

## B Mutual Information Metric

### B.1 Entropy

To introduce the mutual information metric, we present a review of entropy. Let us define  $\Phi$  as a random variable (RV),  $P(\Phi)$  as the probability distribution of  $\Phi$  and  $\rho(\phi)$  as the probability density of  $\Phi$ . So the entropy of  $\Phi$ ,  $H(\Phi)$  is :

$$H(\Phi) = -E[\log(P(\Phi))] \quad (8)$$

where E is the expectation. Rewriting this equation yields the following:

$$H(\Phi) = -\sum_{\phi \in \Phi} \rho(\phi) \log_2 \rho(\phi) \quad (9)$$

This is entropy and it is a measure of randomness. The more random a variable is, the more the entropy. Joint entropy is a statistic that summarizes the degree of dependence of RV  $\Phi$  on another RV  $\Psi$  :

$$H(\Phi, \Psi) = -E_{\phi} [E_{\psi} [\log(\rho(\Phi, \Psi))]] \quad (10)$$

Again rewriting this equation yields:

$$H(\Phi, \Psi) = -\sum_{\phi \in \Phi} \sum_{\psi \in \Psi} \rho(\phi, \psi) \log_2 \rho(\phi, \psi) \quad (11)$$

The conditional entropy is a statistic that summarizes randomness of  $\Psi$  given knowledge of  $\Phi$  :

$$H(\Phi|\Psi) = -E_{\phi} [E_{\psi} [\log(\rho(\Phi|\Psi))]] \quad (12)$$

Two random variables are considered to be independent if:

$$H(\Phi, \Psi) = H(\Phi) + H(\Psi) \quad (13)$$

However if there is any dependency then:

$$H(\Phi, \Psi) < H(\Phi) + H(\Psi) \quad (14)$$

Working through some math we can rewrite the above equation:

$$H(\Psi|\Phi) = \sum_{\phi \in \Phi} \rho(\phi) H(\Psi|\Phi = \phi) \quad (15)$$

$$= -\sum_{\phi \in \Phi} \rho(\phi) \sum_{\psi \in \Psi} \rho(\psi|\phi) \log_2 \rho(\psi|\phi) \quad (16)$$

$$= -\sum_{\phi \in \Phi} \sum_{\psi \in \Psi} \rho(\phi, \psi) \log_2 \rho(\psi|\phi) \quad (17)$$

Now, given the chain rule;

$$H(\Phi, \Psi) = H(\Phi) + H(\Psi|\Phi) \quad (18)$$

We can now flip the variables and get:

$$H(\Psi, \Phi) = H(\Psi) + H(\Phi|\Psi) \quad (19)$$

hence the conditional entropy from Equation 12 becomes;

$$H(\Phi|\Psi) = H(\Psi, \Phi) - H(\Psi) \quad (20)$$

Now that we have defined entropy, joint entropy and conditional entropy we can introduce mutual information (MI).

## B.2 Mutual Information

Mutual Information (MI), between two random variables  $\Phi$  and  $\Psi$  is:

$$MI(\Phi, \Psi) = H(\Psi, \Phi) - H(\Psi|\Phi) \quad (21)$$

$$= H(\Phi) + H(\Psi) - H(\Psi, \Phi) \quad (22)$$

This is a measure of the reduction of the entropy of  $\Psi$  given  $\Phi$  [17,18].

Maximizing the mutual information is documented by [17,18]. If the two distributions are related functionally (through a geometrical transformation  $\mathbf{T}(\Phi)$ ), and we only have an estimate of this transformation, then the mutual information depends on

1. The first distribution, from image  $\Phi$ .
2. The second distribution, from image  $\Psi$ .
3. The estimated transformation that maps one onto the other.

The exact transformation that maps the first image  $u$  (the fixed model) onto the second image  $v$  (the moving image) gives rise to the largest mutual information. Mutual information then becomes an optimization criterion, optimized w.r.t.  $\mathbf{T}$ :

Let  $\Phi = u(\Phi)$ ,  $\Psi = v(\mathbf{T}(\Phi))$  where  $u(\Phi)$  is a voxel of the reference volume,  $v(\Phi)$  is a voxel of the test volume, and  $\Psi = v(\mathbf{T}(\Phi))$  is the test volume voxel associated with the reference volume voxel [18,17].

$$MI(\mathbf{T}) = H(u(\Phi)) + H(v(\mathbf{T}(\Phi))) - H(u(\Phi), v(\mathbf{T}(\Phi))) \quad (23)$$

This method proceeds by a classic gradient-descent optimization technique, and tries to find the transformation that gives the largest mutual information by taking small steps in the direction of the derivative of the criterion [18,17].

$$\frac{d}{d\mathbf{T}} MI(\mathbf{T}) = \frac{d}{d\mathbf{T}} H(v(\mathbf{T}(\Phi))) - \frac{d}{d\mathbf{T}} H(u(\Phi), v(\mathbf{T}(\Phi))) \quad (24)$$