**Influence of autosomal allelic bias on signal transduction through network motifs**

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**Background:** In a typical diploid cell, maternally and paternally derived alleles (copies) of a gene are assumed to be expressed equally. However, in some cases, one or both alleles may not be fully active. Monoallelic expression has been commonly associated with embryonic development via genetic imprinting and X-chromosome inactivation and also with immune cell and sensory receptors. However, recent developments in allele specific sequencing suggest that allelic bias is more widespread and may also include autosomal genes of canonical signaling pathways with diverse signaling and disease roles \([1]\). The exact consequences of having such allelic bias is still unexplored.

**Objectives:** Here, we present a systematic theoretical analysis of different levels of allelic biases and their effects on propagation of signal through network motifs that are commonly present in pathways that control cell survival, proliferation, differentiation and apoptosis.

**Methods:** Dynamics of information flow in diverse signaling motifs were simulated using differential equations. Each protein in the motif was subjected to allelic bias either individually or in combinations with other proteins in the motif. Allelic bias was categorized into three states: biallelic (both alleles equally expressed), monoallelic (10-fold bias between alleles) and intermediate. The variation in dynamical system properties, namely weighted response time, duration and amplitude of the signal was investigated for each allelic bias state. Finally, comparisons were made on the sensitivity of statistical properties of signal outputs to changes in allelic bias state.

**Results and conclusions:** In a simple linear cascade, receptor allelic bias has the most effect on downstream signal. However, perturbation of downstream nodes removes this but at the cost of reduced signal propagation. Addition of positive feedback and feedforward loops lead to a broader impact of allelic bias by skewing the signal output distribution. This study indicates the conditions under which allele specific expression of genes has to be taken into consideration while designing signaling perturbations.

**References:** \([1]\) Gimelbrant, *et al.* Science, 318, 2007