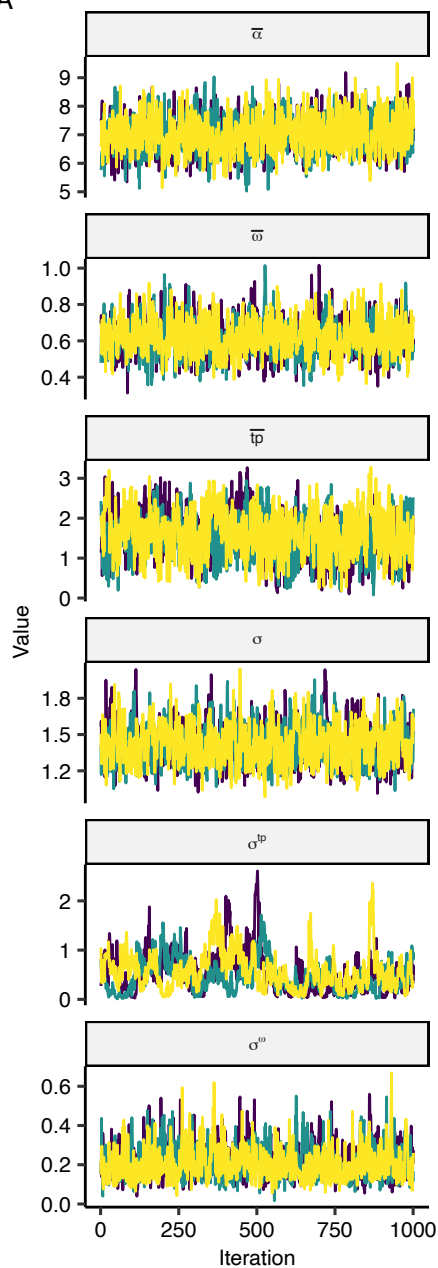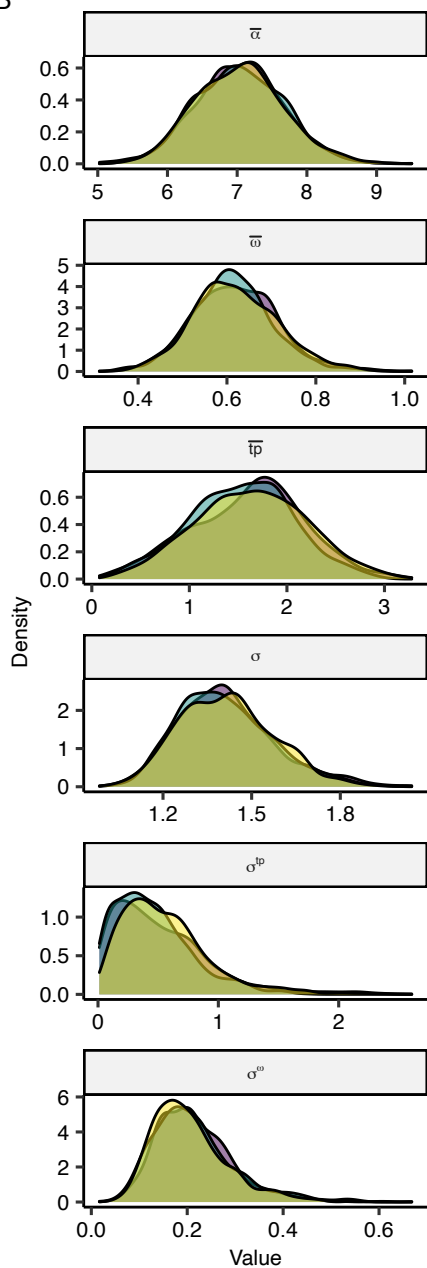Extended Data Figure 2