LIST OF FIGURES

Figure 1.1 Various CDK/cyclin complexes involved at different stages of cell cycle ................................................................. 15
Figure 1.2 Cell cycle control G1/S checkpoints ........................................................ ......................................................... 16
Figure 1.3 CDK2 image showing various flexible loops ...................................................... 17
Figure 1.4 Schematic diagram of the molecular fork. Residues from i to i+2 are Glu81, Phe82, Leu83 for CDK2 ...................................................... 19
Figure 1.5 Image showing phi and psi torsion angles along a protein backbone ...... 20
Figure 1.6 Energy distance curve .............................................................................. 52
Figure 1.7 Energy landscape Biomolecule Curve .......................................................... 57

Figure 3.1 2-Dimensional Structures of selected ligands for energy minimization ... 75
Figure 3.2: Generation of 3dimensional structure of gemcitabine using HyperChem software................................................................................................. 76
Figure 3.3: Image showing various molecular mechanics algorithms applied on ligands .......................................................................................................................... 76
Figure 3.4: 1H1S protein showing ligand (green color, ball and stick model) surrounded by 8.0 Å region of active site amino acids ................................................. 83
Figure 3.5: Image showing multiple sequence alignment of all CDK2 protein using ClustalW tool to find consensus active site residues ................................................. 83
Figure 3.6: Image showing calculation of torsion angles using Dang software ............ 84
Figure 3.7: Image showing the docking of cdk2 proteins with their reference ligands using MVD software .................................................................................... 85
Figure 3.8: Image showing activity values and torsion angles for regression analysis using TSAR software ................................................................................................................. 86
Figure 3.9: Image showing performing of MLR analysis on the complete set .......... 87
Figure 4.1 Screen-shot image of code ........................................................................ 89
Figure 4.2: Image showing various molecular mechanics force fields applied on ligands ................................................................................................................................. 90
Figure 4.3: Image showing selection of parameters for regression analysis ............ 97
Figure 4.4: Image showing 15 variables that entered the regression model after removing outliers ................................................................................................................................. 98
Figure 4. 5: Image showing correlation graph between actual values and predicted values. ................................................................. 99
Figure 4. 6: Image showing 19 variables that entered the final regression model which influences ligand binding within CDK2 active site.................. 100
Figure 4. 7: Image showing the evaluated values of the test set using evaluate function. ................................................................. 103
Figure 4. 8: Image showing statistical validation based on test set .................... 104

LIST OF TABLES
Table 4. 1: Energy minimized data of 1H1S_ligand molecule using various algorithms .................................................................................. 91
Table 4. 2: Energy minimized data of 1OIT_ligand molecule using various algorithms .................................................................................. 92
Table 4. 3: molecular dynamics run of 1H1S_ligand using various run times......... 93
Table 4. 4: molecular dynamics run of 1OIT_ligand using various run times......... 94
Table 4. 5: The Dock score and Activity value of the selected 135 CDK2 proteins... 95

LIST OF PUBLICATIONS