

Metric properties of NMRS

(a) **Non-negativity**

To satisfy non-negativity property, NMRS of two genes should be always greater than zero, i.e.,  $NMRS(a,b) > 0$ , where  $a$  and  $b$  are two gene profiles.

**Proof:**

$$NMRS(a, b) = 1 - \frac{\sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}|}{2 \times \max\{\sum_{i=1}^p |(a_i - a_{mean})|, \sum_{i=1}^p |(b_i - b_{mean})|\}}$$

Suppose

$$\frac{\sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}|}{2 \times \max\{\sum_{i=1}^p |(a_i - a_{mean})|, \sum_{i=1}^p |(b_i - b_{mean})|\}} < 0. \text{ This implies}$$

$$\sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}| < 0.$$

Since absolute value of a quantity is always positive, this contradicts the supposition. Hence, the supposition is false. So

$$\frac{\sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}|}{2 \times \max\{\sum_{i=1}^p |(a_i - a_{mean})|, \sum_{i=1}^p |(b_i - b_{mean})|\}} > 0. \quad (1)$$

Again, suppose

$$\frac{\sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}|}{2 \times \max\{\sum_{i=1}^p |(a_i - a_{mean})|, \sum_{i=1}^p |(b_i - b_{mean})|\}} > 1$$

$$\begin{aligned} \implies \sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}| &> 2 \times \max\{\sum_{i=1}^p |(a_i - a_{mean})|, \sum_{i=1}^p |(b_i - b_{mean})|\} \\ \implies \sum_{i=1}^p |(a_i - a_{mean}) - (b_i - b_{mean})| &> 2 \times \max\{\sum_{i=1}^p |(a_i - a_{mean})|, \sum_{i=1}^p |(b_i - b_{mean})|\} \end{aligned} \quad (2)$$

According to Modulo property  $|a - b| \geq |a| - |b|$ ,

$$\implies \sum_{i=1}^p |(a_i - a_{mean}) - (b_i - b_{mean})| > \sum_{i=1}^p |(a_i - a_{mean})| - \sum_{i=1}^p |(b_i - b_{mean})|.$$

From equation (2)

$$\begin{aligned} \sum_{i=1}^p |(a_i - a_{mean}) - (b_i - b_{mean})| &> \sum_{i=1}^p |(a_i - a_{mean})| - \sum_{i=1}^p |(b_i - b_{mean})| \\ &> 2 \times \max\{\sum_{i=1}^p |(a_i - a_{mean})|, \sum_{i=1}^p |(b_i - b_{mean})|\}. \end{aligned}$$

Since difference between two positive absolute quantities can not be greater than the two times of maximum absolute value of either, this contradicts the supposition. Hence, the supposition is false. So,

$$\frac{\sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}|}{2 \times \max\{\sum_{i=1}^p |(a_i - a_{mean})|, \sum_{i=1}^p |(b_i - b_{mean})|\}} \leq 1. \quad (3)$$

From equation (1) and equation (6)

$$0 < \frac{\sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}|}{2 \times \max\{\sum_{i=1}^p |(a_i - a_{mean})|, \sum_{i=1}^p |(b_i - b_{mean})|\}} < 1.$$

Multiplying by -1,

$$0 > -\frac{\sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}|}{2 \times \max\{\sum_{i=1}^p |(a_i - a_{mean})|, \sum_{i=1}^p |(b_i - b_{mean})|\}} \geq -1.$$

Adding 1 in both sides,

$$\begin{aligned} \Rightarrow 1 + 0 &> 1 - \frac{\sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}|}{2 \times \max\{\sum_{i=1}^p |(a_i - a_{mean})|, \sum_{i=1}^p |(b_i - b_{mean})|\}} \geq 1 - 1 \\ \Rightarrow 1 &> 1 - \frac{\sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}|}{2 \times \max\{\sum_{i=1}^p |(a_i - a_{mean})|, \sum_{i=1}^p |(b_i - b_{mean})|\}} \geq 0 \\ \Rightarrow &1 > N M R S(a, b) \geq 0. \end{aligned} \quad (4)$$

Hence, we have proved that NMRS satisfies the non-negativity property. Moreover, for any two genes, the value of NMRS always lies between 0 and 1.

(b) **Symmetry**

To satisfy the symmetry property, for any two genes a and b,  $NMRS(a,b)$  should be equal to  $NMRS(b,a)$ , i.e.,  $NMRS(a,b) = NMRS(b,a)$ .

**Proof:**

$$N M R S(a, b) = 1 - \frac{\sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}|}{2 \times \max\{\sum_{i=1}^p |(a_i - a_{mean})|, \sum_{i=1}^p |(b_i - b_{mean})|\}} \quad (6)$$

$$N M R S(b, a) = 1 - \frac{\sum_{i=1}^p |b_i - b_{mean} - a_i + a_{mean}|}{2 \times \max\{\sum_{i=1}^p |(a_i - a_{mean})|, \sum_{i=1}^p |(b_i - b_{mean})|\}} \quad (7)$$

According to modulo property,

$$\begin{aligned} |a - b| &= |-(b - a)| = |b - a| \\ \Rightarrow \sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}| &= \sum_{i=1}^p (|-a_i + a_{mean} + b_i - b_{mean}|) \\ \Rightarrow \sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}| &= \sum_{i=1}^p (|b_i - b_{mean} - a_i + a_{mean}|) \\ \Rightarrow 1 - \sum_{i=1}^p |a_i - a_{mean} - b_i + b_{mean}| &= 1 - \sum_{i=1}^p (|b_i - b_{mean} - a_i + a_{mean}|) \\ \Rightarrow N M R S(a, b) &= N M R S(b, a) \text{ (Denominator of both equation (6) and (7) are same)} \end{aligned} \quad (8)$$

Hence, we have proved that NMRS satisfies the symmetry property.

(c) **Subadditivity or Triangle Inequality**

To satisfy triangular inequality property, for any three genes a, b and c, the following condition should hold:

$$N M R S(a, b) + N M R S(b, c) \geq N M R S(a, c).$$

**Proof:**

From equation (5), we have

$$0 \leq NMRS(a, b) < 1 \quad (9)$$

$$0 \leq NMRS(b, c) < 1 \quad (10)$$

$$0 \leq NMRS(a, c) < 1 \quad (11)$$

From (9)+(10), we have

$$0 \leq NMRS(a, b + NMRS(b, c)) < 1 + 1$$

$$0 \leq NMRS(a, b) + NMRS(b, c) < 2 \quad (12)$$

From (11) and (12),

$$NMRS(a, b) + NMRS(b, c) \geq NMRS(a, c)$$

Hence it is proved that NMRS satisfies the triangle inequality property.