confirmed, their 3D structures can be used to identify small molecules that favorably bind into an active or an allosteric site by conducting virtual screening of small molecule libraries, modification of existing drug molecules, or *de novo* design of novel molecules (Simmons et al. 2010):

- Structure-based virtual screening (SBVS) for possible active molecules that forms favorable interactions with selected residues of a target. The SBVS relies on molecular docking of ligands from small molecule libraries into of a known or putative active site on the macromolecule.
- Structure-based *de novo* design provides opportunities to create new chemical entities with adequate molecular properties that could favorably bind into the active site and possibly have novel scaffolds (Hartenfeller and Schneider 2011; Cain et al. 2014).
- The availability of the 3D structure of a drug complexed with the target biomolecule provides a basis for *in silico* structural modifications of the drug molecule to improve the shape and charge complementarity on the binding interface.

On the contrary, ligand-based drug design (LBDD) is utilized when the 3D structure of the drug target is not known, but the effects of a series of molecules on a particular biological process or organism are known. Curation just one of the repositories of the biological activities of small molecules, the ChEMBL database (Gaulton et al. 2012), indicates that over 300 000 compounds were tested for antibacterial activity in cell-based assays, while 110 000 compounds were tested for their inhibitory activity of 500 proteins from different bacterial pathogens. In cases when selected compounds are known to bind into the same active site, the knowledge of their 3D structures enables the development of 3D quantitative structure–activity relationship (3D QSAR) and pharmacophore models, pharmacophore being a structural feature necessary for interaction with the target molecule. Both computer-aided approaches are suitable for lead identification and their further optimization into drug candidates (Acharya et al. 2011). Once the available information is used to generate and validate models, high-throughput virtual screening can be conducted to identify molecules with key molecular properties and/or pharmacophoric features that are essential for the desired biological activity. The identified hit molecules can be reintroduced into ligand-based models for the fine optimization of the structure to improve their efficacy and potency.

The key advantages of the *in silico* approaches to drug design lie in the possibility to generate and evaluate hypotheses before undertaking the extensive and resource demanding experimental projects. As the number of bacterial biomolecules with known 3D structures and availability of the information on the antibacterial activity of small molecules are on the rise, the increase of computational power provides opportunities for the development of new algorithms for the design of novel antibiotics and inhibitors of resistance. The