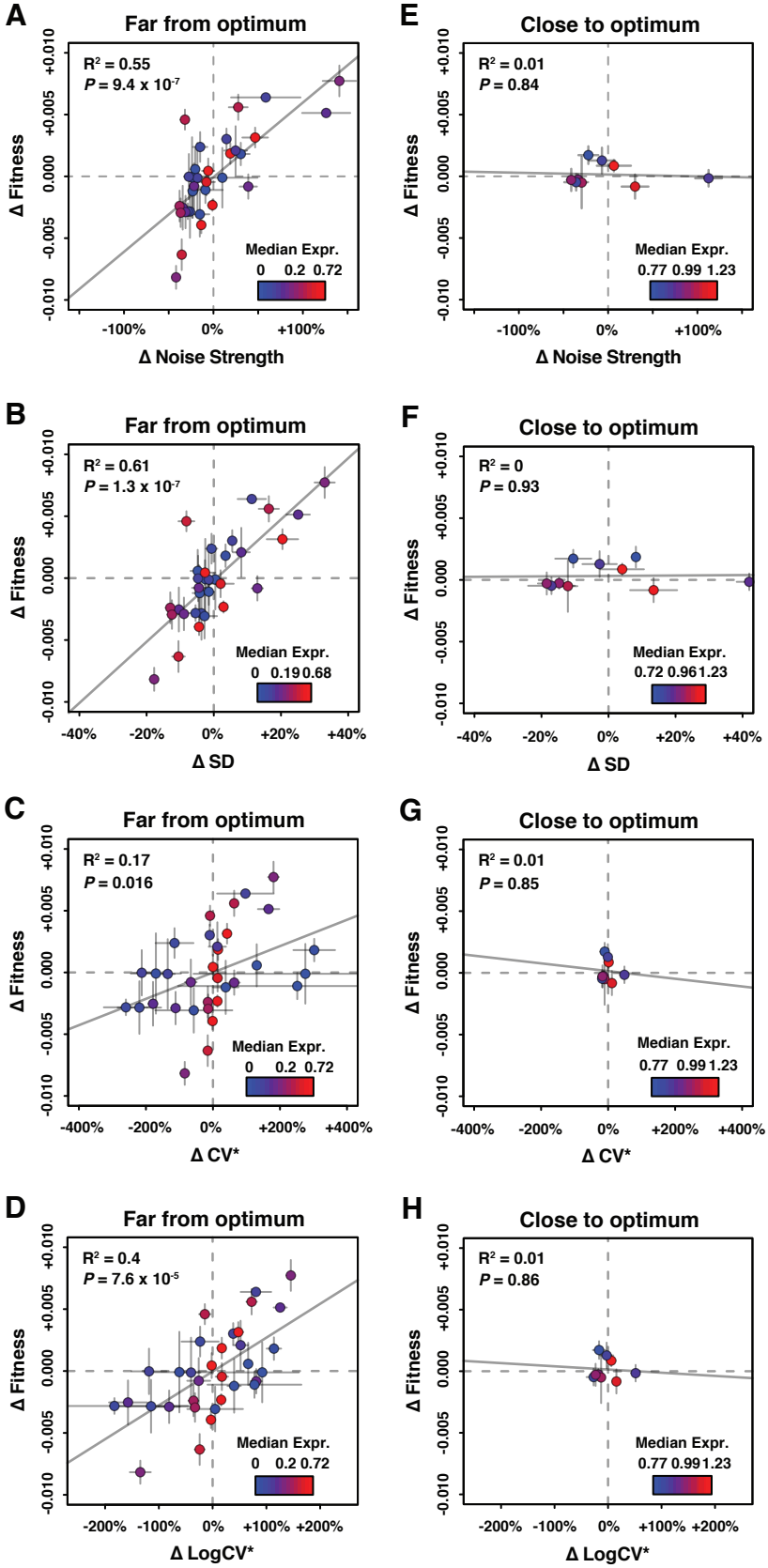Figure 3 - figure supplement 4