Supplementary Figure Legends

Jun et. *al*, Figure S1

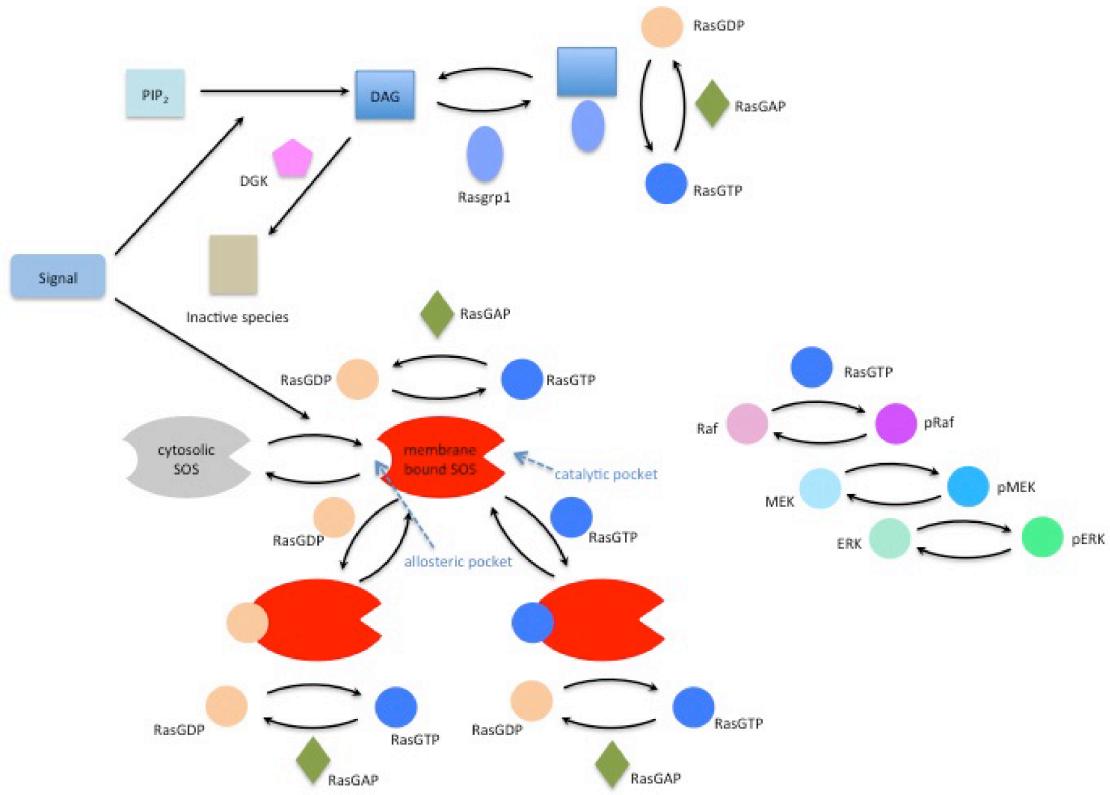

Fig. S1 Coarse-grained model of ERK activation (1-3)

Ras can be activated via both DAG-Rasgrp1-mediated and SOS-mediated pathways. The catalytic rate of SOS depends on the state of its allosteric pocket: empty, bound to RasGDP, or bound to RasGTP, with increasing level of catalytic activities. In particular, the catalytic rate of SOS with RasGTP bound to its allosteric pocket is much larger than that with RasGDP bound to its allosteric pocket. This constitutes a SOS-mediated positive feedback for Ras activation. Ras can be deactivated by RasGAP, while DAG can be metabolized by DGK. Activated Ras can trigger the activation cascade of Ras-Raf-MEK-ERK.

Jun et. *al*, Figure S2

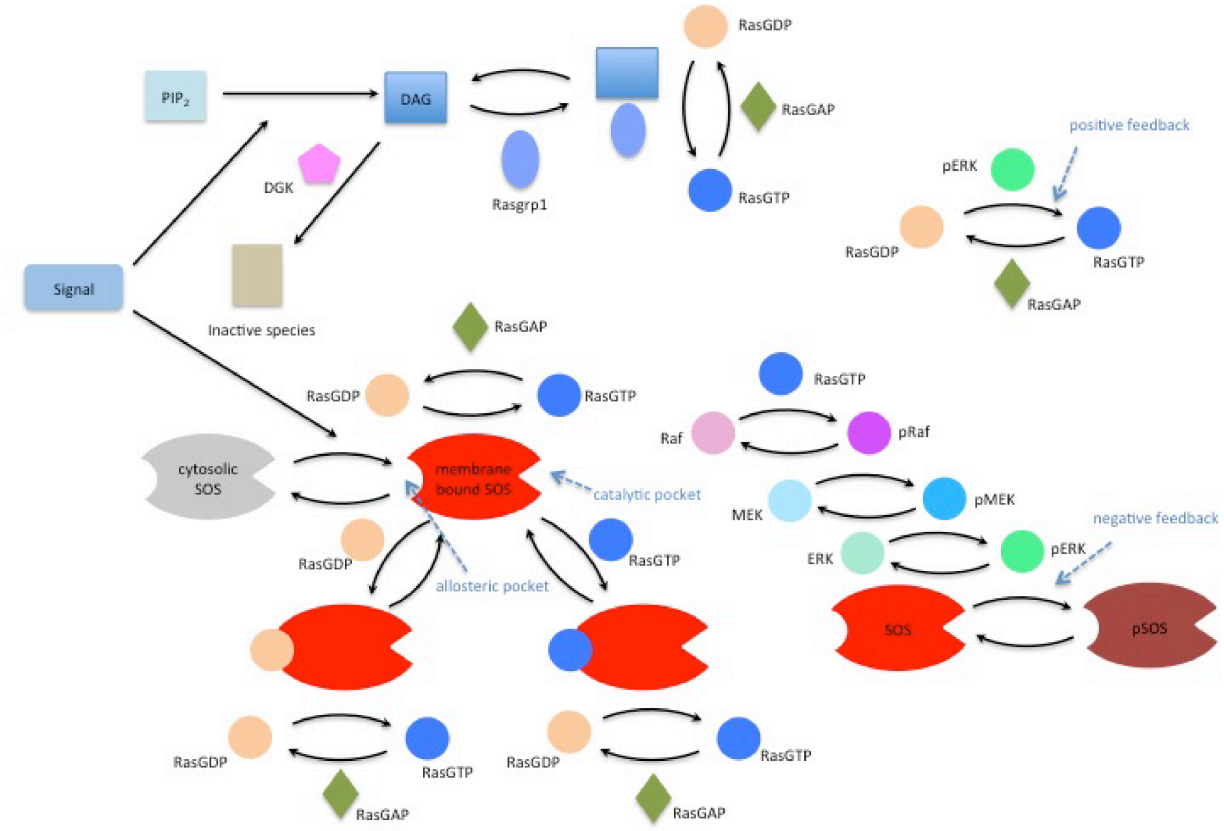

Fig. S2 Coarse-grained model of ERK activation with negative and positive feedback loops (4-5)

Based on the coarse-grained model in Fig. S1, a negative feedback loop and a positive feedback loop are added. The negative feedback loop is generated by the phosphorylation of SOS1 by activated ERK. Ras can also be activated via phospho-ERK, which leads to the positive feedback.

References for Supplementary Information

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