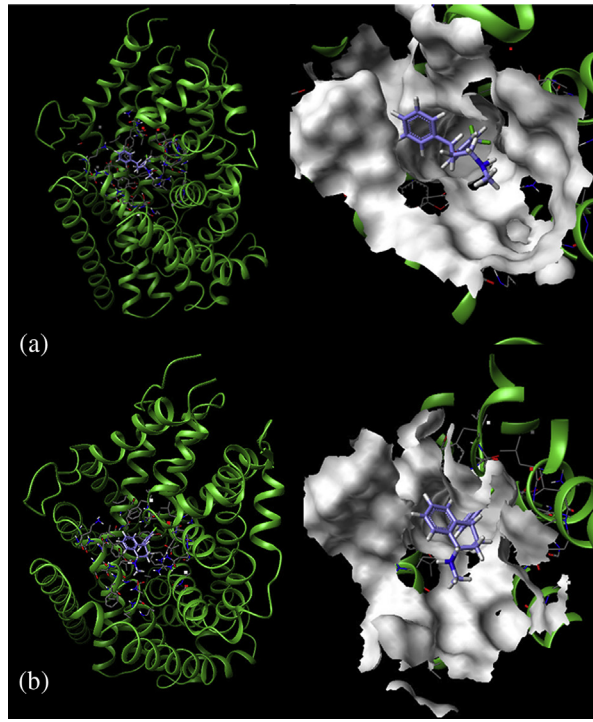

FIGURE 3.45 (a) Leucine transporter with sertraline, full enzyme (left) and binding-site close-up (right) (RCSB 3GWU). (b) Leucine transporter with R-Fluoxetine, full enzyme (left) and binding-site close-up (right) (RCSB 3GWV).

EMERGING TARGETS

Although historically the majority of drugs research has focused on the aforementioned target classes, some new approaches to drug discovery have emerged over the last few decades. Protein/protein, protein/DNA, and protein/RNA interactions have emerged as potential avenues for therapeutic intervention. The importance of protein/protein interactions can be seen in the GPCR pathways, which require the interaction of multiple protein types in order for signal transduction to occur, and interrupting any one of these interactions would alter the physiological outcome. A compound that interfered with binding of the Gα protein to protein kinase C, for example, would block signal transduction through the cAMP pathway, while a compound that stabilized this interaction would augment the signal. In a similar manner, a compound that disrupts the interaction of a regulatory protein with its enzymatic target would increase the amount of free enzyme available to facilitate chemical reactions. In theory, any physiological process that requires the