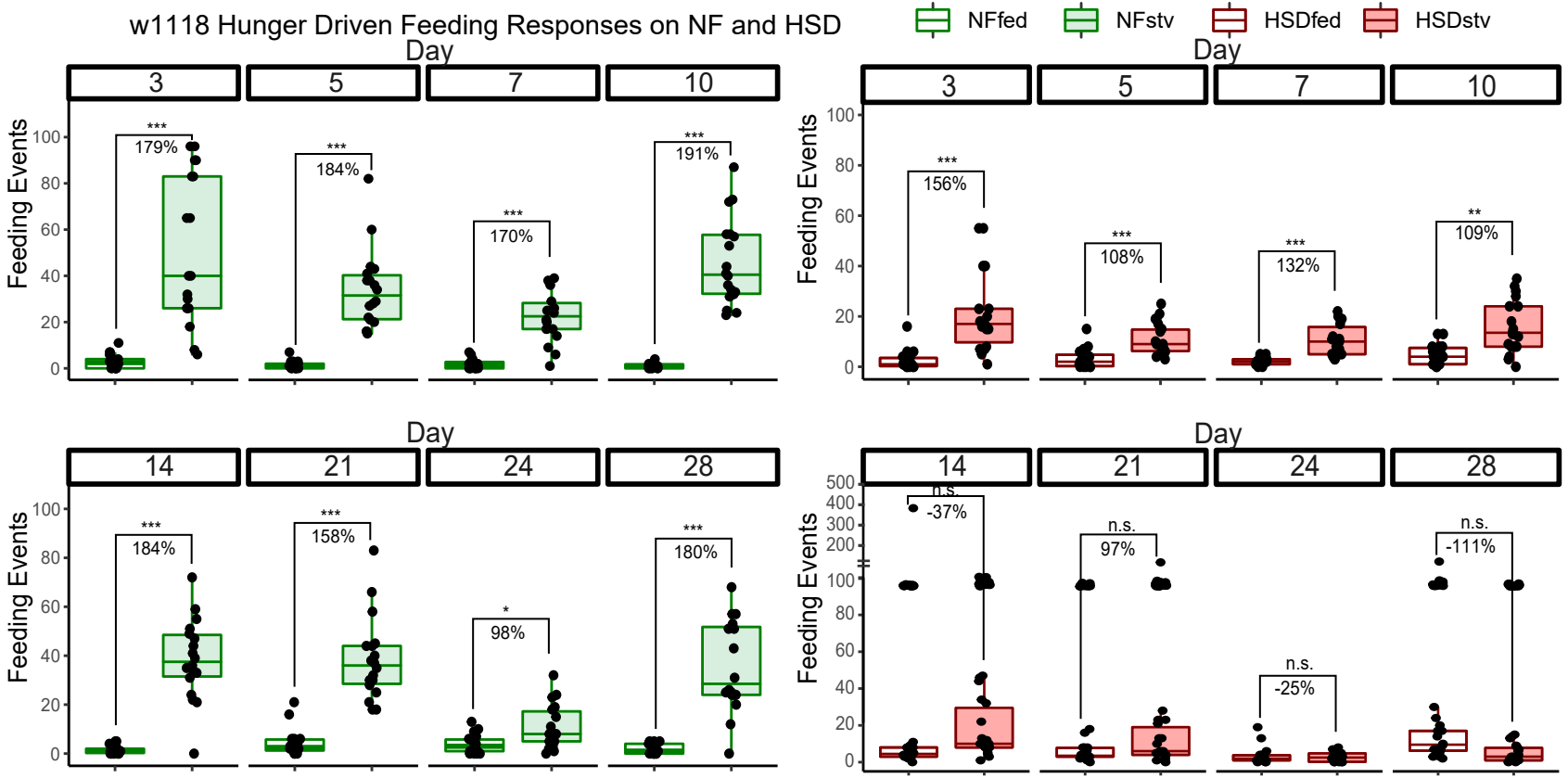Figure 1- figure supplement 1