BAB 5
KESIMPULAN DAN SARAN

5.1. Kesimpulan

Berdasarkan penelitian simulasi dinamika molekul bentuk apo protein FKBP12 (PDB: 1FKB), telah diperoleh hasil data sehingga dapat ditarik kesimpulan. Kesimpulan tersebut dipaparkan sebagai berikut:

1. Simulasi dinamika molekul selama 40 ns menghasilkan perhitungan RMSD yang cukup dengan rata-rata 0,23 nm, sedangkan rata-rata untuk atom penyusun tulang punggung protein adalah 0,15 nm.
2. Efek potensial *flooding* mendestabilisasi struktur protein FKBP12 tetapi setelah potensial *flooding* dihilangkan, struktur protein kembali setimbang.
3. Hasil perhitungan rata-rata RMSF diperoleh untuk semua atom protein memiliki rata-rata sebesar 0,17 nm sedangkan untuk atom penyusun tulang punggung protein memiliki rata-rata sebesar 0,11 nm.
4. Residu Y26, D37, R42, M49 dan E54 menstabilkan struktur protein FKBP12 dengan interaksi ikatan hidrogen.

5.2. Saran

Penelitian ini dapat dilanjutkan dengan:

1. Penelitian simulasi dinamika molekul protein FKBP12 dapat diganti dengan ligan yang lain.

DAFTAR PUSTAKA

Aghdasi, B., Ye, K., Resnick, A., Huang, A., Ha, H.C., Guo, X., Dawson, T.M., Dawson, V. L. and Snyder, S. H. 2001, FKBP12, the 12-kDa FK506-binding protein, is a physiologic regulator of the cell cycle, *Proceedings of the National Academy of Sciences*, **98(5)**: 2425-2430.

Banaszynski, L. A., Liu, C. W., and Wandless, T. J. 2005. Characterization of the FKBP.rapamycin.FRB ternary complex. *Journal of the American Chemical Society*. **127**: 4715–4721

Berendsen, H. J., Van Der Spoel, D., Van Drunen, R. 1995. GROMACS: a message-passing parallel molecular dynamics implementation. *Computer Physics Communications*, **91(1-3)**: 43-56.

Brooks, B. R., Bruccoleri, R. E., Olafson, B. D., States, D. J., Swaminathan, S. A., Karplus, M. 1983. CHARMM: a program for macromolecular energy, minimization, and dynamics calculations. *Journal of Computational Chemistry*, **4(2)**: 187-217.

Delves, P.J. and Roitt, I.M. 2000, The Immune System, New England Journal of Medicine, **343(1)**:37–49.

Eriksson, M. A. L., Pitera, J., & Kollman, P. A. 1999, Prediction of the binding free energies of new TIBO-like HIV-1 reverse transcriptase inhibitors using a combination of PROFEC, PB/SA, CMC/MD, and free energy calculations. *Journal of Medicinal Chemistry*, **42(5)**:868–881.

Fireman, M., Dimartini, A.F., Armstrong, S. C., & Cozza, K. L. 2004. Immunosuppressants. Psychosomatics, **45(4)**: 354-360.

Frenkel, D. and Smit, B. 2002, *Understanding Molecular Simulation from Algorithms to Applications*, Academic Press, New York.

Griffith, J. P., Kim, J. L., Kim, E. E., Sintchak, M. D., Thomson, J. A., Fitzgibbon, M. J., *et al*. (1995). X-ray structure of calcineurin inhibited by the immunophilin-immunosuppressant FKBP12 FK506 complex. Cell, **(82)**: 507–522.

Grzesiek, S. & Edwin, D. B. 2011. Hydrogen bonding. *Encyclopedia of Magnetic Resonance*, Switzerland.

Halloran PF. Immunosuppressive drugs for Kidney Transplantation. *The New England Journal of Medicine*. 2004; **352(10)**:1056

Huldani. 2018. Pengantar Imunologi dari Imunoseluler ke Exercise Imunologi. **(1)**: 2-3

Hess, B., Bekker, H., Berendsen, H. J., Fraaije, J. G. 1997. LINCS: a linear constraint solver for molecular simulations. *Journal of Computational Chemistry*, **18(12)**:1463-1472.

Holtje, H. D., Sippl, W., Rognan, D., and Folkers, G., 2008. *Molecular Modeling Basic Principle and Application*, ed 3rd , WILEY – VCH Verlag GmbH & Co. KgaA, Germany, 16 – 18.

Kang, C.B., Hong, Y., Dhe-Paganon, S. and Yoon, H.S. 2008, FKBP family proteins: immunophilins with versatile biological functions, *Neurosignals*, **16(4)**:318-325.

Karplus, M., McCammon, J. A. 2002. Molecular dynamics simulations of biomolecules. *Nature Structural Biology*, **9(9)**:646-652.

Kolos, J. M., Voll, A. M., Bauder, M., Hausch, F. 2018. FKBP Ligands Where We Are and Where to Go? Frontiers in Pharmacology:9.

Lange, O. F., Schäfer, L. V., & Grubmüller, H. (2006). Flooding inGROMACS: Accelerated barrier crossings in molecular dynamics. Journal of Computational Chemistry, **27(14)**, 1693–1702.

Liang, J., Choi, J., and Clardy, J. 1999. Refined structure of the FKBP12-rapamycin-FRB ternary complex at 2.2 angstrom resolution. Acta Crystallogr. D: *Biological Crystallography*, **(55)**:736–744

Mackay, F., Mackay, C. R. 2002. The role of BAFF in B-cell maturation, T-cell activation and autoimmunity. Trends in Immunology, **23(3)**:113–115

Nicholson, L.B. (2016) "The immune system," *Essays in Biochemistry*, **60(3)**:275–301.

Rosen, M. K., and Schreiber, S. L. 1992. Natural-products as probes of cellular function - studies of immunophilins. Angewandte Chemie International Edition in English, **(31)**: 384–400

Suardana, I.B.K. (2017) *Diktat Imunologi Dasar Sistem Imun*. Denpasar: Universitas Udayana.

Van Der Spoel, D., Lindahl, E., Hess, B., Groenhof, G., Mark, A. E., & Berendsen, H. J. C. 2005. GROMACS: Fast, flexible, and free. Journal of Computational Chemistry, **26(16)**: 1701–1718.

Van Duyne, G.D., Standaert, R.F., Schreiber, S.L. and Clardy, J. 1991, Atomic structure of the rapamycin human immunophilin FKBP-12 complex, Journal of the American Chemical Society, **113(19)**: 7433-7434.

Van Gunsteren, W. F., & Mark, A. E. 1998. Validation of molecular dynamics simulation. The Journal of Chemical Physics, **108(15)**: 6109-6116.

Waickman, A. T., and Powell, J. D. 2012. Mammalian target of rapamycin integrates diverse inputs to guide the outcome of antigen recognition in T cells. The Journal of Immunology. **(188)**: 4721–4729.

Weiner, P.K., & Kollman, P.A. 1981. AMBER: Assisted model building with energy refinement. A general program for modeling molecules and their interactions. Journal of Computational Chemistry, 2.

Wang, J., Wolf, R.M., Caldwell, J.W., Kollman, P.A. and Case, D.A. 2004, Development and Testing of a General Amber Force Field, *Journal of Computational Chemistry*, **25(9)**: 1158-1171.

Wu, W. and Owino, J. 2014, Applying Periodic Boundary Conditions in Finite Element Analysis, *Simulia Community Conference*, Amerika Serikat.