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Supplementary Materials for

Systematic modification of functionality in disordered elastic networks through free energy surface tailoring

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Figs. S1 to S9

Rotation of the 2d plane spanned by the top HLDA eigenvectors

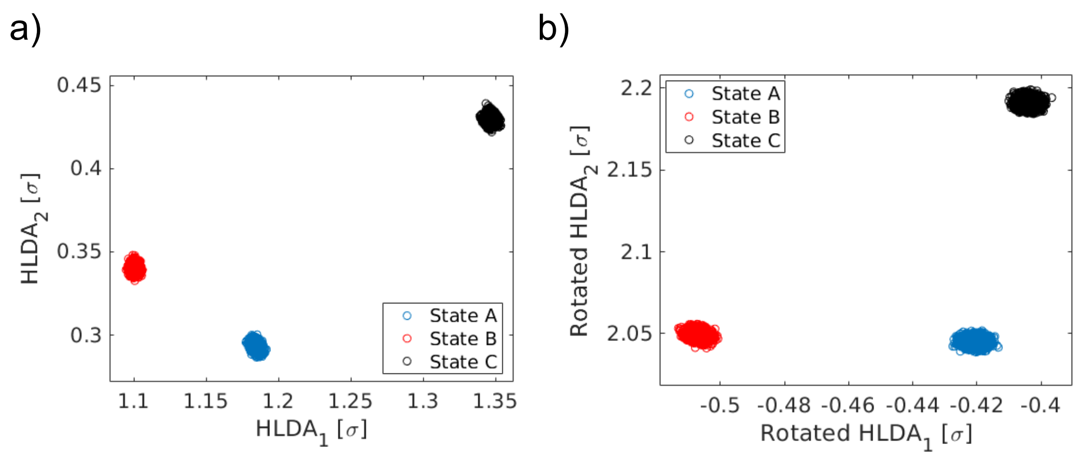

Figure S1: **Rotation of the 2d plane spanned by the top HLDA eigenvectors.** a) Projection of the data sampled in the training simulations of the three considered states (A being the inactivated state, B the activated state, and C the inhibiting state) on the plane spanned by the top two HLDA eigenvectors. b) The HLDA eigenvector plane after rotation. It can be seen that states A and B are now predominantly separated with respect to the rotated $HLDA_2$, while states A and C are predominantly separated with respect to the rotated $HLDA_1$.

Sorted HLDA vectors for the cases of the allosteric response and the network's strain fluctuations

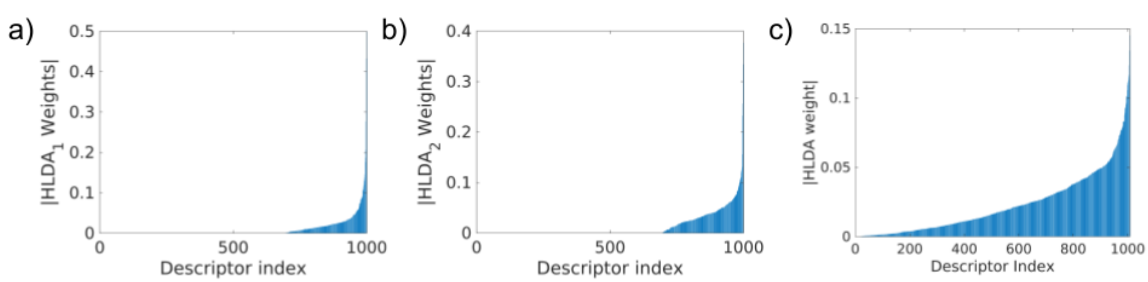

Figure S2: **Sorted HLDA eigenvectors in absolute value for the first HLDA iteration for the case of the network's allosteric response:** a)$HLDA_1$, b)$HLDA_2$ and, c) the case of the network's strain fluctuations. The HLDA vector distribution can be seen to me more broad in the latter case, reflecting the less local nature of the phenomenon.

Example of time dependence behavior in a WTMD simulation in which d_s is the biased CV

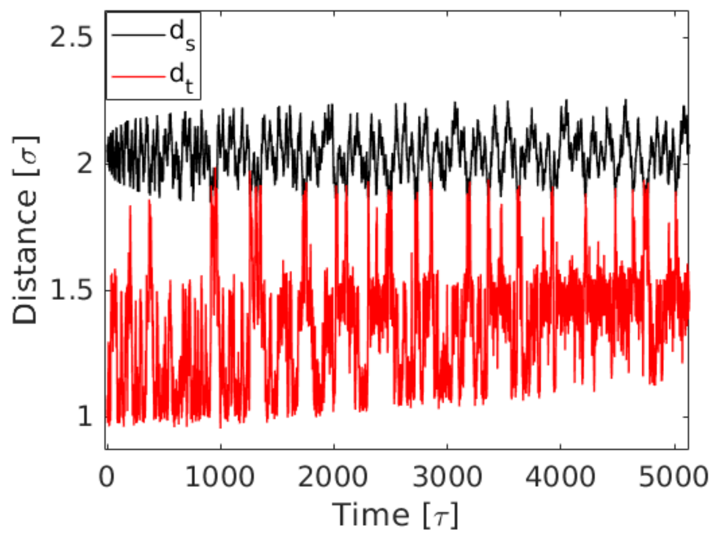

Figure S3: **A time dependence excerpt from a WTMD simulation.** The simulation was run at $T = 8.6 \cdot 10^{-6}$ ($k_B = 1$). d_s, the distance between the source nodes was used as the biased CV. It can be seen that upon passing a threshold value, the allosteric response of the target beads (measured by the distance between them, d_t) is triggered.

Time dependence behavior in WTMD simulations for a pristine and modified network

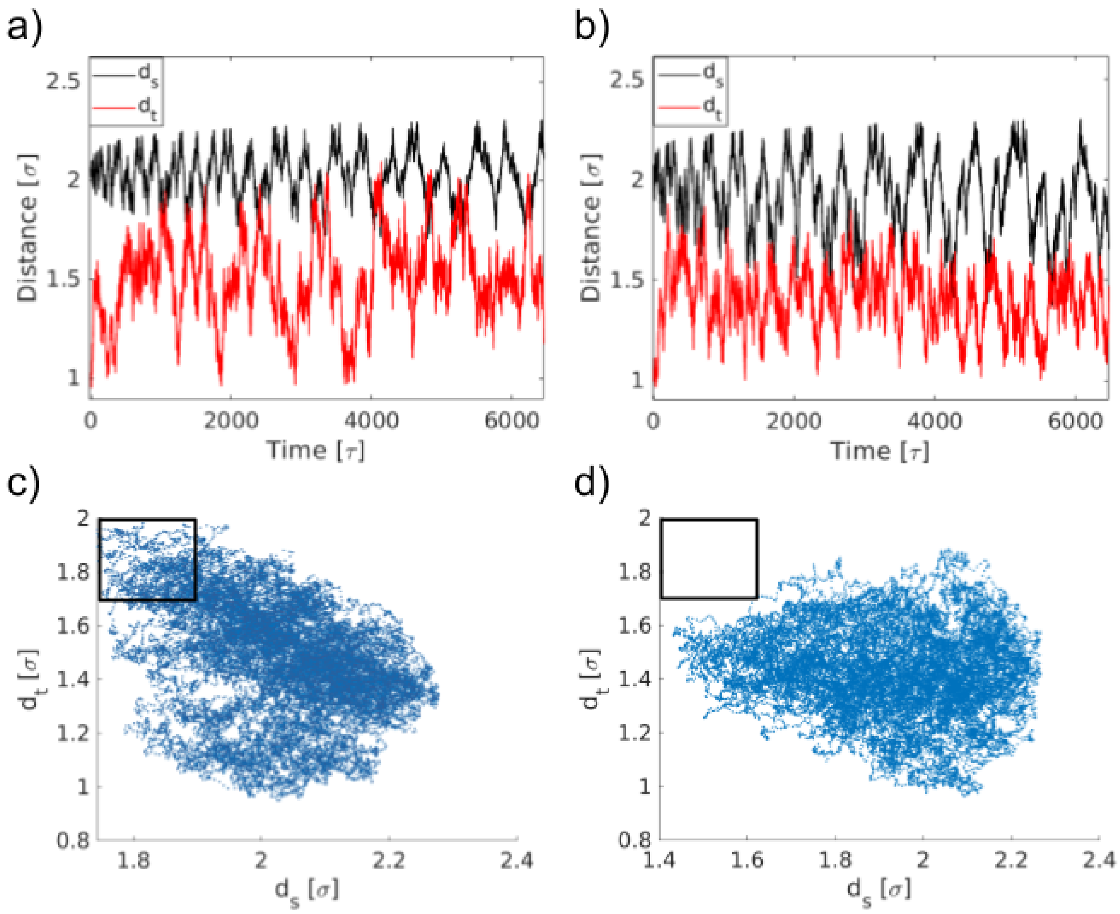

Figure S4: **Time dependence behavior in WTMD simulations for a pristine and modified network.** a) Time dependence excerpt from a WTMD simulation of the pristine network run at $T = 4.3 \cdot 10^{-5}$ in which d_s, the distance between the source nodes is the biased CV. It can be seen that upon passing a threshold value, the allosteric response of the target beads (measured by the distance between them, d_t) is triggered. b) Time dependence excerpt from a WTMD simulation run at $T = 4.3 \cdot 10^{-5}$ of a modified network for which the bonds ranked 12-27 in the HLDA_1 weight hierarchy were weakened. As can be seen the activated state is inhibited in the modified network whereby for values $d_s < 1.7$ the target beads do not access the activated region of $d_t > 1.7$. c) and d) showing the same data corresponding to a) and b), respectively, whereby the distance between target beads is plotted as function of the distance between the source beads. The rectangles indicate approximate region in phase space in which the allosteric site activation is initially triggered.

Allosteric activation distance as function of the stiffness of the single top ranked HLDA bond (the case of a single 'mutation')

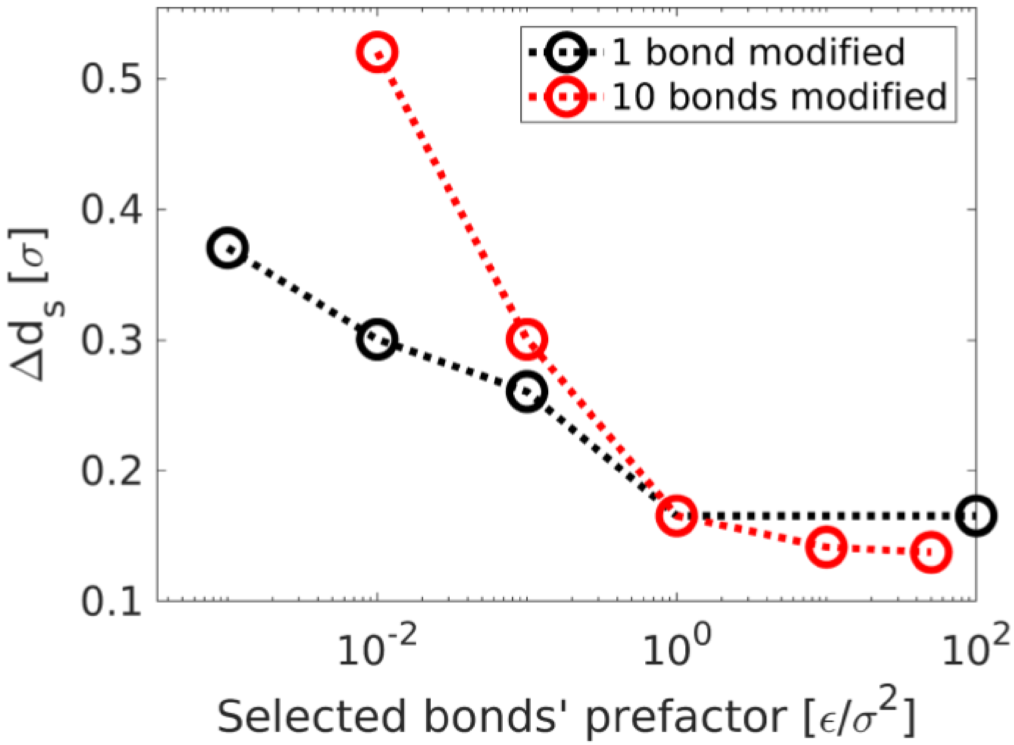

Figure S5: **Allosteric activation distance as function of the stiffness of the single top ranked HLDA bond.** The measured allosteric minimal activation distance between the source beads for the case in which the top ranked $HLDA_1$ bond is modified (single mutation) vs.the case in which the top 10 $HLDA_1$ bonds are modified.

Modifications made to the network's FES corresponding to its strain fluctuations

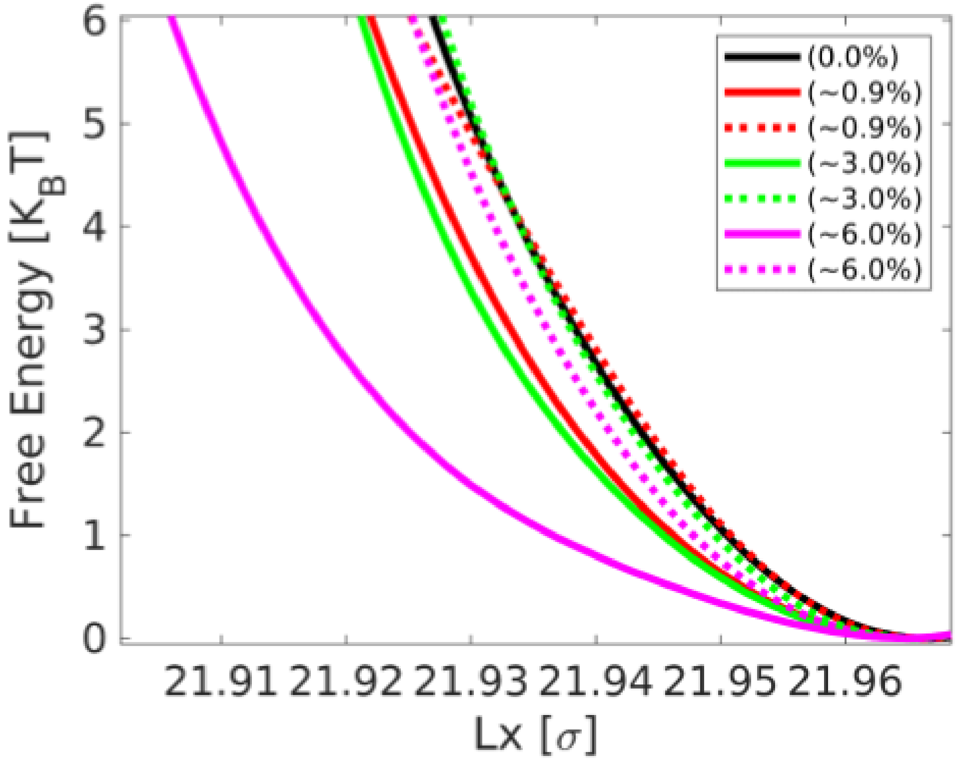

Figure S6: **The network's FES corresponding to its strain fluctuations for different percentage of bond modifications.** The computed FES of the simulated pristine network as function of L_x (solid black) **aligned** according to their minima with the FES of modified realizations of the network in which the bond coefficient of the highest weighted HLDA bonds was reduced to $0.01\epsilon/\sigma^2$ (solid lines) or in which the bond coefficient of randomly selected bonds was reduced to $0.01\epsilon/\sigma^2$ (doted lines). In parenthesis, the percentage of bonds that was modified in the network in each case. As can be seen the effect of the random modifications on the network's FES is comparably small.

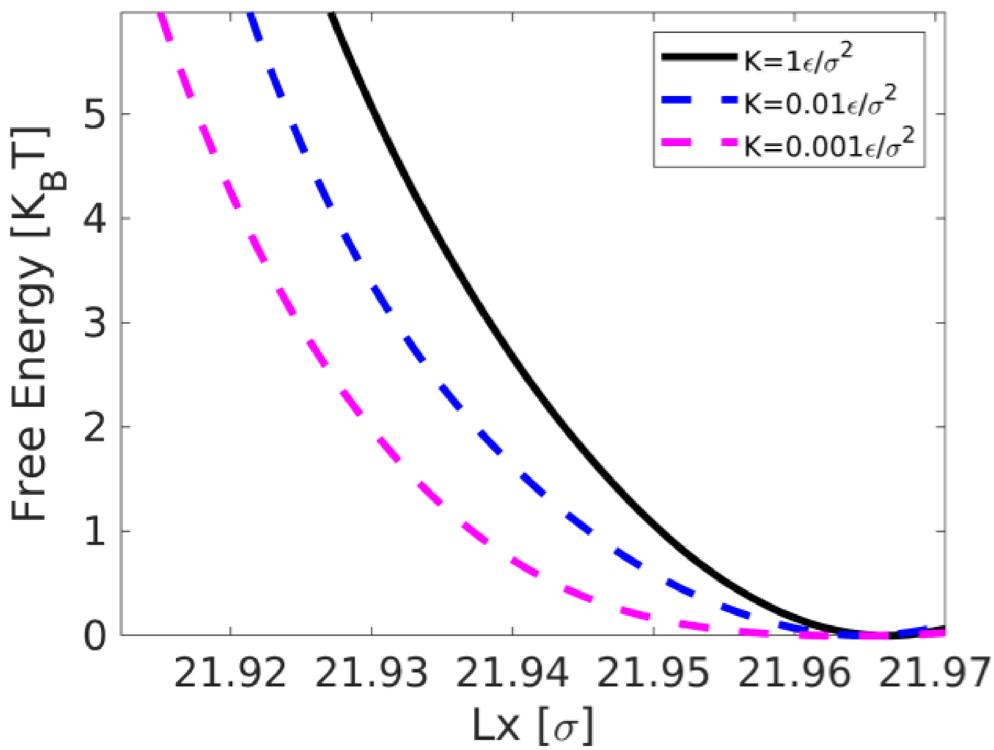

Figure S7: **The network's FES corresponding to its strain fluctuations in which the top 3 percent ranked HLDA bonds are weakened by a differing value.** The computed FES of the simulated pristine network as function of L_x (solid black) aligned according to their minima with the FES of modified realizations of the network in which the top 30 (3 percent) ranked HLDA bonds are weakened.

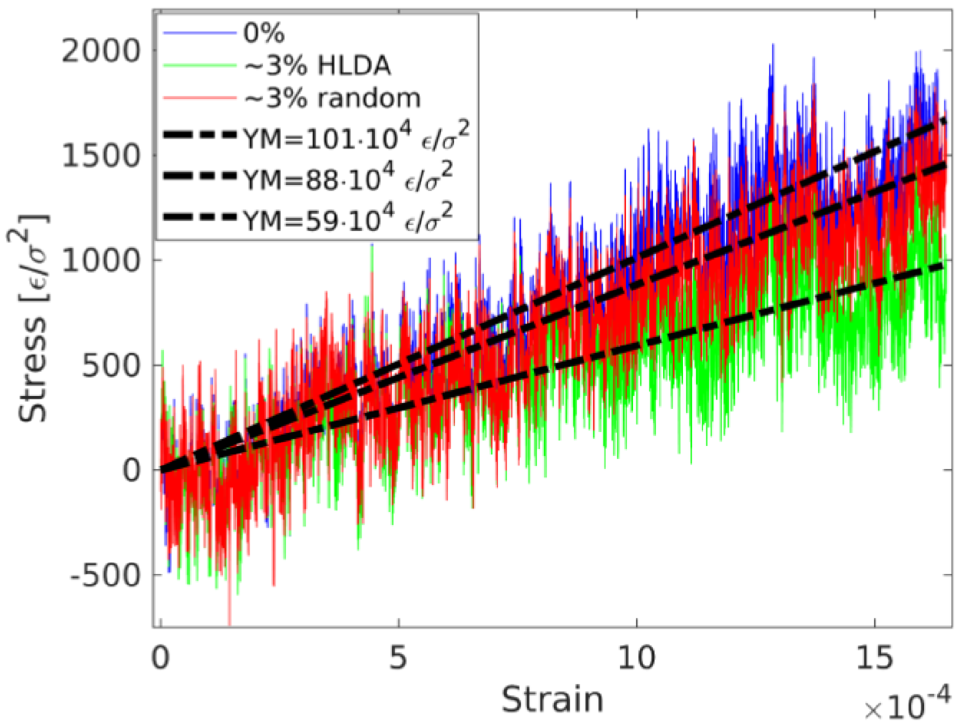

Figure S8: **Stress-strain curves for different network realizations.** The stress-strain curve for the pristine network and the networks in which 3 percent of the bonds were weakened using CV-FEST or randomly. The Young's Modulus of the networks (corresponding to the curves' slopes are given, respectively, in the legend.

Induced entropic modifications in the context of the network strain fluctuations

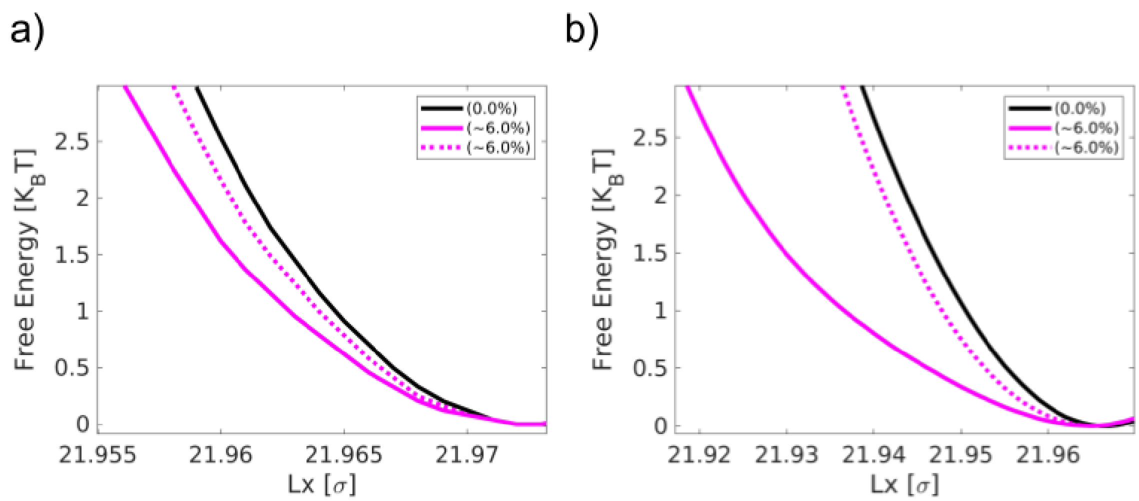

Figure S9: **Induced entropic modifications in the context of the network strain fluctuations.** The computed FES of the simulated pristine network as function of L_x (solid black) aligned (according to their minima) with the FES of modified realizations of the network in which 6 percent of the network bonds were weakened to $0.01\epsilon/\sigma^2$. In the colored solid lines, the FES of the CV-FEST modified network while in the dotted lines, the FES of the randomly modified network. a) In the case where the system was run at a temperature of T=0.01, and b) in which it was run at T=0.1. The relative effect of the CV-FEST targeted selection can be seen to increase with temperature, indicating that the system's free energy surface change in the case of CV-FEST is largely due to an alteration to its entropy.

Equation for the calculation of the free energy difference ΔF between any two states A and B

$$\Delta F_{AB} = -\frac{1}{\beta}\log\frac{\int_A d\mathbf{s}e^{-\beta F(\mathbf{s})}}{\int_B d\mathbf{s}e^{-\beta F(\mathbf{s})}} \tag{S1}$$