical imaging for image registratic reference image, this image is deformed until the mutual informati
- Detection of phase synchronization in time series analysis
- In the infomax method for neural-net and other machine learning,

Engineering, biology, computer science, physics, medicine

Comparing $I(X;Y)$ with Pearson correlation



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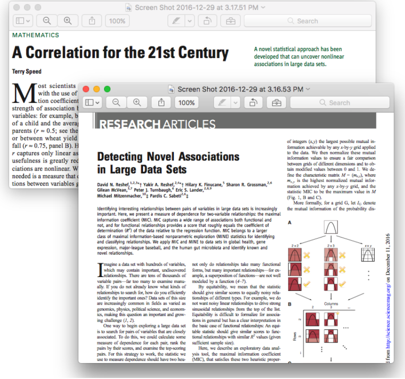

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- Only mutual information (and derived quantities) measures dependence directly

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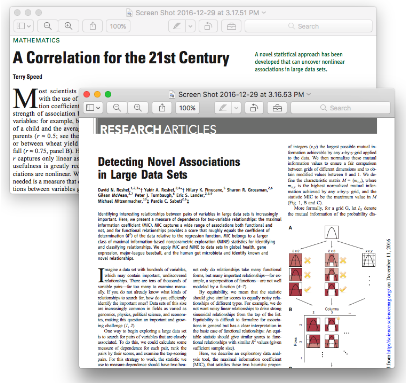

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- Only mutual information (and derived quantities) measures dependence directly

Problems with mutual information

- Hard to interpret (compared to R^2)
- Hard to estimate (compared to R^2)

Can we make $I(X; Y)$ easier to interpret?

- Define the "informational correlation" (Linfoot 1957)

$$\text{Cor}_{Info}(X, Y) = \sqrt{1 - e^{-2I(X;Y)}}$$

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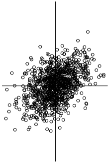
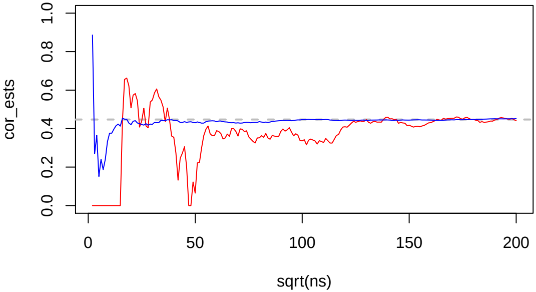
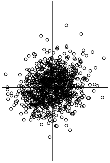
Example with $\text{Cor}_{Pearson}(X,Y) = \text{Cor}_{Info}(X,Y) = 0.44$.

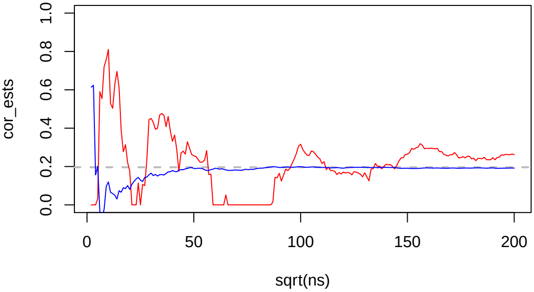




Difficulty of estimating $I(X; Y)$

Example with $\text{Cor}_{Pearson}(X, Y) = \text{Cor}_{Info}(X, Y) = 0.2.$





How to estimate $I(X; Y)$

Suppose we observe pairs $(X_i, Y_i)_{i=1}^n$ iid from density $p(x, y)$

- Definition of mutual information:

$$I(X; Y) = \int \log \left(\frac{p(x, y)}{p(x)p(y)} \right) p(x, y) dxdy$$

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- Kernel density estimate approaches estimate $p(x, y)$ (Beirlant et al. 2001, Ivanov and Rozhkova 1981)
- Nearest neighbor estimators rely on distance-based computations (Mnatsakanov et al. 2008, Goria et al. 2005, Singh et. al. 2003)

Problems in high dimensions

- Density estimation is known to have *exponential complexity* with respect to dimensionality.
  - E.g. to get the same precision, you need 10 observations for univariate X, Y but 1000 for trivariate $\vec{X}, \vec{Y}$.

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  - Gene expression time series
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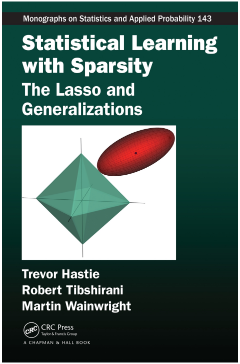
- One approach is to assume joint multivariate normality of X, Y, but this reduces mutual information to a linear statistic.
- Other approaches: binning (Bialek et al. 1991, Paninski 2003), confusion matrix of a classifier (Treves 1997, Quiroga et al. 2009)

First idea: Use sparsity!



- Suppose that $Y \approx f(X) + \epsilon$, where f depends *sparsely* on X.
- Can we exploit the sparsity to obtain an estimate of $I(X;Y)$?

Second idea: link prediction accuracy to mutual information

- If $I(X;Y) > 0$, then X carries information about Y and vice-versa.

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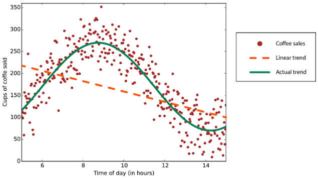
- If $I(X;Y) > 0$, then X carries information about Y and vice-versa.
- Therefore, we can *predict* Y from X (or X from Y)
- We know that often *prediction accuracy* implies a lower bound for *mutual information* (e.g. Fano 1952)

Background: Regression



- Suppose you observe $(\vec{X}^{(i)}, Y^{(i)})_{i=1}^n$ where $Y^{(i)} = f(\vec{X}^{(i)}) + \epsilon$, where f is an unknown function and ϵ is noise. (Also, assume $\mathbf{E}[\epsilon] = 0$.)

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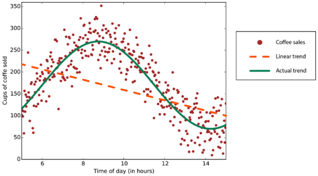

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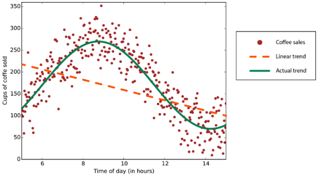

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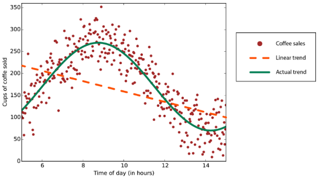

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- if we do not assume a particular form for f, we can use *nonparametric regression*.

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	Classical	*Sparse*
Linear	Ordinary Least-Squares (Gauss 1975?)	Elastic net (Zou 2008)
Nonpar.	LOWESS (Cleveland 1979)	Random forests (Breiman 2001)

Our proposal

Suppose we observe pairs $(X_i, Y_i)_{i=1}^n$ iid from density $p(x, y)$.

1. Estimate a (sparse) regression model for $\mathbf{E}[y|x]$.
2. Assess the *prediction accuracy* of the model using *identification risk*
3. Use the identification risk to obtain a lower bound for the mutual information $I(X; Y)$

Multiple-response regression

- Pairs $(x_i, y_i)_{i=1}^n$, where X is p-dimensional and Y is q-dimensional.
- Data matrices $\boldsymbol{X}_{n \times p}$, $\boldsymbol{Y}_{n \times q}$.
- For each column of Y, fit sparse model $Y^{(i)} \approx X^T \beta^{(i)} + \epsilon$, e.g. by using elastic net (Zou 2008),

$$\hat{\beta}^{(i)} = \text{argmin}_\beta ||\boldsymbol{X}^T \beta^{(i)} - Y^{(i)}||^2 + \lambda_2 ||\beta^{(i)}||_2^2 + \lambda_1 ||\beta^{(i)}||_1$$

- Or, fit a *random forest* model for each column of Y (Breiman 2001)

Regression vs Identification loss

- Independent *test set* $(x_i^*, y_i^*)_{i=1}^k$.
- Use model to predict $\hat{y}_i^* = (x_i^*)^T \hat{B}$ for $i = 1, \ldots, k$.

Two ways to evaluate the predictive accuracy of the regression model:

- Regression (mean squared-error) loss:

$$\text{MSE} = \frac{1}{k} \sum_{i=1}^k ||y_i^* - \hat{y}_i^*||^2.$$

- Identification loss (Kay 2008):

$$\text{IdLoss}_k = \frac{1}{k} \sum_{i=1}^k (1 - I\{\hat{y}_i^* \text{ is nearest neighbor of } y_i^*\}).$$

[note: point out that while idloss was introduced by Kay, that we are the first to consider theory, and add slide about 1d example/robustness]

Identification loss and mutual information

- Define the identification risk as the expected identification loss

$$\text{IdRisk}_k = \mathbf{E}[\text{IdLoss}_k]$$

- Define the Bayes risk as the identification risk given the *true* model parameters. Hence,

$$\text{BayesRisk}_k \leq \text{IdRisk}_k.$$

- **Theorem.** (Z., Benjamini 2016) There exists a function g_k such that

$$I(X;Y) \geq g_k(\text{BayesRisk}_k).$$

- Resulting estimator:

$$\hat{I}_{IdLoss}(X;Y) = g_k(\text{IdLoss}_k).$$

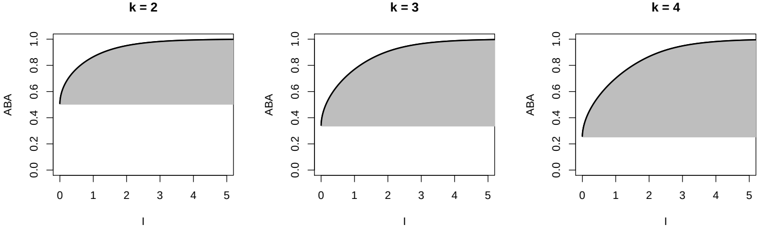
Cross-validated loss

Leave-k-out cross-validation (LkoCV) can be used for both squared-error loss and identification loss.

- Start with a dataset $(x_i, y_i)_{i=1}^N$.
- Let $n = N - k$. Consider all $\binom{N}{k}$ partitions of the dataset into a test set $(\boldsymbol{X}, \boldsymbol{Y})$ and training set $(\boldsymbol{X}^*, \boldsymbol{Y}^*)$.
- For each partition, compute the loss.
- Define the LkoCV loss as the average loss over $\binom{N}{k}$ partitions.

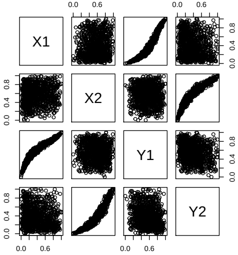
Computational note. One can subsample to avoid computing all $\binom{N}{k}$ partitions. In particular, if $m = N/k$, then one can use m-fold cross-validation which uses m partitions that have disjoint test sets.

Illustration of $C_k = g_k^{-1}$



As information increases, the maximal identification risk goes to 0. [note: pictures need to be rotated]

Simulation



- Generate data: $(Y_1, Y_2) = f(X_1, X_2, \epsilon)$ where f is nonlinear.
- Add extra noise dimensions $X_3, X_4, \ldots$.
- $n = 1000$.
- Compare Nearest-Neighbor estimator (Mnatsakov et al, 2008, implemented in `FNN`) with our method using *Random Forest*.

Simulation Results

True $I(X;Y) = 4.615$.

Extra dim	NN	RF $k = 10$	RF $k = 20$
0	**4.445**	3.989	3.924
1	3.040	**3.645**	3.610
2	1.773	**3.249**	3.182

Section 2

Theory

Functional formulation

Bayes identification risk $\text{BayesRisk}_k[p(x,y)]$ and mutual information $\text{I}[p(x,y)]$ are both *functionals* of $p(x,y)$.

$$\text{BayesAcc}_k[p(x,y)] = \frac{1}{k}\int p_X(x_1)\dots p_X(x_k)\max_{i=1}^{k} p(y|x_i)dx_1\dots dx_k dy.$$

$$\text{I}[p(x,y)] = \int p(x,y)\log\frac{p(x,y)}{p(x)p(y)}dxdy.$$

where $\text{BayesAcc}_k = 1 - \text{BayesRisk}_k$.

Problem formulation

Take $\iota > 0$, and fix $k \in \{2, 3, ...\}$. Let $p(x, y)$ be a joint density (where (X, Y) could be random vectors of any dimensionality.) Supposing

$$\mathrm{I}[p(x, y)] \leq \iota,$$

then can we find an upper bound, $g_k^{-1}(\iota)$, on $\text{BayesAcc}_k[p(x, y)]$?

Proof outline

1. Reduce problem to optimization over univariate densities.
2. Define the Lagrangian functional

$$\mathcal{L}[q(x)] = -\text{BayesAcc}_k[q(x)] + \lambda \int_0^1 q(x)dx + \nu \mathrm{I}[q(x)]$$

   which maps the univariate density $q(x)$ to a real number.
3. Compute the functional derivative of the Lagrangian

$$\nabla\mathcal{L}[q](x) = -t^{k-1} + \lambda + \nu(1 + \log q(x))$$

4. Set $\nabla\mathcal{L}[q](x) = 0$, yielding

$$q^*(t) = \alpha e^{\beta t^{k-1}}.$$

5. Check that local minimizer is global minimizer.

Result

Theorem. For any $\iota > 0$, there exists $\beta_\iota \geq 0$ such that defining

$$q_\beta(t) = \frac{\exp[\beta t^{k-1}]}{\int_0^1 \exp[\beta t^{k-1}]},$$

we have

$$\int_0^1 q_{\beta_\iota}(t) \log q_{\beta_\iota}(t) dt = \iota.$$

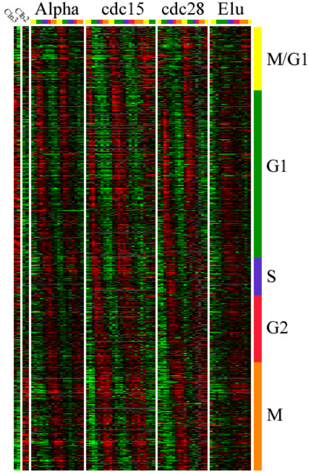
Then,

$$\sup_{I(X;Y)=\iota} \text{BayesAcc}_k = \int_0^1 q_{\beta_\iota}(t) t^{k-1} dt = g_k^{-1}(\iota).$$

Section 3

Conclusion

Application to gene expression time series



- Data for expression levels of 6178 yeast genes during cell cycle
- Total 73 time points per gene

Groups of genes

Group	No. genes
unknown	396
cell cycle	27
DNA replication	27
transport	19
cytoskeleton	17
chromatin structure	16

Total 145 different categories (only top 6 shown).

Canonical correlations between time series

Top canonical correlation (Hotelling 1936)

	CC	DR	Tr	Cy	CS
CC		1	1	1	1
DR			1	0.99	0.99
Tr				0.99	0.98
Cy					0.98
CS					

CC = cell cycle, DR = DNA replication, Tr = transport,
Cy = cytoskeleton, CS = chromatin structure

Sparse canonical correlations between time series

Using sparse CCA* (Witten and Tibshirani 2009).

	CC	DR	Tr	Cy	CS
CC		0.93	0.79	0.88	0.87
DR			0.76	0.76	0.91
Tr				0.65	0.68
Cy					0.83
CS					

CC = cell cycle, DR = DNA replication, Tr = transport,
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*: Default settings in R package `PMA`

Information correlations between time series

Taking the max of $\hat{I}(X;Y)$ and $\hat{I}(Y;X)$.

	CC	DR	Tr	Cy	CS
CC		0.92	0.79	0.97	0.81
DR			0.85	0.90	0.92
Tr				0.73	0.71
Cy					0.93
CS					

CC = cell cycle, DR = DNA replication, Tr = transport,
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Related work and future directions

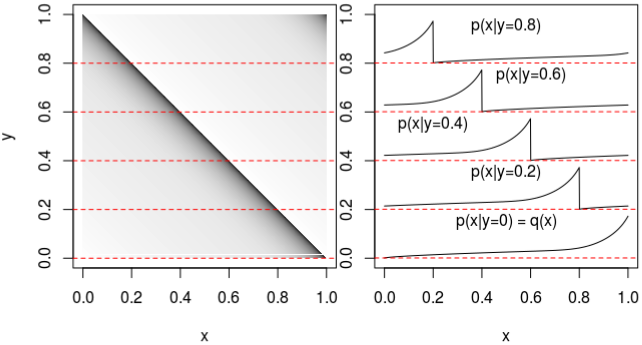
to be contd

Section 4

The End

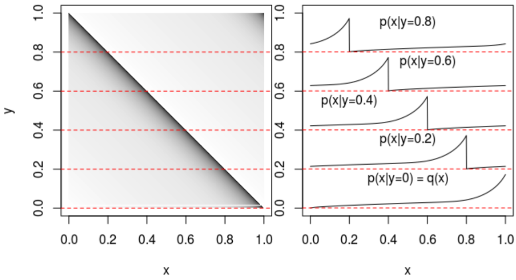
Reduced Problem

Rather than show the whole proof, we consider a simplified problem to illustrate the methods.



Actually, the simplified problem is equivalent to the full problem and we get the same answer (but this is non-trivial).

Reduced Problem



- $p(x, y)$ on unit square with uniform marginals.
- The conditional distributions $p(x|y)$ are just "shifted" copies of a common density, $q(x)$, on $[0, 1]$

$$p(x|y) = q(x - y + I\{x < y\})$$

- Furthermore, $q(x)$ is increasing in x.

Simplified formulae

The information and average Bayes error can be written in terms of $q(x)$.

$$\mathrm{I}[p(x,y)] = \int_0^1 q(x) \log q(x) dx$$

$$\text{BayesAcc}_k[p(x,y)] = \int_{[0,1]^k} \max_{i=1}^{k} q(x_i) dx_1 \cdots dx_k$$

Simplified formulae

Overload the notation and "redefine" information and average Bayes error as functionals of $q(x)$.

$$\mathrm{I}[q(x)] \stackrel{def}{=} \int_0^1 q(x) \log q(x) dx$$

$$\text{BayesAcc}_k[q(x)] \stackrel{def}{=} \frac{1}{k} \int_{[0,1]^k} \max_{i=1}^{k} q(x_i) dx_1 \cdots dx_k$$

Optimization problem

We now pose the question: how do we find $q(x)$ which maximizes $\text{BayesAcc}_k[q(x)]$ subject to $\mathrm{I}[q(x)] \leq \iota$?

- *Domain of the optimization*: Recall that $q(x)$ satisfies $q(x) \geq 0$, $\int_0^1 q(x)dx = 1$, and is increasing in x. Let $\mathcal{Q}$ denote the space of functions on $[0,1] \to [0,\infty)$ which are increasing in x.
- *Constraints*: We have two remaining constraints, $\mathrm{I}[q(x)] \leq \iota$ and $\int_0^1 q(x)dx = 1$.

Hence the problem is

$$\text{maximize}_{q(x)\in\mathcal{Q}} \text{ BayesAcc}_k[q(x)] \text{ subject to } \int_0^1 q(x)dx = 1 \text{ and } \mathrm{I}[q(x)] \leq \iota.$$

Optimization problem

$$\text{maximize}_{q(x)\in\mathcal{Q}} \text{ BayesAcc}_k[q(x)] \text{ subject to } \int_0^1 q(x)dx = 1 \text{ and } \mathrm{I}[q(x)] \leq \iota.$$

- Does a solution exist? *Yes*, because the space of measures with density $q(x)$ satisfying $\mathrm{I}[q(x)] \leq \iota$ is tight, and both the constraints and objective are continuous wrt to the topology of weak convergence.
- Given a solution $q^*(x)$ exists, there exist Lagrange multipliers $\lambda \in \mathbb{R}$ and $\nu > 0$ such that q^* minimizes

$$\mathcal{L}[q(x)] = -\text{BayesAcc}_k[q(x)] + \lambda \int_0^1 q(x)dx + \nu \mathrm{I}[q(x)]$$

$$= \int_0^1 (-t^{k-1} + \lambda + \nu \log q(x))q(x)dx.$$

Functional derivatives

- Taylor explansions are a useful trick for computing functional derivatives
- We can compute the functional derivative of $\mathcal{L}[q(x)]$ by writing

$$\begin{aligned}
&\mathcal{L}[q(x) + \epsilon\xi(x)] \\
&\quad = \int_0^1 (-t^{k-1} + \lambda + \nu \log(q(x) + \epsilon\xi(x)))(q(x) + \epsilon\xi(x))dx. \\
&\quad \approx \int (q(x) + \epsilon\xi(x))(-t^{k-1} + \lambda + \nu\{\log q(x) + \frac{\epsilon\xi(x)}{q(x)}\})dx \\
&\quad \approx \mathcal{L}[q(x)] + \int_0^1 (-t^{k-1} + \lambda + \nu(1 + \log q(x))\epsilon\xi(x)dx.
\end{aligned}$$

- Hence

$$\nabla\mathcal{L}[q](x) = -t^{k-1} + \lambda + \nu(1 + \log q(x))$$

Variational magic!

Suppose we set the functional derivative to 0,

$$0 = \nabla \mathcal{L}[q](t) = -t^{k-1} + \lambda + \nu + \nu \log q(t).$$

Then we conclude that the optimal $q^*(t)$ takes the form

$$q^*(t) = \alpha e^{\beta t^{k-1}}$$

for some $\alpha > 0$, $\beta > 0$.
From the constraint $\int q(t)dt = 1$, we get

$$q_\beta(t) = \frac{e^{\beta t^{k-1}}}{\int e^{\beta t^{k-1}} dt}.$$

Result

Theorem. For any $\iota > 0$, there exists $\beta_\iota \geq 0$ such that defining

$$q_\beta(t) = \frac{\exp[\beta t^{k-1}]}{\int_0^1 \exp[\beta t^{k-1}]},$$

we have

$$\int_0^1 q_{\beta_\iota}(t) \log q_{\beta_\iota}(t) dt = \iota.$$

Then,

$$\sup_{I(X;Y)=\iota} \text{BayesAcc}_k = \int_0^1 q_{\beta_\iota}(t) t^{k-1} dt = g_k^{-1}(\iota).$$