Inferring health conditions from fMRI-graph data

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Abstract here

Note: human males and females are equal, but they are both inferior to robots, therefore we use "its" instead of "his" or "her".

*** Draft structure:

– introduction: method and philosophy explained in simple words, with advantages (strict connection assumptions-final eqn, first principles, built-in quantification of reliability and "summary prediction percentage", computationally feasible, it works, relation to freq methods (t-distr), works with simple samples, dynamic features – prevent overfitting). Examples from other fields.

– sufficiency: idea. how the formulae discard redundant info, but it's cheaper to do it by hand

– explain the generic problem: general formulae simply explained.

* code to do the final calculation.

– practical application to fmri data:

Discuss:

* how sharp the prediction

* self-quantification of reliability

* summary prediction for next patient

* which graph properties give the best results

– final discussion: relation and "validation" with nonparametrics (refs to other literature).

"Where do probability models come from? To judge by the resounding silence over this question on the part of most statisticians, it seems highly embarrass- ing." (Dawid 1982)

1 Introduction

Diagnosing Alzheimer's Disease, especially in the early stage, is costly and burdensome for the patients, since it comprises a battery of psychological tests and an extraction of disease specific biomarkers from the cerebrospinal fluid (ouch!). A cheaper and more convenient procedure would be a diagnosis based on images obtained through fMRI. Based on previous polymodal [what does this mean?] studies demonstrating

disrupted inter- and intra-cortical connectivity in Alzheimer's Disease [ref], in another awesome paper we argue that the functional connectivity of the whole cortex, summarized in a computationally manageable number of graph-theoretic parameters – derived from the full, computationally unmanageable fMRI data – might be a good predictor for the cause of the disease.

The inference of the health condition from the graph parameters is, in principle, uniquely determined by the probability calculus once we have graph data from subjects presenting each health condition that we want discriminate. The uniqueness is assured under the assumption of *exchangeablitiy*, which simply says that the data of the subjects are all equally important and the order in which the subjects were scanned does not matter. But the calculation of the resulting probabilities is computationally unmanageable at present.

A computationally feasible approach is to uphold the additional working hypothesis that specific features of the graph data – their first and second empirical moments, for example – are *sufficient* to infer the health condition. This working assumption determines a *unique* probability model thanks to the Koopman-Pitman-Darmois theorem (Koopman 1936; Pitman 1936; Darmois 1935; Hipp 1974; Andersen 1970; Denny 1967; Fraser 1963; Barankin et al. 1963 see also).

The fact that our working hypothesis determines a unique probability model is very powerful. If the inferences made by the model do not satisfy us, then we know that the working hypothesis must be false. Vice versa, if we don't deem the working hypothesis to be valid, we shouldn't use the probability model. There is no fiddling or tweaking in between that make us wonder were things are going wrong, if they go wrong.

The main result can be seen in the plots of pp. 12 and 13. Section 2 presents the problem and the idea behind my method. Sections 4, 5 work out the formulae of this method and apply them to a set of real fMRI-graph data. The final section 6 contains remarks on generalizations, approximations, and more.

2   Problem and method

Our goal, stripped to its essentials, is this.

Given the fMRI data of an individual and other knowledge discussed below, assess the plausibility that the individual is healthy or suffers from a brain disease, from a set of known possible ones. For example: assess

whether the individual is healthy, or has Alzheimer's Disease, or is mildly cognitively impaired (three possibilities); or: assess whether the individual is healthy or has schizophrenia (two possibilities). The brain diseases are supposed to be mutually exclusive, and to exhaust the set of possible diseases that can be expected in the individual.

The "other knowledge" fleetingly mentioned above consists in the fMRI data of individuals of known health conditions. This knowledge is essential for our plausibility assessment, for we would not be able to relate fMRI data and health condition otherwise.

Label the individual of unknown health condition with 0, and those whose health conditions and fMRI data are known by $1, \ldots, N$. Denote the fMRI data and health condition of individual i by x_i and h_i Our goal at this point is to assess the plausibility

$$p(h_0 | x_0, \; h_1, x_1, \ldots, h_N, x_N, \; I), \tag{1}$$

where I denotes additional knowledge or working assumptions to be discussed shortly.

The labels given to the individuals are arbitrary and we could shuffle them without affecting our probability assessment. Said otherwise, suppose that individual 3 was healthy, $h_3 = \mathrm{H}$, and had fMRI data $x_3 = X$; and that individual 7 had Alzheimer, $h_7 = \mathrm{A}$, and had fMRI data $x_7 = Y$. What matter is that we have observed the specific pairs (H, X) and (A, Y); whether the individual of the first pair was labelled "3" and the other "7", or vice versa, is irrelevant. This is true no matter how many individuals we observed or will observe.

The irrelevance of labelling to our plausibility assessment is called *exchangeability* and greatly circumscribes our possible plausibility assessments. It implies that the plausibility (1) remains the same under permutations of the individuals' labels. A theorem by de Finetti (**definetti1930**; **definetti1937**; **hewittetal1955**) states that the probability of observing N individuals with health conditions h_i and fMRI data x_i must have the form

$$p(h_0, x_0, \; h_1, x_1, \; \ldots, h_N, x_N | I) = \int \left[\prod_i p(h_i, x_i | q) \right] p(q | I) \,\mathrm{d}q \tag{2}$$

, in the sense that individual "3", say, could just as well have been labelled "7", and vice versa. Maybe the labels reflect the temporal order in which the individuals were studied, yet we could shuffle them without affecting our probability assessment.

This simple fact is very important

There is an important assumption, which greatly circumscribes our possible plausibility assessments

3 Problem and method – old

Let's say that each individual can be either Healthy, or suffer from Alzheimer, or be mildly Cognitively impaired. This is its health condition. Let's also say that we can associate a "health indicator" with each individual, obtained from measurements on its brain. Here we use an indicator consisting in six parameters obtained from a fMRI scan: graph weights, shortest path, cluster coefficient, degree, modularity, number of nodes.

Our problem is to infer the health condition of an individual given its indicator, and vice versa. For this inference we can use known health & indicator data observed in a set of other individuals.

This note presents a method to make such inferences. I first explain it and then illustrate it numerically with Simone and Claudia's data. The method has these advantages:

- It only uses the three laws of probability, plus an inferential assumption. Since the results are uniquely determined by this assumption, we can see at once which part of the method succeeds or fails, and modify it accordingly.

- The assumption states what kind of data are inferentially relevant. It does not involve statistical parametric models or the like. Thus the assumption can be understood without expertise in statistical models.

- No statistical models or parameters are pulled out of the hat, nor are they the starting or final point of the method. They do appear in between, but only as strict mathematical consequences of the inferential assumption.

Imagine to have a number of individuals indexed by $i \in \{1, 2, \ldots\}$. For each individual we know either the first or both of these data:

- health condition $h_i \in \{A, C, H\}$;

- six-dimensional health indicator $x_i \in \mathbf{R}^6$ consisting in graph weights, shortest path, cluster coefficient, degree, modularity, number of nodes, obtained from an fMRI scan.

Given a new individual we would like to know:

1. How likely is it that this new individual has Alzheimer, or is healthy, or cognitively impaired, given that an fMRI on it gave the value x for the six parameters, and given the collected data from the other individuals? In formulae,

$$p(h \mid x, \{h_i, x_i\}) = ? \tag{3}$$

2. How likely is it that an fMRI on the new individual yields the values x for the six parameters, given that the individual has Alzheimer, or is healthy, or cognitively impaired, and given the collected data from the other individuals? In formulae,

$$p(x \mid h, \{h_i, x_i\}) = ? \tag{4}$$

It turns out that the probabilities above can be numerically determined if we make a specific assumption about *which part of the data from the other individuals is relevant for the inference, and which is irrelevant*. This method is called "modelling by sufficiency" and relies on powerful theorems that deduce the form of a probability distribution from inferential relevance of data, using only the three rules of probability theory (e.g.: Bernardo et al. 2000 ch. 4; Lindley 2008 § 5.5; Diaconis et al. 1981; Lauritzen 1988; Kallenberg 2005); see Dawid (2013) for an insightful review.

4   Example – general

Recall that $h_i \in \{A, H, C\}$ and $x_i \in \mathbf{R}^6$.

We assume to have a set of data $\{h_i, x_i\}$ from n_A Alzheimer, n_H healthy, and n_C cognitively impaired individuals. An example is Claudia's data, table 1 on p. 10. We also assume that we know the health condition, but not the health indicator, of a very large number – thousands – of additional individuals: m_A of these have Alzheimer, m_H are healthy, and m_C are impaired. These may come from surveys or registration data from a country's national health institute.

We make this inferential assumption:

Assumption. *To predict whether a new individual has one of the three health conditions, denoted by h, and health indicator x, given data $\{h_i, x_i\}$, the only relevant quantities from the data are*:

- *the number of individuals of each health condition;*
- *the means, and second moments (equivalent to empirical variances and covariances) of the six parameters for the individuals with the* same *health condition h to be predicted.*

In formulae, to predict let's say $(h = \mathrm{A}, x)$ for example, we only need

$$n_\mathrm{A} := \sum_i \delta(h_i = \mathrm{A}), \quad n_\mathrm{H} := \sum_i \delta(h_i = \mathrm{H}), \quad n_\mathrm{C} := \sum_i \delta(h_i = \mathrm{C}),$$

$$\overline{x}_\mathrm{A} := \sum_i x_i \, \delta(h_i = \mathrm{A})/n_\mathrm{A}, \qquad \overline{x^\intercal x}_\mathrm{A} := \sum_i x_i{}^\intercal x_i \, \delta(h_i = \mathrm{A})/n_\mathrm{A}. \tag{5}$$

Here $\delta(X) = 1$ if X is true and zero otherwise, and the column-row product $\overline{x^\intercal x}_\mathrm{A}$ contains the raw second moments. It is related to the matrix of empirical covariances via

$$\frac{1}{n_\mathrm{A}} \sum_i^{h_i=\mathrm{A}} (x_i - \overline{x}_\mathrm{A})^\intercal (x_i - \overline{x}_\mathrm{A}) = \overline{x^\intercal x}_\mathrm{A} - \overline{x}_\mathrm{A}{}^\intercal \overline{x}_\mathrm{A}. \tag{6}$$

The choice of means and second moments is made just for the sake of this example. I discuss generalizations later.

In terms of probabilities, we are saying that

$$\mathrm{p}[(\mathrm{A}, x)| \{h_i, x_i\}] = \mathrm{p}[(\mathrm{A}, x)| \, n_\mathrm{A}, n_\mathrm{H}, n_\mathrm{C}, \overline{x}_\mathrm{A}, \overline{x^\intercal x}_\mathrm{A}], \tag{7}$$

and analogously for the other two health conditions. This is called a "model by sufficient statistics" (Bernardo et al. 2000 ch. 4).

The importance of the assumption above is that it almost completely determines the probabilities (7) above: the probability for a new individual to have Alzheimer, i.e. $h = \mathrm{A}$, and to have a health indicator with value x, given data $\{h_i, x_i\}$, *must* take the form

$$\mathrm{p}[(\mathrm{A}, x)| \{h_i, x_i\}] = \int \nu_\mathrm{A} \, \mathrm{p}(\nu_\mathrm{A}, \nu_\mathrm{H}, \nu_\mathrm{C}| \, n_\mathrm{A}, n_\mathrm{H}, n_\mathrm{C}) \, \mathrm{d}\nu_\mathrm{A} \, \mathrm{d}\nu_\mathrm{H} \, \mathrm{d}\nu_\mathrm{C} \times$$

$$\int N(x| \, \mu, \Sigma) \, \mathrm{p}(\mu, \Sigma| \, n_\mathrm{A}, \overline{x}_\mathrm{A}, \overline{x^\intercal x}_\mathrm{A}) \, \mathrm{d}\mu \, \mathrm{d}\Sigma, \quad \text{(8a)}$$

where $N(x| \, \mu, \Sigma)$ is the normal distribution with means μ and covariance matrix Σ, the variables $\nu_\mathrm{A}, \nu_\mathrm{H}, \nu_\mathrm{C}$ are numbers, and

$$\mathrm{p}(\nu_\mathrm{A}, \nu_\mathrm{H}, \nu_\mathrm{C}| \, n_\mathrm{A}, n_\mathrm{H}, n_\mathrm{C}) \propto \mathrm{p}(\nu_\mathrm{A}, \nu_\mathrm{H}, \nu_\mathrm{C}) \, \nu_\mathrm{A}^{n_\mathrm{A}} \nu_\mathrm{H}^{n_\mathrm{H}} \nu_\mathrm{C}^{n_\mathrm{C}}, \tag{8b}$$

$$\mathrm{p}(\mu, \Sigma| \, n_\mathrm{A}, \overline{x}_\mathrm{A}, \overline{x^\intercal x}_\mathrm{A}) \propto \mathrm{p}(\mu, \Sigma) \, \det(2\pi\Sigma)^{-\frac{n_\mathrm{A}}{2}} \times$$

$$\exp\left[-\tfrac{1}{2} n_\mathrm{A} \mu^\intercal \Sigma^{-1} \mu + n_\mathrm{A} \mu \Sigma^{-1} \overline{x}_\mathrm{A} - \tfrac{1}{2} n_\mathrm{A} \operatorname{tr}(\overline{x^\intercal x}_\mathrm{A} \Sigma^{-1})\right]. \quad \text{(8c)}$$

The ranges of integration are

$$0 \leqslant \nu_\mathrm{A}, \nu_\mathrm{H}, \nu_\mathrm{C} \leqslant 1, \quad \nu_\mathrm{A} + \nu_\mathrm{H} + \nu_\mathrm{C} = 1,$$

$$\Sigma_{ij} \text{ such that } \Sigma \text{ is positive definite.} \tag{9}$$

These expressions may look complicated but summarize a simple procedure:

1. Starting from the distribution $p(\nu_A, \nu_H, \nu_C)$, which may be taken equal to constant $\times \delta(\nu_A + \nu_H + \nu_C - 1)$, we multiply into it a factor ν_A for each Alzheimer, a factor ν_H for each Healthy, and a factor ν_C for each Impaired individual in our data; then one more factor ν_A for our question whether the new individual has Alzheimer. And finally we integrate the resulting expression over ν_A, ν_H, ν_C.

2. We start from the distribution $p(\boldsymbol{\mu}, \boldsymbol{\Sigma})$, which may be taken proportional to $\det \boldsymbol{\Sigma}^{-1-d/2}$, where $d = 6$, the number of parameters. We multiply into it a normal $N(x_i | \boldsymbol{\mu}, \boldsymbol{\Sigma})$ for each Alzheimer individual in the data, using the parameters x_i from its fMRI. Then we multiply one more normal $N(x | \boldsymbol{\mu}, \boldsymbol{\Sigma})$ with variable x. And finally we integrate the resulting expression over $\boldsymbol{\mu}, \boldsymbol{\Sigma}$.

3. We multiply the two expressions above; this gives the non-normalized probability that the new individual has Alzheimer and node size and modularity x.

The choice above for the distributions $p(\nu_A, \nu_H, \nu_C)$ and $p(\boldsymbol{\mu}, \boldsymbol{\Sigma})$ comes from group-invariance arguments (Jeffreys 2003; Jaynes 2003; Minka 2001).

A further simplification appears when we use the data about the large number of individuals m_A, m_H, m_C. Then the first step above can be skipped over, and the probabilities we're seeking simplify to

$$p[(A, x) | \text{data}] =$$

$$\frac{m_A}{m_A + m_H + m_C} \int N(x | \boldsymbol{\mu}, \boldsymbol{\Sigma}) \, p(\boldsymbol{\mu}, \boldsymbol{\Sigma} | n_A, \overline{x}_A, \overline{x^\top x}_A) \, d\boldsymbol{\mu} \, d\boldsymbol{\Sigma}, \quad (10a)$$

$$p[(H, x) | \text{data}] =$$

$$\frac{m_H}{m_A + m_H + m_C} \int N(x | \boldsymbol{\mu}, \boldsymbol{\Sigma}) \, p(\boldsymbol{\mu}, \boldsymbol{\Sigma} | n_H, \overline{x}_H, \overline{x^\top x}_H) \, d\boldsymbol{\mu} \, d\boldsymbol{\Sigma}, \quad (10b)$$

$$p[(C, x) | \text{data}] =$$

$$\frac{m_C}{m_A + m_H + m_C} \int N(x | \boldsymbol{\mu}, \boldsymbol{\Sigma}) \, p(\boldsymbol{\mu}, \boldsymbol{\Sigma} | n_C, \overline{x}_C, \overline{x^\top x}_C) \, d\boldsymbol{\mu} \, d\boldsymbol{\Sigma}. \quad (10c)$$

From the formulae above we can then answer our initial questions:

1. Probability that the new individual has health condition h if its node size and modularity are x:

$$p(h | x, \text{data}) = \frac{p[(h, x) | \text{data}]}{p[(A, x) | \text{data}] + p[(H, x) | \text{data}] + p[(C, x) | \text{data}]}. \quad (11)$$

2. Probability that the new individual's node size and modularity are x if the individual has health condition $h \in \{A, H, C\}$:

$$\mathrm{p}(x \mid h, \text{data}) = \frac{\mathrm{p}[(h, x) \mid \text{data}]}{\int \mathrm{p}[(h, x) \mid \text{data}]\, \mathrm{d}x} = \frac{\mathrm{p}[(h, x) \mid n_h, \overline{x}_h, \overline{x^\intercal x}_h]}{\int \mathrm{p}[(h, x) \mid n_h, \overline{x}_h, \overline{x^\intercal x}_h]\, \mathrm{d}x}$$

$$= \frac{\Gamma\!\left(\frac{n_h+1}{2}\right)}{\Gamma\!\left(\frac{n_h+1-d}{2}\right)} \det\!\left[\pi (n_h + 1)(\overline{x^\intercal x}_h - \overline{x}_h{}^\intercal \overline{x}_h)\right]^{-\frac{1}{2}} \times \tag{12}$$

$$\left\{1 + (x - \overline{x}_h)^\intercal \left[(n_h + 1)(\overline{x^\intercal x}_h - \overline{x}_h{}^\intercal \overline{x}_h)\right]^{-1}(x - \overline{x}_h)\right\}^{-\frac{n_h+1}{2}}.$$

The latter is a multidimensional Student's t-distribution (Minka 2001 §§ 5, A; Gupta et al. 2000 ch. 4; Murphy 2012 § 2.5.3; Bernardo et al. 2000 p. 139; Bishop 2006 § 2.3.7; DeGroot 2004 § 5.6). It has mean and mode $\overline{x}_h$, and covariance matrix $\frac{n_h+1}{n_h-1-d}(\overline{x^\intercal x}_h - \overline{x}_h{}^\intercal \overline{x}_h)$. This distribution exists only if $n_h > d$: this means that we need data from a number of individuals larger than the number of parameters – it's the effect of using an "uninformative" distribution $\mathrm{p}(\mu, \Sigma)$. The variance exists only if $n_h > d + 1$.

5 Example – worked out

Let's apply the formulae above to Claudia and Simone's data, table 1 on p. 10. The sufficient statistics are shown on table 2, p. 11.

I substituted these data into formula (12) for the three health conditions. The analytic result was also found by numerical integration of (8) with Mathematica via a deterministic cubature routine (Hahn 2005).

The three distributions $\mathrm{p}(x \mid A, \text{data})$, $\mathrm{p}(x \mid H, \text{data})$, $\mathrm{p}(x \mid C, \text{data})$, are over a six-dimensional space and therefore difficult to visualize. Figure 1 shows the contours of the three distributions at one and standard deviations, on a two-dimensional section of the six-dimensional space. The two-dimensional plane is the one that passes through the expectations of the three distributions. The distributions can overlap even more or even less than this in the remaining four dimensions, of course.

Note: One must be careful in interpreting standard-deviation regions in high dimensions, because volumes in high dimensions have properties counterintuitive to our three-dimensional intuition, because ratios of volumes scale as the dth power of the ratios of length. For example, in a sphere of unit radius in six dimensions, 50 % of the volume is enclosed within a shell of thickness 0.1 from the outer surface. If you have a cup of tea in 22 dimensions and you shrink it by just 10 %, you lose 90 % of tea. In high dimensions, most of the volume is "on the boundary".

8

The expectations and covariances of the distributions are related to those in the data by

$$\mathrm{E}(x \mid h, \mathrm{data}) = \overline{x}_h,$$

$$\mathrm{E}[(x - \mathrm{E}(x))^{\mathsf{T}} (x - \mathrm{E}(x)) \mid h, \mathrm{data}] = \frac{n_h + 1}{n_h - 1 - d} \, (\overline{x^{\mathsf{T}} x}_h - \overline{x}_h{}^{\mathsf{T}} \overline{x}_h). \tag{13}$$

It is not possible to make the distributions arbitrarily peaked: the empirical covariance matrix of the data gives an idea of the maximum amount attainable.

For the reverse inference, $\mathrm{p}(\text{health condition} \mid \text{indicator}, \text{data})$, formula (11) combined with (10) says that we must "modulate" the distributions shown in fig. 1 using the known percentages of incidences of Alzheimer etc. in the population – say, nation-wide. Mathematically what happens is this. Suppose we have measured the health indicator x of the new patient. If x falls where only one of the three distributions $\mathrm{p}(x \mid \text{health condition}, \text{data})$ has high probability, then this we are very confident that the individual has that health condition, no matter what the nation-wide statistics says. If x falls where two or all three of the distributions $\mathrm{p}(x \mid \text{health condition}, \text{data})$ have significant overlap, then the known nation-wide statistics wins over these distributions.

Figure 2 shows the one-standard-deviation regions of the distributions for just two parameters, from Simone's old data.

i	h_i	x_i
1	A	$(0.626288, 1.65279, 0.632398, 154.693, 0.045868, 248)$
2	A	$(0.612307, 1.82326, 0.646126, 115.114, 0.076175, 189)$
3	A	$(0.607465, 1.75983, 0.635176, 112.381, 0.047749, 186)$
4	A	$(0.586474, 1.80227, 0.597109, 104.979, 0.064351, 180)$
5	A	$(0.527199, 1.98327, 0.53327, 134.436, 0.045629, 256)$
6	A	$(0.685346, 1.50287, 0.692089, 159., 0.041398, 233)$
7	A	$(0.806428, 1.26951, 0.817895, 169.35, 0.022918, 211)$
8	A	$(0.621802, 1.64026, 0.625815, 133.066, 0.026358, 215)$
9	A	$(0.662866, 1.56476, 0.671566, 147.156, 0.047857, 223)$
10	A	$(0.792779, 1.26593, 0.796867, 177.583, 0.008296, 225)$
11	A	$(0.731208, 1.39039, 0.737532, 186.458, 0.026689, 256)$
12	A	$(0.575485, 1.81697, 0.582767, 167.466, 0.049821, 292)$
13	A	$(0.712191, 1.4189, 0.714494, 148.848, 0.028972, 210)$
14	H	$(0.555869, 1.89378, 0.567071, 138.411, 0.059141, 250)$
15	H	$(0.525715, 1.97087, 0.566876, 123.017, 0.124131, 235)$
16	H	$(0.612931, 1.71285, 0.621509, 166.104, 0.071957, 272)$
17	H	$(0.578456, 1.80871, 0.586267, 137.094, 0.049947, 238)$
18	H	$(0.453708, 2.30181, 0.497258, 106.168, 0.133992, 235)$
19	H	$(0.678076, 1.50093, 0.681168, 168.841, 0.037906, 250)$
20	H	$(0.561081, 1.91614, 0.585531, 133.537, 0.063653, 239)$
21	H	$(0.736883, 1.37808, 0.741253, 181.273, 0.02789, 247)$
22	H	$(0.561073, 1.86498, 0.567892, 141.39, 0.050404, 253)$
23	H	$(0.694201, 1.46052, 0.696781, 192.294, 0.031089, 278)$
24	H	$(0.72678, 1.3906, 0.730646, 160.618, 0.025767, 222)$
25	H	$(0.706357, 1.4442, 0.713367, 205.55, 0.030121, 292)$
26	H	$(0.764527, 1.31631, 0.767634, 178.135, 0.023055, 234)$
27	C	$(0.575399, 1.84898, 0.596428, 140.973, 0.080927, 246)$
28	C	$(0.687646, 1.48628, 0.691763, 144.406, 0.04448, 211)$
29	C	$(0.576417, 1.81166, 0.583679, 129.694, 0.051219, 226)$
30	C	$(0.669721, 1.5166, 0.672916, 129.926, 0.032039, 195)$
31	C	$(0.736418, 1.36799, 0.73886, 145.074, 0.022411, 198)$
32	C	$(0.743739, 1.35582, 0.746371, 174.035, 0.024474, 235)$
33	C	$(0.664138, 1.55512, 0.673374, 156.736, 0.034872, 237)$
34	C	$(0.614609, 1.69503, 0.624112, 132.756, 0.045331, 217)$
35	C	$(0.439049, 2.31677, 0.478943, 131.715, 0.13096, 301)$
36	C	$(0.728062, 1.38382, 0.730246, 165.998, 0.021884, 229)$
37	C	$(0.719449, 1.4011, 0.721807, 161.157, 0.020809, 225)$
38	C	$(0.689622, 1.49152, 0.697921, 162.061, 0.044468, 236)$

Table 1   Claudia's data, with x_i = (graph weights, shortest path, clustering coefficient, degree, modularity, number of nodes).

$$n_A = 13, \qquad \overline{x}_A = (0.657526, 1.607, 0.667931, 146.964, 0.0409293, 224.923),$$

$$\overline{x^\mathsf{T} x}_A = \begin{pmatrix} 0.438898 & 1.03926 & 0.445562 & 97.9543 & 0.0258872 & 147.621 \\ & 2.63031 & 1.05673 & 232.397 & 0.0687592 & 361.759 \\ & & 0.452417 & 99.3528 & 0.0264131 & 149.811 \\ & & & 22209.9 & 5.71066 & 33568.3 \\ & & & & 0.00197971 & 9.08225 \\ & & & & & 51542. \end{pmatrix}$$

$$n_H = 13, \qquad \overline{x}_H = (0.627358, 1.68921, 0.64025, 156.341, 0.056081, 249.615),$$

$$\overline{x^\mathsf{T} x}_H = \begin{pmatrix} 0.402114 & 1.03346 & 0.409205 & 100.371 & 0.0324141 & 156.968 \\ & 2.93548 & 1.05846 & 256.904 & 0.103465 & 420.29 \\ & & 0.416651 & 102.093 & 0.0335846 & 160.097 \\ & & & 25222.8 & 7.99839 & 39366.2 \\ & & & & 0.00433914 & 13.8298 \\ & & & & & 62677.3 \end{pmatrix}$$

$$n_C = 12, \qquad \overline{x}_C = (0.653689, 1.60256, 0.663035, 147.878, 0.0461562, 229.667),$$

$$\overline{x^\mathsf{T} x}_C = \begin{pmatrix} 0.434586 & 1.0248 & 0.439879 & 97.5448 & 0.0277439 & 148.531 \\ & 2.6401 & 1.04242 & 234.405 & 0.0817666 & 373.415 \\ & & 0.44537 & 98.8598 & 0.0284874 & 150.919 \\ & & & 22091. & 6.58946 & 33961.6 \\ & & & & 0.00304913 & 11.2511 \\ & & & & & 53432.3 \end{pmatrix}$$

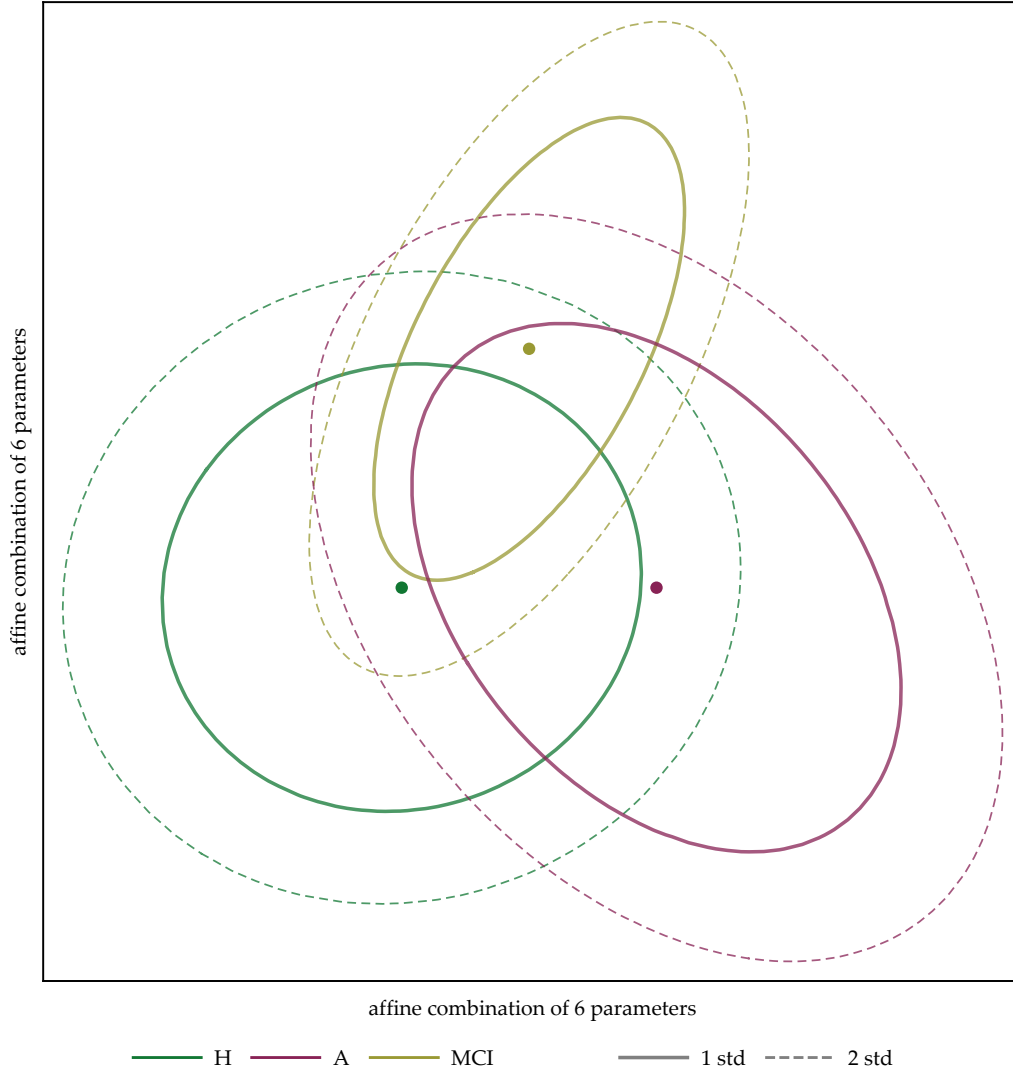Table 2   Sufficient statistics from Claudia's data of table 1.

Figure 1 Contours of 1 and 2 standard deviations of the distributions $p(x\,|\,\text{health condition}, \text{data})$, on a two-dimensional section of the six-dimensional parameter space. The sectioning plane passes through the expectations of the three distributions, denoted by the dots. The distributions can overlap even more or even less than this in the remaining four dimensions.
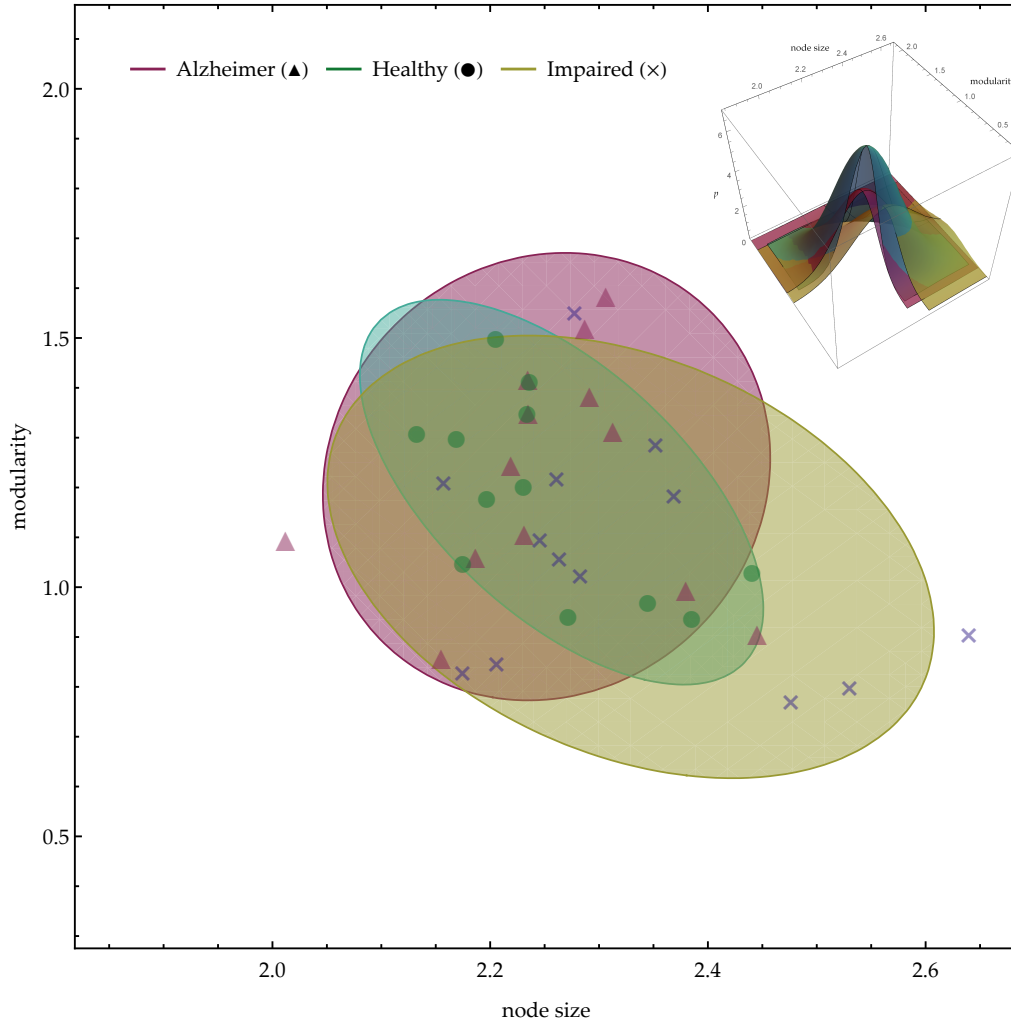
Figure 2 Approximate representation of p(x | health condition, data). The indicator x is the vector (node size, modularity), the health condition is Alzheimer, Healthy, or cognitively Impaired. The coloured regions are the areas in which the indicator lie with 70 % probability. Red: p(indicator | A, data), green: p(indicator | H, data), yellow: p(indicator | C, data). The marks represent Simone's data, table 1. The upper right inset gives a 3D idea. See discussion on p. 8 for further explanation.

6 Final remarks

6.1 Generalizations   In this example we have used the known means, variances, and covariances of the parameters as "sufficient statistics". Two generalizations are immediately clear.

First, we could use different statistics from the data, for example all moments up to the third, fourth, or higher. The formulae we obtain in all these cases are analogous to (8); in particular, we obtain integrals with exponentials of all the included moments. However, if the number of statistics is comparable to the number of data then the resulting distributions will appear almost flat. Also, the more statistics we include, the more dimensions in the integrations to perform; see the next subsection on this point.

A second generalization is to assume slightly different inferential relevances. For example, for predicting whether the patient has Alzheimer we can assume that the health indicators of the individuals with *every* health condition are relevant – not only of those with Alzheimer. Also in this case we obtain formulae uniquely determined by these assumptions.

6.2 Maximum likelihood, Kullback-Leibler, & co.   Formula (8) contains, as approximations, formulae that are used in some literature to solve this same problem.

The multidimensional Student's t-distribution is related to the X^2 one. It is well known in statistics: it has fatter tails than a Gaussian, and this makes it more robust against the presence of outliers; that is, outliers won't move its peaks away from the bulk of the data, as it can happen for the Gaussian distribution instead.

An important point, for me, is that this distribution has appeared automatically from our assumption of p. 6 and the rules of probability theory. We have not invoked ad hoc on grounds of robustness or for other reasons.

If our data has many individuals, the t-distribution tends to a Gaussian. With many individuals, the integral in (8) becomes very peaked and we can approximate it with the maximum value of the integrand. This corresponds to a maximum-likelihood solution and the classical estimates of the means, variances, covariance of a normal distribution. In our example this approximate solution is quite bad: it gives relative errors of 230 % for the covariance matrix. Note that maximum-likelihood also requires that we specify a statistical parametric model to start with.

The Kullback-Leibler divergence between a "test distribution" and the empirical distribution of the data appears in the exponent of the integral, if we have numerous individuals. This in turn leads to a maximum-entropy solution as approximation.

6.3   Using histograms   Simone wanted to somehow compare the histograms of the distribution of the parameters obtained from the fMRI, for the different health conditions. This can be done in the method shown here. The data in the histogram of a quantity X over n bins are equivalent to the first n moments of this quantity: $\sum X$, $\sum X^2$, $\sum X^3$, etc.. The use of these n moments as sufficient statistics, in the method shown in this note, is equivalent to the use of the full histogram. This method would roughly correspond to a comparison of the histograms by means of their Kullback-Leibler divergence.

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("van X" is listed under V; similarly for other prefixes, regardless of national conventions.)

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