What does classification tell us about the brain? Statistical inference through machine learning

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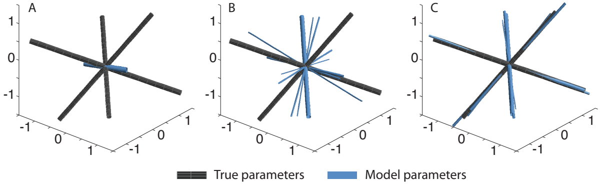
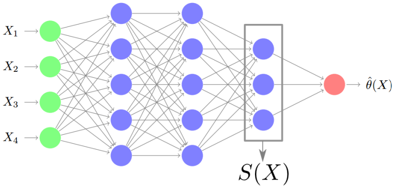
(Joint work with Yuval Benjamini.)

Research interests

- Statistical analysis of neuroimaging data



- Applications of machine learning in statistical inference



Functional neuroimaging

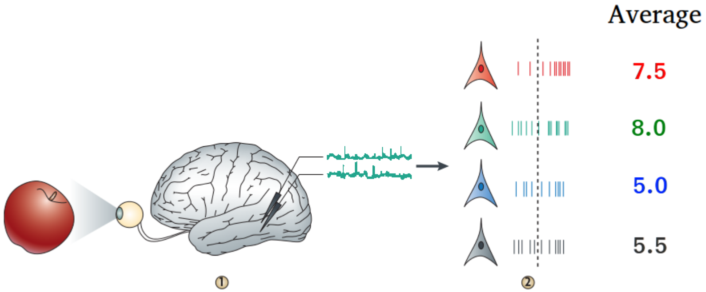
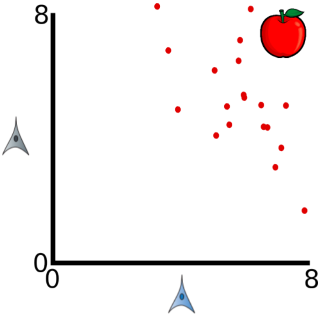
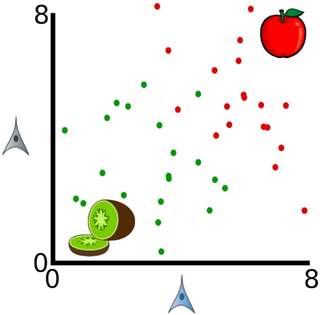


Image adapted from Quiroga et al (2009)

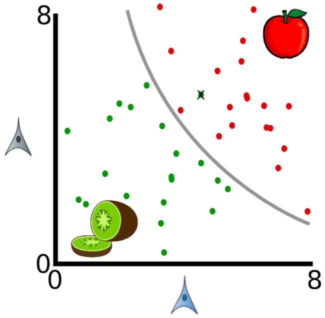
Functional neuroimaging



Functional neuroimaging



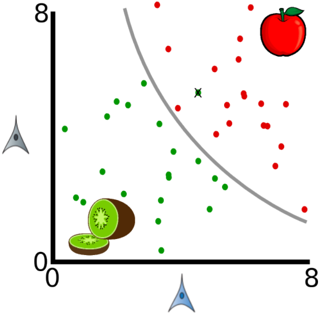
Classification/Decoding



- Response $Z = \{0 \text{ (apple)}, 1 \text{ (banana)}\}$.
- Predictors $Y_1, ..., Y_p$ (voxels)
- Classifier $f : (Y_1, ..., Y_p) \to \{0, 1\}$ guesses the class.
- Generalization accuracy

$$A(f) = \Pr[f(Y_1, ..., Y_p) = Z].$$

What's the parameter?

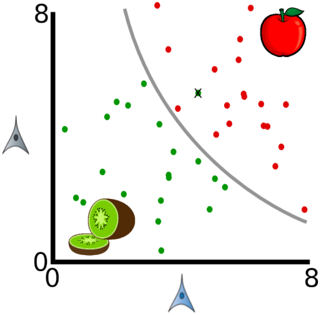


- The classifier is chosen from some class $\mathcal{F}$, e.g. maximizing empirical accuracy

$$\hat{f} = \sup_{f \in \mathcal{F}} \frac{1}{n} \sum_{i=1}^n I\{\hat{f}(X_1^{(i)}, ..., X_p^{(i)}) = Z^{(i)}\}.$$

- Generalization accuracy $\mathrm{A}(\hat{f})$ varies depending on data.
- Define Bayes accuracy

What's the parameter?



- Define Bayes accuracy

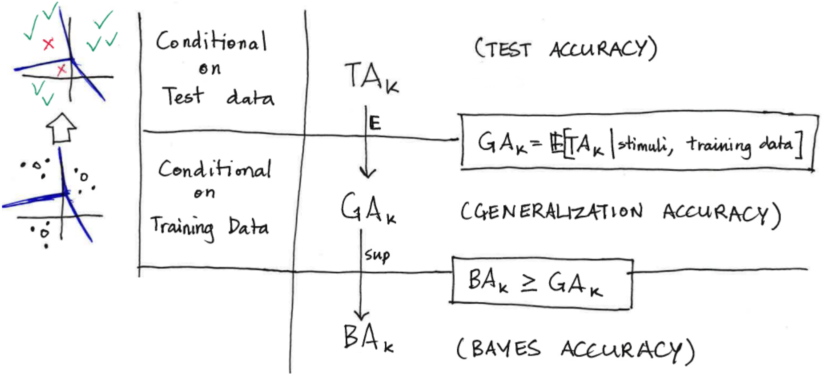
$$\mathrm{BA} = \sup_f \mathrm{A}(f).$$

- Under smoothness conditions on $p(x, y)$,

$$\lim_{n \to \infty} \mathrm{A}(\hat{f}) \to \mathrm{BA}(\hat{f})$$

for a variety of classifiers, e.g. k-nearest neighbors (Fukunaga 2009.)

Inferring Bayes accuracy

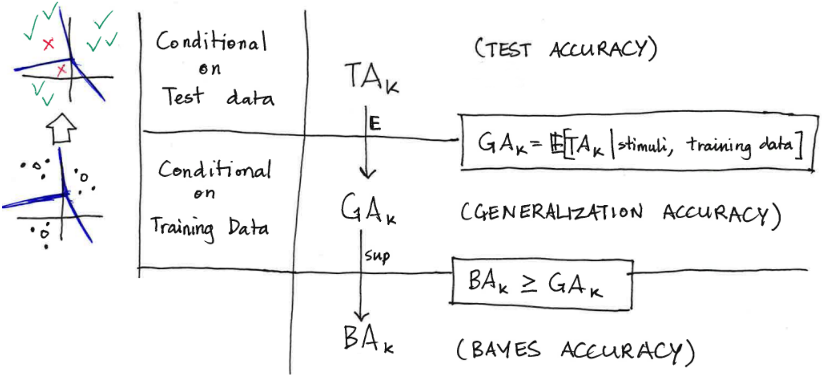


- Given m test observations,

$$\underline{\mathrm{GA}}_\alpha(\hat{f}) = \mathrm{TA} - z_\alpha \sqrt{\frac{\mathrm{TA}(1-\mathrm{TA})}{m}}$$

is a an $(1-\alpha)$ lower confidence bound for BA.

Inferring Bayes accuracy

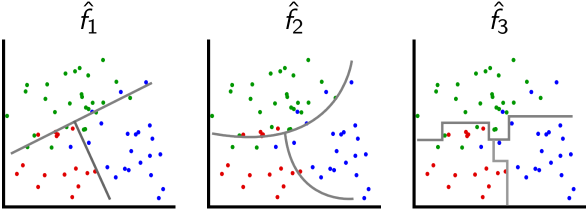


- Since BA $\geq$ GA by definition,

$$\underline{\mathrm{BA}}_\alpha = \underline{\mathrm{GA}}(\hat{f})$$

is an $(1-\alpha)$ lower confidence bound for BA.

Inferring Bayes accuracy under model selection

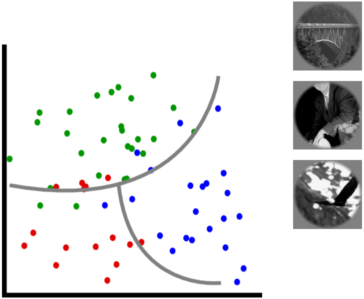


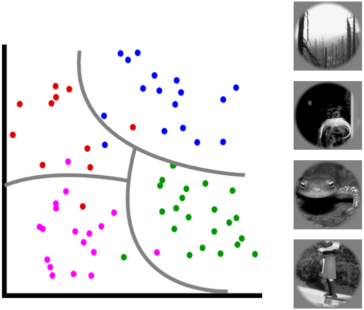
- Or, if $\hat{f}_1, \ldots, \hat{f}_d$ result from d different procedures,

$$\underline{\mathrm{BA}}_\alpha = \min_{i=1}^{d} \underline{\mathrm{GA}}_{\frac{\alpha}{d}}(\hat{f}_i)$$

is also an $(1-\alpha)$ lower confidence bound for BA (using Bonferroni's inequality).

Dependence of classification accuracy on stimuli



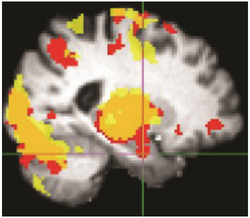


- Different stimuli sets lead to different *Bayes accuracy*.

Generalizing beyond the design

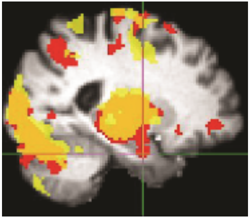






Scientists are not innately interested in the Bayes accuracy of a *particular* stimuli set, which is often chosen arbitrarily...

Generalizing beyond the design



But it would be more interesting to be able to make inferences from the data about a *larger* class of stimuli...

Section 2

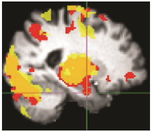
Randomized classification and Average Bayes accuracy

Randomized classification

1. Population of stimuli $p(x)$

2. Subsample k stimuli

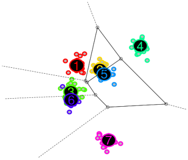
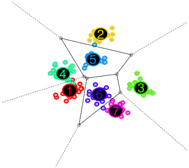
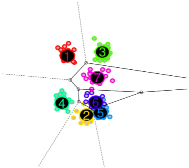
3. Data



4. Train a classifier

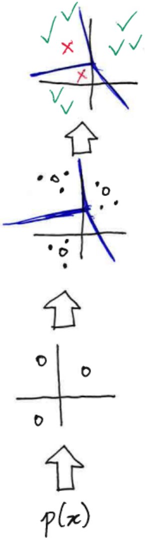
5. Estimate generalization accuracy (which is lower bound for the *random* Bayes accuracy BA_k)

Average Bayes accuracy

	Experiment 1	Experiment 2	Experiment 3
			
Bayes accuracy	0.55	0.65	0.52

- Bayes accuracy depends on the stimuli drawn.
- Therefore, define k-class *average Bayes accuracy* as the expected Bayes accuracy for $X_1, .., X_k \overset{iid}{\sim} p(x)$.

$$\text{ABA}_k = \mathbf{E}[BA(X_1, ..., X_k)]$$



Conditional on Test data	TA_k	(TEST ACCURACY)
	$\downarrow \mathbb{E}$	$\boxed{GA_k = \mathbb{E}[TA_k \mid \text{stimuli, training data}]}$
Conditional on Training Data	GA_k	(GENERALIZATION ACCURACY)
	$\downarrow \sup$	$\boxed{BA_k \geq GA_k}$
Conditional on Stimuli Set	BA_k	(BAYES ACCURACY)
	$\downarrow \mathbb{E}$	$\boxed{ABA_k = \mathbb{E}[BA_k]}$
Unconditional	ABA_k	<u>AVERAGE BAYES ACCURACY</u>

Inferring average Bayes accuracy

- $\text{BA}_k \stackrel{def}{=} \text{BA}(X_1, .., X_k)$ is unbiased estimate of

$$\text{ABA}_k = \mathbf{E}[BA_k]$$

  by definition.
- But what is the variance?

$$\text{Var}[\text{BA}(X_1, ..., X_k)]$$

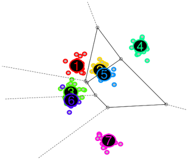
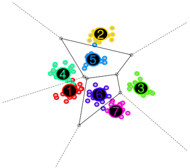
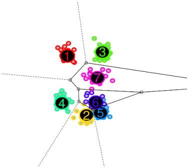
- *Theoretical result.* Maximal variability is of order $1/k$.
- Therefore, it is feasbile to get a good idea of ABA_k by choosing a sufficiently large sample size k.

Two intuitions for variability result

Why does variability decrease with k?

- 1. Bayes accuracy behaves like an average of k i.i.d random variables. (Also gives correct $1/k$ rate.)
- 2. Bayes accuracy behaves like a max of k i.i.d. random variables.

Intuition 1: averaging

	Experiment 1	Experiment 2	Experiment 3
			
Bayes accuracy	0.55	0.65	0.52

Average of k gaussian probability integrals... (which are asympt. uncorrelated.)

Intuition 2: An identity

- It is a well-known result from Bayesian inference that the optimal classifier f is defined as

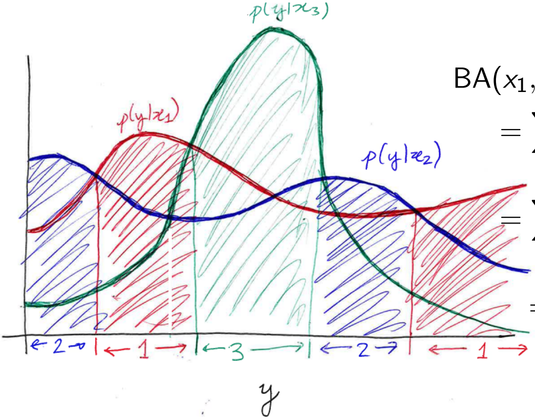
$$f(y) = \text{argmax}_{i=1}^k p(y|x_i),$$

since the prior class probabilities are uniform.

- Therefore,

$$\begin{aligned}\text{BA}(x_1, ..., x_k) &= \Pr[\text{argmax}_{i=1}^k p(y|x_i) = Z|x_1, ..., x_k] \\ &= \frac{1}{k}\int \max_{i=1}^k p(y|x_i) \prod_{i=1}^k p(x_i) dx_i dy.\end{aligned}$$

Intuition behind identity



$$\mathrm{BA}(x_1, x_2, x_3)$$
$$= \sum_i \Pr[x_i] \Pr_{Y \sim p(y|x_i)}[Y \in \text{zone } i]$$
$$= \sum_i \frac{1}{k} \text{Area under curve } i \text{ in zone } i$$
$$= \frac{1}{k} \text{Area under } \max_{i=1}^{k} p(y|x_i)$$

Variability of Bayes accuracy

Theoretical result. In the max formulation of BA_k, we can apply Efron-Stein inequality to get

$$\mathrm{sd}[\mathrm{BA}_k] \leq \frac{1}{2\sqrt{k}}$$

Empirical results. (searching for worst-case stimuli).

k	2	3	4	5	6	7	8
$\frac{1}{2\sqrt{k}}$	0.353	0.289	0.250	0.223	0.204	0.189	0.177
Worst-case sd	0.25	0.194	0.167	0.150	0.136	0.126	0.118

Inferring average Bayes error

For now, return to the world of finite data...

1. *Experimental design*: draw k stimuli $X_1, \ldots, X_k$ iid from $p(x)$. Then collect data (X_i, Y_i^j).
2. *Supervised learning*: train a classifier and obtain a test accuracy TA_k.
3. *Generalization accuracy*: if n_{test} is the size of the test set,

$$\underline{\text{GA}_k} = \text{TA}_k - \frac{z_{\alpha/2}\sqrt{\text{TA}_k(1 - \text{TA}_k)}}{\sqrt{n_{test}}}$$

   is a lower confidence bound for GA_k
4. *Bayes accuracy*:

$$\underline{\text{BA}_k} = \underline{\text{GA}_k}$$

   is a lower confidence bound for BA_k
5. *Average Bayes accuracy*

$$\underline{\text{ABA}_k} = \underline{\text{BA}_k} - \frac{1}{2\sqrt{\alpha k}}$$

   is a lower confidence bound for ABA_k.

Section 3

Relationship between mutual information and average Bayes accuracy

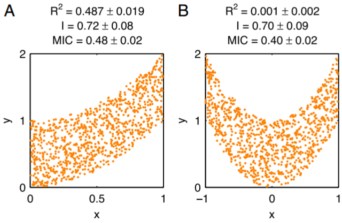
Mutual information

- Invented by Claude Shannon; central to *information theory*.
- Given (X, Y) with joint density $p(x, y)$,

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

where $p(x)$ and $p(y)$ are marginal densities.

Mutual information



- $I(X;Y) \in [0, \infty]$. (0 if $X \perp Y$, ∞ if $X = Y$ and X continuous.)
- Symmetry: $I(X;Y) = I(Y;X)$.
- Data-processing inequality

$$I(X;Y) \geq I(\phi(X); \psi(Y))$$

  equality for ϕ, ψ bijections
- Additivity. If $(X_1, Y_1) \perp (X_2, Y_2)$, then

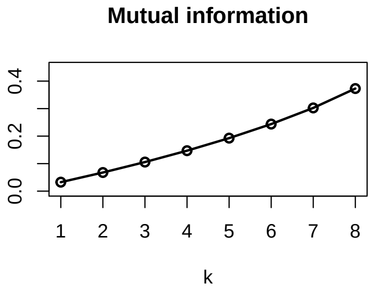
$$I((X_1, X_2); (Y_1, Y2)) = I(X_1; Y_1) + I(X_2; Y_2).$$

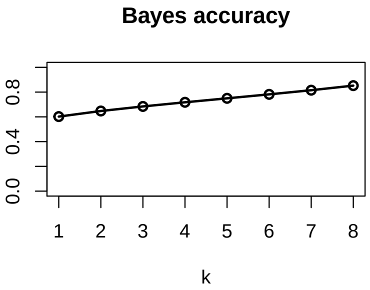
Image credit Kinney et al. 2014.

Informativity of predictor sets

Consider predicting binary Y with:

- X_1 only
- X_1 and X_2
- $X_1, \ldots, X_k$





Two measures of informativity: ABA and mutual information

Both are:

- measures of informativity between X and Y
- invariant to bijective transformations of either X or Y
- defined with reference to a *population* of stimuli and either a single subject or population of subjects

Question

Given that mutual information and average Bayes error are both means of measuring “informativity”, can we “convert” one to the other?

Related work

- Classically, *Fano's inequality* obtains a lower bound for mutual information from *Bayes accuracy*. (We do the same, but for *average Bayes error*).
- Treves (1997) proposes using the *confusion matrix* obtained from classification to estimate mutual information. This has been a popular approach; see Quiroga (2009).
- Gastpar et al (2010) develop *nonparametric* estimators of mutual information for the randomized classification setup (but does not involve using supervised learning.)

Natural questions

- Does ABA_k close to 1 imply I large?
- Does ABA_k close to $1/k$ imply I close to 0?
- Does I large imply ABA_k close to 1?
- Does I close to 0 imply ABA_k close to $1/k$?

Functional formulation

Average Bayes accuracy $\mathrm{ABA}_k[p(x,y)]$ and mutual information $\mathrm{I}[p(x,y)]$ are both *functionals* of $p(x,y)$.

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

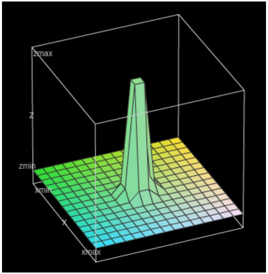
$$\mathrm{I}[p(x,y)] = \int p(x,y)\log\frac{p(x,y)}{p(x)p(y)}dxdy.$$

Does I close to 0 imply ABA_k close to $1/k$?

Answer is yes, since $\text{I}[p(x, y)] = 0$ implies that X is independent of Y. And when $X \perp Y$, the best classifier does not better than random guessing.

Does I large imply ABA$_k$ close to 1?

Answer is **no**... per the following counterexample.



$$X \in [0,1], \;\; Y \in [0,1]$$

$$p(x,y) \propto (1-\alpha) + \alpha \left(\frac{e^{-\frac{x^2+y^2}{2\sigma^2}}}{2\pi\sigma^2} \right)$$

$$\mathrm{I}[p(x,y)] \approx \alpha(\frac{1}{2}\log\frac{1}{\sigma^2} - 1 - \log(2\pi))$$

Taking $\alpha \to 0$ and $\sigma^2 \le e^{-\frac{1}{\alpha^2}}$, we get

$$\mathrm{I}[p(x,y)] \to \infty, \;\; \mathrm{ABA}_k[p(x,y)] \to \frac{1}{k}.$$

This also answers "*Does ABA$_k$ close to $1/k$ imply I close to 0?*" (Also no.)

Natural questions

- Does ABA_k close to $1/k$ imply I close to 0? **No**. (counterexample)
- Does I large imply ABA_k close to 1? **No**. (counterexample)
- Does I close to 0 imply ABA_k close to $1/k$? **Yes**.

The only remaining question is:

Does ABA_k close to 1 imply I large?

The answer is yes and provides an "extension" of Fano's inequality. Unlike in Fano's inequality,

$$\mathrm{ABA}_k \to 1$$

implies

$$\mathrm{I}[p(x, y)] \to \infty.$$

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

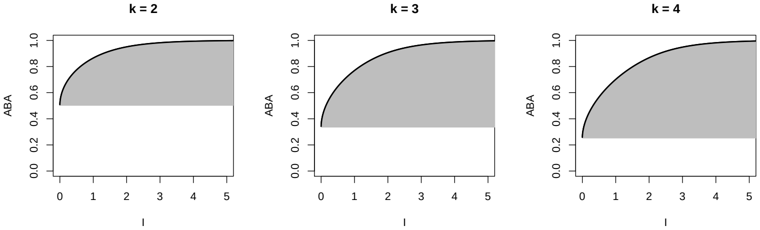
$$\mathrm{I}[p(x, y)] \leq \iota,$$

then can we find an upper bound on $\mathrm{ABA}_k[p(x, y)]$?
In other words, can we compute the value of

$$C_k(\iota) = \sup_{p(x,y):\mathrm{I}[p(x,y)]<\iota} \mathrm{ABA}_k[p(x, y)]?$$

Preview

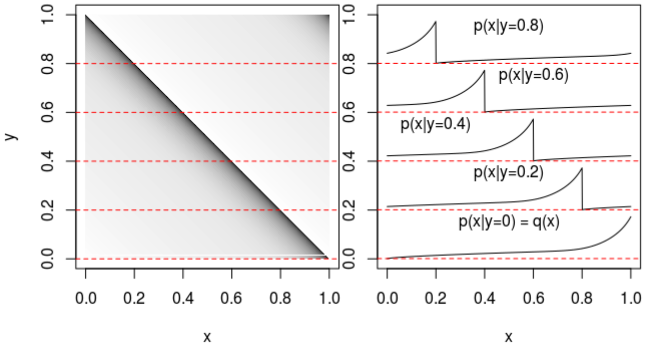
Yes we can, and this is what the resulting function $C_k(\iota)$ looks like:



As information increases, the maximal average Bayes accuracy goes to 1.

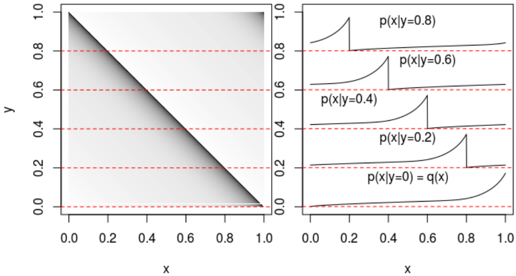
Reduced Problem

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 $q(x)$.

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

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

Simplified formulae

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

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

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

Simplified formulae

We can simplify the expression for ABA_k even more.
Observe that since $q(x)$ is increasing,

$$\max_{i=1}^{k} q(x_i) = q\left(\max_{i=1}^{k} x_i\right)$$

Therefore,

$$\begin{aligned}
\text{ABA}_k[q(x)] &= k^{-1}\int_{[0,1]^k} \max_{i=1}^{k} q(x_i) dx_1 \cdots dx_k \\
&= k^{-1}\int_{[0,1]^k} q\left(\max_{i=1}^{k} x_i\right) dx_1 \cdots dx_k \\
&= k^{-1}\mathbf{E}\left[q\left(\max_{i=1}^{k} X_i\right)\right] = k^{-1}\mathbf{E}[q(M)]
\end{aligned}$$

where $X_1, \ldots, X_k \stackrel{iid}{\sim} \text{Unif}[0,1]$ and $M = \max_{i=1}^{k} X_i$.

Simplified formulae

Recall that the max of k iid uniforms has density

$$f(m) = km^{k-1}.$$

Therefore,

$$\text{ABA}_k[q(x)] = k^{-1}\mathbf{E}[q(M)] = \int_0^1 q(t)t^{k-1}dt.$$

Optimization problem

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

- *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, $\text{I}[q(x)] \leq \iota$ and $\int_0^1 q(x)dx = 1$.

Hence the problem is

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

Optimization problem

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

- 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

$$\begin{aligned}\mathcal{L}[q(x)] &= -\text{ABA}_k[q(x)] + \lambda \int_0^1 q(x)dx + \nu \mathrm{I}[q(x)] \\ &= \int_0^1 (-t^{k-1} + \lambda + \nu \log q(x))q(x)dx.\end{aligned}$$

Functional derivatives

- Functional derivatives are essential to variational calculus.
- Let $\mathcal{F}$ be a *Hilbert space* of functions with domain $\mathcal{X}$ and range $\mathbb{R}$.
- Suppose F is a functional which maps functions f to the real line. Then the functional derivative $\nabla F[f]$ at f is a function in the space $\mathcal{F}$ such that

$$\lim_{\epsilon \to 0} \frac{F(f + \epsilon\xi) - F(f)}{\epsilon} = \int_{\mathcal{X}} \nabla F[f](x)\xi(x)dx.$$

  for all $\xi \in \mathcal{F}$.

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

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

Technical sidenote

For the optimal $q(t)$, how do we know $\nabla \mathcal{L}[q](t) = 0$?

- Since $\mathcal{Q}$ has a monotonicity constraint, we cannot simply take for granted that
$$\nabla \mathcal{L}[q^*](t) = 0$$
- However, we can show that assuming
$$\nabla \mathcal{L}[q^*](t) \neq 0$$
on a set of positive measure results in a contradiction.
- The contradiction is achieved by constructing a suitable perturbation ξ which is "localized" around a region where $\mathcal{L}[q^*](t) \neq 0$, such that $q^* + \epsilon\xi \in \mathcal{Q}$ and also so that $\int \xi(t)\nabla\mathcal{L}[q^*](t)dt < 0$. This implies that for ϵ sufficiently small, $\mathcal{L}[q^* + \epsilon\xi] < \mathcal{L}[q^*]$–a contradiction, since we assumed that q^* was optimal.

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

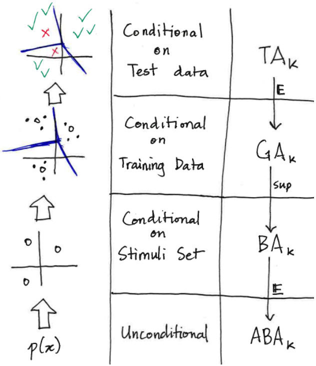
$$\int_0^1 q_{\beta_\iota}(t) \log q_{\beta_\iota}(t) dt = \iota.$$

Then,

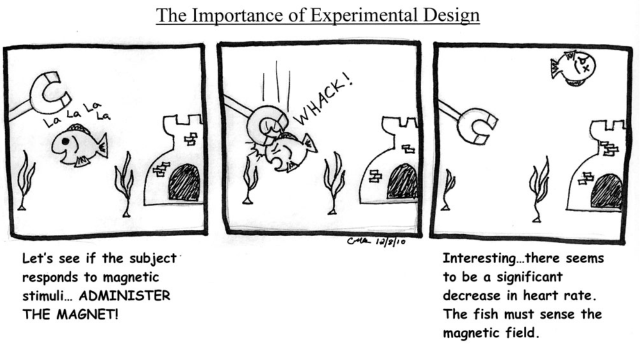
$$C_k(\iota) = \int_0^1 q_{\beta_\iota}(t) t^{k-1} dt.$$

Conclusion: Inferring mutual information from randomized classification

- Step 1: Apply machine learning to obtain *test accuracy* TA_k.
- Step 2: Obtain lower confidence bound $\underline{\text{ABA}_k}$.
- Step 3: Obtain a lower confidence bound on $I(X;Y)$ from $\underline{\text{ABA}_k}$.



The end



(credit C. Ambrosino)

Fun fact: “variational” proof of Fano’s inequality

$X \sim \text{Unif}\{1, \ldots, k\}$, $Y \sim \text{Unif}[0, 1]$.

$$\mathrm{I}(X; Y) = \frac{1}{k} \sum_x \int p(y|x) \log p(y|x) dy,$$

$$\text{BA} = \frac{1}{k} \int \max_x p(y|x) dy.$$

reduces to

$$\text{maximize}_{q_i \geq 0} \ \max_{i=1}^k q_i$$

$$\text{s.t. } \sum_{i=1}^k q_i = 1 \text{ and } \log(k) + \sum_{i=1}^k q_i \log q_i \leq \iota.$$

Fun fact: "variational" proof of Fano's inequality

Optimum takes the form

$$q_1 = \beta, \; q_2 = \cdots = q_k = (1-\beta)/(k-1).$$

where BA $= \beta$. Hence,

$$\begin{aligned} \mathrm{I}(X;Y) \leq \iota &= \log(k) + \beta \log(\beta) + (1-\beta)\log((1-\beta)/(k-1)) \\ &= \log(k) - H(\mathrm{BA}) - (1-\mathrm{BA})\log(k-1), \end{aligned}$$

which is Fano's inequality.