Plasticity and contextually dependent-regulation of the relationships between cell motion, morphology and nuclear-Golgi polarity

Hamdah Shafqat^, Ulrich Berge^, Xiaowei Gong, John Lock*, Staffan Stromblad*
Dept. of Biosciences and Nutrition, Karolinska Institutet, Novum, 141 83 Huddinge Sweden
John.Lock@ki.se (^, * equal contribution)

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Abstract

Reorientation of the nuclear-Golgi polarity-axis often coincides with the establishment of the cell motion-axis, as canonically observed in classical wound healing assays. Yet it has also recently been indicated that there is little correspondence between these axes during random cell migration. In addition, Golgi orientation has been observed alternately leading or trailing the nucleus under various experimental conditions, implying potentially distinct polarity organization states. We hypothesize that these conflicting indications result from a combination of plasticity and contextual sensitivity in the dynamic relationship between cell migration and polarity. To explore the putative adaptability of this system we have therefore performed a quantitative analysis of the spatiotemporal relationships between cell motion, morphology and polarity in single randomly migrating cells over a two-dimensional experimental array composed of twenty conditions wherein intra-cellular tension (modulated via ROCK-signalling) and extra-cellular matrix ligand density are progressively co-varied.
By analysing the distributions of measured motion, morphology and polarity features, the steady-state correlation of these features, and time-resolved cross-correlation between motion and polarity dynamics, we find that: 1) forward polarity orientation represents an ordered and regulated state, while backward polarity shows little response to regulation and is disordered (i.e. not a defined state); 2) measured features show highly plastic responses over the 2D condition array, with many of these responses showing contextual dependence such that the impacts of one experimental modulation are inverted depending on the second modulation; 3) inter-feature correlative relationships are often non-linear and non-monotonic, as well as frequently being decoupled by reductions in tension and adhesion levels, and; 4) motion dynamics and polarity are coupled ~60-70% of the time, with the frequency of positive and negative cross-correlation being condition-dependent. Likewise, the tendency for polarity dynamics to temporally lead motion dynamics, or *vice versa*, is also regulated, as is the time delay between these events.