

Calculation of modulator mode of action by statistical test

To determine the modulator mode of action, we tested the significance of the difference between two populations \mathcal{RE}_{jk}^+ and \mathcal{RE}_{jk}^- where \mathcal{RE}^+ and \mathcal{RE}^- are the subsets of $RE_{jk\alpha}$ in which the modulator values are in its top and bottom 5 % range, respectively, by the Wilcoxon rank-sum test. The modulator mode of action for the relationships between the j -th regulator and the k -th target is then classified into five modes:

1. A modulator increased the activation of the k -th target by the j -th regulator, if the hypothesis $H_1 : \mathcal{RE}_{jk}^+ > \mathcal{RE}_{jk}^-$ is accepted at 5% level and $RE_{jk\alpha} \geq 0, \forall \alpha$.
2. A modulator decreased the inhibition of the k -th target by the j -th regulator, if the hypothesis $H_1 : \mathcal{RE}_{jk}^+ > \mathcal{RE}_{jk}^-$ is accepted at 5% level and $RE_{jk\alpha} \leq 0, \forall \alpha$.
3. A modulator decreased the activation of the k -th target by the j -th regulator, if the hypothesis $H_1 : \mathcal{RE}_{jk}^+ < \mathcal{RE}_{jk}^-$ is accepted at 5% level and $RE_{jk\alpha} \geq 0, \forall \alpha$.
4. A modulator increased the inhibition of the k -th target by the j -th regulator, if the hypothesis $H_1 : \mathcal{RE}_{jk}^+ < \mathcal{RE}_{jk}^-$ is accepted at 5% level and $RE_{jk\alpha} \leq 0, \forall \alpha$.
5. The modulator mode of action is not determined, if it is not the case of 1, 2, 3, or 4.