Advanced brain imaging methods: Tutorial 0

3rd February 2014

1 Linear algebra: warm up

1.1 Adding noise to an image

Say that for some reason you want to add normally distributed noise to an image. Given an image defined by the matrix A and the matrix B containing normally distributed noise, what would be the matrix C of the image to which this noise has been added ?

$$A = \begin{bmatrix} 136 & 37 & 45 & 158 \\ 28 & 69 & 78 & 55 \\ 227 & 75 & 196 & 170 \\ 212 & 34 & 23 & 125 \end{bmatrix} ; B = \begin{bmatrix} -1 & 6 & 2 & 12 \\ -14 & -6 & -4 & -1 \\ -3 & 1 & 3 & -15 \\ -13 & -4 & 5 & -6 \end{bmatrix}$$

Simply add each value of A to its corresponding value of B:

$$A + B = \begin{bmatrix} 135 & 43 & 47 & 170 \\ 14 & 63 & 74 & 54 \\ 224 & 76 & 199 & 155 \\ 199 & 30 & 28 & 119 \end{bmatrix}$$

1.2 Rigid body transformation: translations

The transformation matrix of an image is the matrix that allows you to say what are the coordinates [x,y,z] in world space of the voxel with indices [i,j,k] in voxel space.

What is the matrix B that will translate an image by 15 mm along the x dimension, -58 mm along the y dim and 65 mm along the z dimension?

$$B = \begin{bmatrix} 1 & 0 & 0 & 15 \\ 0 & 1 & 0 & -58 \\ 0 & 0 & 1 & 65 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

Given the transformation matrix A below, what would be the values of A' the new transformation matrix once the translation performed by B has been applied?

$$A = \begin{bmatrix} 5 & 0 & 0 & 125 \\ 0 & 2 & 0 & 118 \\ 0 & 0 & 1 & 10 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

The new matrix will be given to you by the matrix multiplication $A \times B$ which will simplifies to this (but do not take my word for it, check it yourself):

$$A' = A \times B = \begin{bmatrix} 5 & 0 & 0 & 125 + 15 * 5 \\ 0 & 2 & 0 & 118 - 58 * 2 \\ 0 & 0 & 1 & 10 + 65 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

Given this new transformation matrix, what would be the real world coordinates of the voxel with indices [10,25,45] and for any voxel with indices [i,j,k]?

These coordinates will be given to you by this matrix multiplication:

$$A' \times \begin{bmatrix} i & j & k & 1 \end{bmatrix}^T = A' \times \begin{bmatrix} i \\ j \\ k \\ 1 \end{bmatrix} = \begin{bmatrix} 5 & 0 & 0 & 200 \\ 0 & 2 & 0 & 2 \\ 0 & 0 & 1 & 75 \\ 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} 10 \\ 25 \\ 45 \\ 1 \end{bmatrix}$$
$$= \begin{bmatrix} 5 * 10 + 200 * 1 \\ 2 * 25 + 2 * 1 \\ 1 * 45 + 75 * 1 \\ 1 \end{bmatrix} = \begin{bmatrix} 250 \\ 52 \\ 120 \\ 1 \end{bmatrix}$$

The center of this voxel will occupy the coordinates $x = 250$ mm ; $y = 52$ mm ; $z = 120$ mm.

1.3 Rigid body transformation: rotations

What is the matrix C that will rotate an image by 90 degrees around the x axis (pitch)?

$$C = \begin{bmatrix} cos(90) & sin(90) & 0 & 0 \\ -sin(90) & cos(90) & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} = \begin{bmatrix} 0 & 1 & 0 & 0 \\ -1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

Given the transformation matrix A below, what would be the values of A", the new transformation matrix, after this rotation has been applied?

$$A = \begin{bmatrix} 5 & 0 & 0 & 125 \\ 0 & 2 & 0 & 118 \\ 0 & 0 & 1 & 10 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

The new matrix will be given to you by the matrix multiplication $A \times C$ which will simplifies to this (but do not take my word for it, check it yourself):

$$A'' = A \times C = \begin{bmatrix} 0 & 5 & 0 & 125 \\ -2 & 0 & 0 & 118 \\ 0 & 0 & 1 & 10 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

1.4 Rigid body transformation: order of transformation

For the point with coordinates [14,58,23], what would be its coordinates if:

1. you applied the translation defined by B then the rotation defined by C,
2. you applied the rotation defined by C and then the translation defined by B?

For the first case we have to do the following matrix multiplication:

$$C \times B \times \begin{bmatrix} 14 & 58 & 23 & 1 \end{bmatrix}^T$$

$$= \begin{bmatrix} 0 & 1 & 0 & 0 \\ -1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} 1 & 0 & 0 & 15 \\ 0 & 1 & 0 & -58 \\ 0 & 0 & 1 & 65 \\ 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} 15 \\ 58 \\ 23 \\ 1 \end{bmatrix}$$

$$= \begin{bmatrix} 0 & 1 & 0 & 0 \\ -1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} 15+15 \\ 58-58 \\ 23+65 \\ 1 \end{bmatrix}$$

$$= \begin{bmatrix} 58-58 \\ -(15+15) \\ 23+65 \\ 1 \end{bmatrix} = \begin{bmatrix} 0 \\ -30 \\ 88 \\ 1 \end{bmatrix}$$

For the second case we have to do the following matrix multiplication:

$$B \times C \times \begin{bmatrix} 14 & 58 & 23 & 1 \end{bmatrix}^T$$

$$= \begin{bmatrix} 1 & 0 & 0 & 15 \\ 0 & 1 & 0 & -58 \\ 0 & 0 & 1 & 65 \\ 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} 0 & 1 & 0 & 0 \\ -1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} 15 \\ 58 \\ 23 \\ 1 \end{bmatrix}$$

$$= \begin{bmatrix} 1 & 0 & 0 & 15 \\ 0 & 1 & 0 & -58 \\ 0 & 0 & 1 & 65 \\ 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} 58 \\ -15 \\ 23 \\ 1 \end{bmatrix}$$

$$= \begin{bmatrix} 58+15 \\ -15-58 \\ 23+65 \\ 1 \end{bmatrix} = \begin{bmatrix} 73 \\ -73 \\ 88 \\ 1 \end{bmatrix}$$

This illustrates that the order which you apply the transformation to an image does matter.

2 General linear model

In class we have seen how to find the equation that defines the ordinary least-square estimate of the $\hat{\beta}$ value of the following model:

$y = \beta x + \varepsilon$

For each value of x_i, the residual error (ε_i) is given by the difference between the predicted value of the model ($\hat{y}_i = \hat{\beta} x_i$) and the actual empirical value (y_i). We want to minimize the sum of the squared residual:

$$\sum_{i=1}^{N} \varepsilon_i^2 = \sum_{i=1}^{N} (y_i - \hat{y}_i)^2 = \sum_{i=1}^{N} (y_i - \hat{\beta} x_i)^2 = \sum_{i=1}^{N} (y_i^2 - 2\hat{\beta} x_i y_i + \hat{\beta}^2 x_i^2)$$

At the value of $\hat{\beta}$ that minimize this function, we know that its derivative with respect to β will be equal to 0. So to find $\hat{\beta}$, we derived this function with respect to $\hat{\beta}$, and rearranged this derivative to have the value of $\hat{\beta}$ expressed in terms of x and y.

Let's now try to do the same with this model:

$$y = \hat{\beta}_1 x + \hat{\beta}_0 + \varepsilon$$

Do this by the following steps:

1. Write down the sum of the squared residual of this model.
2. Derive this function with respect to $\hat{\beta}_1$ and rearranged this derivative to have the value of $\hat{\beta}_1$ expressed in terms of x, y and $\hat{\beta}_0$.
3. Do the same with respect to $\hat{\beta}_0$.
4. You will find the values that minimize your errors when both of those partial derivatives are equal to zero. So you have now a system of 2 equations with 2 unknowns. Substitute $\hat{\beta}_0$ in the function found in step 2 by the solution of step 3.

The sum of the squared residual (RSS) of this new model is:

$$RSS(\hat{\beta}_1, \hat{\beta}_0) = \sum_{i=1}^{N} \varepsilon_i^2 = \sum_{i=1}^{N} (y_i - \hat{y}_i)^2 = \sum_{i=1}^{N} (y_i - (\hat{\beta}_1 x_i + \hat{\beta}_0))^2 = \sum_{i=1}^{N} (y_i - \hat{\beta}_1 x_i - \hat{\beta}_0)^2$$

This can be rewritten as:

$$RSS(\hat{\beta}_1, \hat{\beta}_0) = \sum_{i=1}^{N} (y_i^2 + \hat{\beta}_1^2 x_i^2 + \hat{\beta}_0^2 - 2\hat{\beta}_0 y_i - 2\hat{\beta}_1 x_i y_i + 2\hat{\beta}_0 \hat{\beta}_1 x_i)$$

$$= \sum_{i=1}^{N} y_i^2 + \sum_{i=1}^{N} \hat{\beta}_1^2 x_i^2 + \sum_{i=1}^{N} \hat{\beta}_0^2 - \sum_{i=1}^{N} 2\hat{\beta}_0 y_i - \sum_{i=1}^{N} 2\hat{\beta}_1 x_i y_i + \sum_{i=1}^{N} 2\hat{\beta}_0 \hat{\beta}_1 x_i$$

$$= \sum_{i=1}^{N} y_i^2 + \hat{\beta}_1^2 \sum_{i=1}^{N} x_i^2 + n\hat{\beta}_0^2 - 2\hat{\beta}_0 \sum_{i=1}^{N} y_i - 2\hat{\beta}_1 \sum_{i=1}^{N} x_i y_i + 2\hat{\beta}_0 \hat{\beta}_1 \sum_{i=1}^{N} x_i$$

If with derive with respect to $\hat{\beta}_0$, we get:

$$\frac{\partial RSS(\hat{\beta}_1, \hat{\beta}_0)}{\partial \hat{\beta}_0} = 2n\hat{\beta}_0 - 2\sum_{i=1}^{N} y_i + 2\hat{\beta}_1 \sum_{i=1}^{N} x_i$$

If with derive with respect to $\hat{\beta}_1$, we get:

$$\frac{\partial RSS(\hat{\beta}_1, \hat{\beta}_0)}{\partial \hat{\beta}_1} = 2\hat{\beta}_1 \sum_{i=1}^{N} x_i^2 - 2\sum_{i=1}^{N} x_i y_i + 2\hat{\beta}_0 \sum_{i=1}^{N} x_i$$

If we set both equations as equal to 0, we get:

$$n\hat{\beta}_0 - \sum_{i=1}^{N} y_i + \hat{\beta}_1 \sum_{i=1}^{N} x_i = 0 \quad (1)$$

$$\hat{\beta}_1 \sum_{i=1}^{N} x_i^2 - \sum_{i=1}^{N} x_i y_i + \hat{\beta}_0 \sum_{i=1}^{N} x_i = 0 \quad (2)$$

From 1 we can extract $\hat{\beta}_0$:

$$\hat{\beta}_0 = \frac{1}{n}\sum_{i=1}^{N} y_i - \hat{\beta}_1 \frac{1}{n}\sum_{i=1}^{N} x_i \quad (3)$$

By substituting equation 3 in equation 2, we have:

$$\hat{\beta}_1 \sum_{i=1}^{N} x_i^2 - \sum_{i=1}^{N} x_i y_i + (\frac{1}{n}\sum_{i=1}^{N} y_i - \hat{\beta}_1 \frac{1}{n}\sum_{i=1}^{N} x_i)\sum_{i=1}^{N} x_i = 0$$

$$\hat{\beta}_1 \sum_{i=1}^{N} x_i^2 - \sum_{i=1}^{N} x_i y_i + \frac{1}{n}\sum_{i=1}^{N} y_i \sum_{i=1}^{N} x_i - \hat{\beta}_1 \frac{1}{n}(\sum_{i=1}^{N} x_i)^2 = 0$$

$$\hat{\beta}_1 (\sum_{i=1}^{N} x_i^2 - \frac{1}{n}(\sum_{i=1}^{N} x_i)^2) = \sum_{i=1}^{N} x_i y_i - \frac{1}{n}\sum_{i=1}^{N} y_i \sum_{i=1}^{N} x_i$$

$$\hat{\beta}_1 = \frac{\sum_{i=1}^{N} x_i y_i - \frac{1}{n}\sum_{i=1}^{N} y_i \sum_{i=1}^{N} x_i}{\sum_{i=1}^{N} x_i^2 - \frac{1}{n}(\sum_{i=1}^{N} x_i)^2} \quad (4)$$

As by definition $\frac{1}{n}\sum_{i=1}^{N} x_i$ is equal to the mean of x, $\bar{x}$, and $\frac{1}{n}\sum_{i=1}^{N} y_i$ is equal to the mean of y, $\bar{y}$, it is possible to rewrite 4 like this:

$$\hat{\beta}_1 = \frac{\sum_{i=1}^{N}(x_i - \bar{x})(y_i - \bar{y})}{\sum_{i=1}^{N}(x_i - \bar{x})^2} \quad (5)$$

You can recognize that the numerator is the covariance of X and Y and the denominator is the variance of X. Given the values for all the x_i and y_i, you can then compute β_1 and substitute this value in the equation 3 to find β_0.

3 Design matrices

The General Linear Model described by $Y = X\beta + \varepsilon$. Define the design matrices (X) of the following:

1. a two-sample t-test with 2 subjects in group A and 3 subjects in B,
2. a paired t-test with 5 subjects with two conditions a and b,

3. an ANOVA with three groups of subjects and 3 subjects in each group,
4. a repeated-measures ANOVA for 3 subjects and with three within-subject levels (a, b, c).

Here are some advices:

- Do not panic!
- For 1:
  1. write for each subject the equation that describes that subject's y in terms of:
     - the average of the group A (μ_A) times a certain weighting factor,
     - the average of the group B (μ_B) times a certain weighting factor,
     - an error term ε specific to that subject.
  2. go from the equation form to the matrix form, by putting together a) the y of all subjects, b) the weighting factors, c) the 2 averages and d) the error terms.
  3. the design matrix is the one that contains the weighting factors.
- For 2, the process will the same as for 1 but you will have to describe each subject's y in each condition in terms of:
  - the average of the condition a (μ_a) times a certain weighting factor,
  - the average of the condition b (μ_b) times a certain weighting factor,
  - as many subject specific variable (τ) as there are subjects each time multiplied by a certain weighting factor,
  - an error term specific to that subject and that condition.
- For 3 and 4, you can geneleralize by remembering that a two sample t-test is in fact an ANOVA with only two groups and that a paired t-test is in fact a repeated-measures ANOVA with only two levels.

Let's do this ! First the two sample t-test:

$$
\begin{aligned}
Y_{A1} &= 1 \times \mu_A + 0 \times \mu_B + \varepsilon_{A1} \\
Y_{A2} &= 1 \times \mu_A + 0 \times \mu_B + \varepsilon_{A2} \\
Y_{B1} &= 0 \times \mu_A + 1 \times \mu_B + \varepsilon_{B1} \\
Y_{B2} &= 0 \times \mu_A + 1 \times \mu_B + \varepsilon_{B2} \\
Y_{B3} &= 0 \times \mu_A + 1 \times \mu_B + \varepsilon_{B3}
\end{aligned}
$$

Then we reorganize this in matrix notation:

$$
\begin{bmatrix} Y_{A1} \\ Y_{A2} \\ Y_{B1} \\ Y_{B2} \\ Y_{B3} \end{bmatrix} = \begin{bmatrix} 1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \end{bmatrix} \times \begin{bmatrix} \mu_A \\ \mu_B \end{bmatrix} + \begin{bmatrix} \varepsilon_{A1} \\ \varepsilon_{A2} \\ \varepsilon_{B1} \\ \varepsilon_{B2} \\ \varepsilon_{B3} \end{bmatrix}
$$

In this case X is:

$$\begin{bmatrix} 1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \end{bmatrix}$$

By generalizing this process to an ANOVA with three groups of subjects and 3 subjects in each group, we have:

$$\begin{bmatrix} 1 & 0 & 0 \\ 1 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 1 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \end{bmatrix}$$

Now the paired t-test:

$$\begin{aligned}
Y_{a1} &= 1 \times \mu_a + 0 \times \mu_b + 1 \times \tau_1 + 0 \times \tau_2 + 0 \times \tau_3 + 0 \times \tau_4 + 0 \times \tau_5 + \varepsilon_{a1} \\
Y_{a2} &= 1 \times \mu_a + 0 \times \mu_b + 0 \times \tau_1 + 1 \times \tau_2 + 0 \times \tau_3 + 0 \times \tau_4 + 0 \times \tau_5 + \varepsilon_{a2} \\
Y_{a3} &= 1 \times \mu_a + 0 \times \mu_b + 0 \times \tau_1 + 0 \times \tau_2 + 1 \times \tau_3 + 0 \times \tau_4 + 0 \times \tau_5 + \varepsilon_{a3} \\
Y_{a4} &= 1 \times \mu_a + 0 \times \mu_b + 0 \times \tau_1 + 0 \times \tau_2 + 0 \times \tau_3 + 1 \times \tau_4 + 0 \times \tau_5 + \varepsilon_{a4} \\
Y_{a5} &= 1 \times \mu_a + 0 \times \mu_b + 0 \times \tau_1 + 0 \times \tau_2 + 0 \times \tau_3 + 0 \times \tau_4 + 1 \times \tau_5 + \varepsilon_{a5} \\
Y_{b1} &= 0 \times \mu_a + 1 \times \mu_b + 1 \times \tau_1 + 0 \times \tau_2 + 0 \times \tau_3 + 0 \times \tau_4 + 0 \times \tau_5 + \varepsilon_{b1} \\
Y_{b2} &= 0 \times \mu_a + 1 \times \mu_b + 0 \times \tau_1 + 1 \times \tau_2 + 0 \times \tau_3 + 0 \times \tau_4 + 0 \times \tau_5 + \varepsilon_{b2} \\
Y_{b3} &= 0 \times \mu_a + 1 \times \mu_b + 0 \times \tau_1 + 0 \times \tau_2 + 1 \times \tau_3 + 0 \times \tau_4 + 0 \times \tau_5 + \varepsilon_{b3} \\
Y_{b4} &= 0 \times \mu_a + 1 \times \mu_b + 0 \times \tau_1 + 0 \times \tau_2 + 0 \times \tau_3 + 1 \times \tau_4 + 0 \times \tau_5 + \varepsilon_{b4} \\
Y_{b5} &= 0 \times \mu_a + 1 \times \mu_b + 0 \times \tau_1 + 0 \times \tau_2 + 0 \times \tau_3 + 0 \times \tau_4 + 1 \times \tau_5 + \varepsilon_{b5}
\end{aligned}$$

Then we reorganize this in matrix notation before we get dizzy:

$$\begin{bmatrix} Y_{a1} \\ Y_{a2} \\ Y_{a3} \\ Y_{a4} \\ Y_{a5} \\ Y_{b1} \\ Y_{b2} \\ Y_{b3} \\ Y_{b4} \\ Y_{b5} \end{bmatrix} = \begin{bmatrix} 1 & 0 & 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 1 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} \mu_A \\ \mu_B \\ \tau_1 \\ \tau_2 \\ \tau_3 \\ \tau_4 \\ \tau_5 \end{bmatrix} + \begin{bmatrix} \varepsilon_{a1} \\ \varepsilon_{a2} \\ \varepsilon_{a3} \\ \varepsilon_{a4} \\ \varepsilon_{a5} \\ \varepsilon_{b1} \\ \varepsilon_{b2} \\ \varepsilon_{b3} \\ \varepsilon_{b4} \\ \varepsilon_{b5} \end{bmatrix}$$

This means that in this case X is:

$$\begin{bmatrix} 1 & 0 & 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 1 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

By generalizing this process to a repeated-measures ANOVA for 3 subjects and with three within-subject levels (a, b, c), we have:

$$\begin{bmatrix} 1 & 0 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 0 & 0 & 1 \\ 0 & 1 & 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 0 & 1 & 0 \\ 0 & 1 & 0 & 0 & 0 & 1 \\ 0 & 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 & 0 & 1 \end{bmatrix}$$