Mathematical modeling the eukaryotic heat shock response: Dynamics of the *hsp70* promoter

Supplementary information

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Translation rate knockdown at 43°C

At 43°C, eukaryotic translation elongation factors are inhibited leading to inefficient translation of proteins (Duncan and Hershey, 1984; Duncan and Song, 1999). The model presented in the manuscript does not consider translation to be a function of temperature (unlike mRNA degradation rate). When the 43°C heat shock is simulated with the translation rate constant (κ_{ta}) reduced below the baseline value used in the model, the dynamics of the attenuation phase are

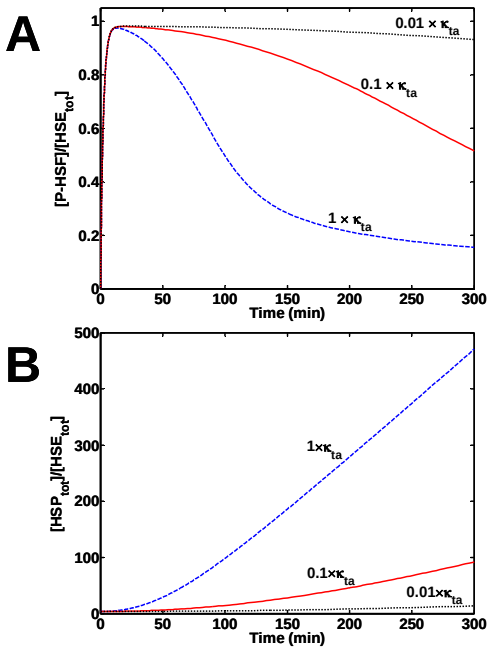

Figure S1. Effect of fold reduction on κ_{ta} under continual 43°C heat shock. (A) Phosphorylated HSF versus time with 0.01× (dotted line), 0.1× (solid line), 1× baseline κ_{ta} (dashed line) (B) Total HSP versus time. Fold changes to κ_{ta} same as (A).

changed significantly (Fig. S1A). In line with experimental observations (Abravaya et al., 1991), the induction phase is rapid, the peak of phosphorylated HSF1 is very high and the system fails to attenuate the heat shock response (manuscript Fig. 3D).

Regulation of the heat shock response by the kinase phosphatase balance

Six of the eleven parameters in Table 4 are related to the activities and binding affinities of the stress kinase (κ_S, Γ_2) and phosphatases (κ_I, Γ_4) that modify HSF1. Given the ubiquity and interconnected nature of kinase cascades in transcriptional regulation, and the sensitivity of the heat shock response to the activity of the kinase(s) of HSF1, the impairment of the stress kinase is a likely target for deregulation of the heat shock response. The dynamic responses to a reduction in the stress kinase's activity (κ_S) are shown in Fig. S2A-B. The concentration of HSP's at 250 minutes is decreased by 0.5 fold when the stress kinase's activity is reduced by

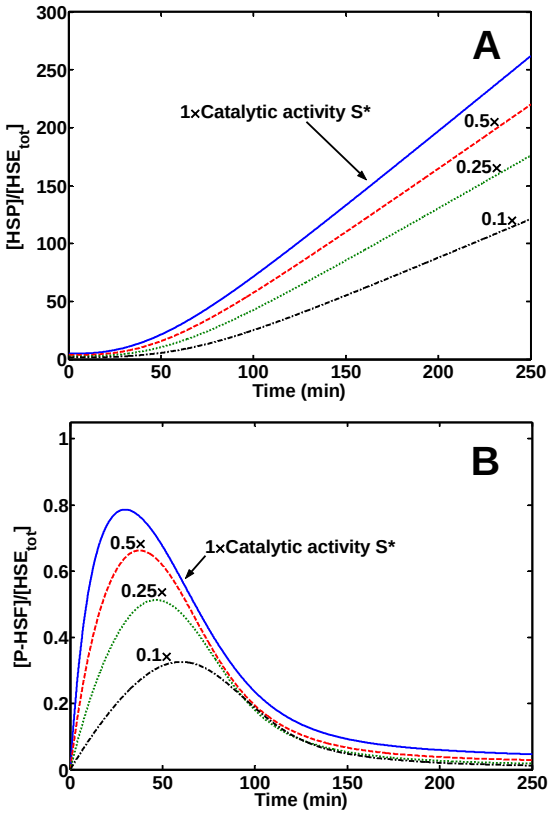

Figure S2. Regulation of the heat shock response by the activity of the kinase. (A) The effect of a fold reduction in stress kinase catalytic activity on dimensionless HSP concentration versus time. The catalytic activity of the stress kinase was reduced by 1 (solid), 0.5 (dashed line), 0.25 (dash-dot line), and 0.1 (dotted line) fold. (B) The effect of a fold reduction in stress kinase catalytic activity on phosphorylated HSF versus time. Fold reductions same as in (A).

0.1 fold, compared to the baseline case (Fig. S2A). Consistent with this reduction in HSP's, the peak of HSF1 phosphorylation is observed to decrease 0.4 fold under a 0.1 fold reduction in stress kinase activity (Fig. S2B).

Supplemental References

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Duncan, R., and J.W. Hershey. 1984. Heat shock-induced translational alterations in HeLa cells. Initiation factor modifications and the inhibition of translation. *J Biol Chem* 259(19):11882-11889.

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