"networking" concept (Stadler, Schweins, Zaccai, & Lindner, 2010). The main idea is that if the protein or mAbs are interacting in a long-range network, then displacement of a single mAb requires movement of the other network-associated mAbs resulting in a larger viscous drag. The formation of a network would require involvement of multiple binding sites on a mAb and such interactions could occur through Fab–Fc, Fab–Fab or both interactions. Fc–Fc interactions were ruled out since both mAb1 and mAb2 have the same Fc amino acid sequence, and yet mAb2 does not have aberrantly high viscosity at the high concentration.

In order to determine which regions of the mAb are involved, the viscosity of the $F(ab')_2$ fragments (Figure 9.7(a)) of mAb_1 and mAb_2 was determined. Overall

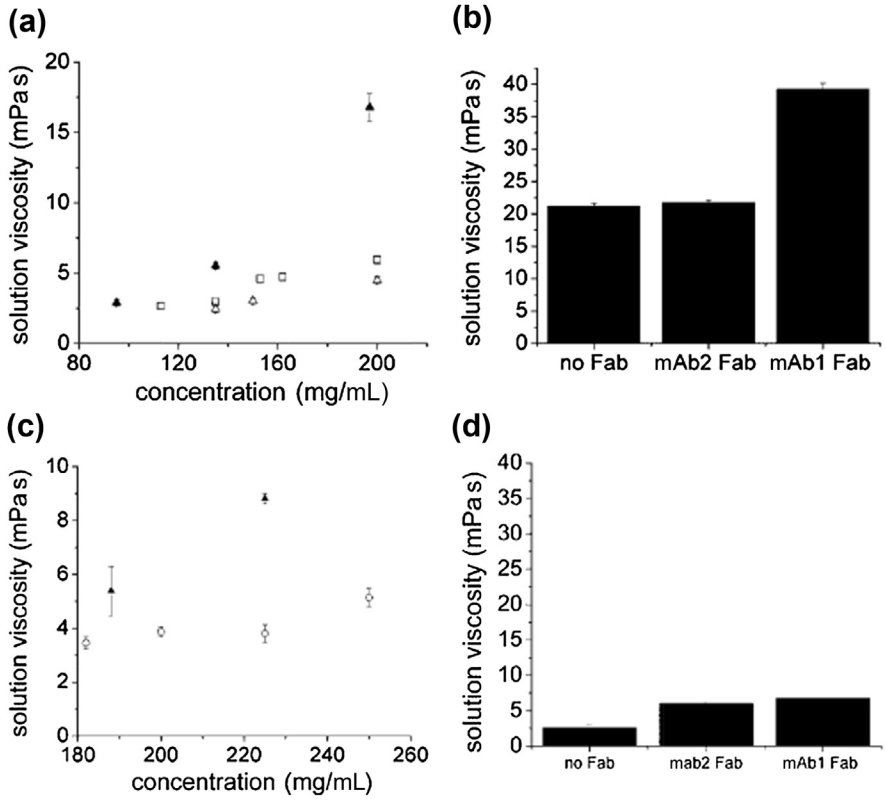

Figure 9.7 (a) Viscosity of mAb1 and mAb2 $F(ab')_2$ fragments in 30 mM histidine buffer at pH 6.0, mAb1 $F(ab')_2$ (solid triangles) and mAb2 $F(ab')_2$ (open squares) and mAb1 $F(ab')_2$ in buffer with 200 mM NaSCN (open triangles). (b) Viscosity of full-length mAb1 mixed with Fab fragments as indicated. The full-length mAb1 concentration is 110 mg/mL and Fab concentration is 100 mg/mL in 30 mM histidine buffer at pH 6.0. (c) Viscosity of mAb1 (solid triangles) and mAb2 Fab (open circles) fragments in 30 mM histidine, pH 6.0. (d) Viscosity of full-length mAb2 mixed with Fab fragments as indicated. The full-length mAb2 concentration is 100 mg/mL and Fab concentration is 100 mg/mL in 30 mM histidine buffer at pH 6.0.
From Kanai et al. (2008).