# BAB 5
## KESIMPULAN DAN SARAN

### 5.1. Kesimpulan

Berdasarkan penelitian pada simulasi dinamika molekul bentuk apo protein FKBP12(PDB:2PPN), sudah memperoleh hasil data sehingga dapat ditarik kesimpulan.Simulasi dinamika molekul selama 40 ns menghasilkan rata-rata nilai RMSD untuk semua atom protein yang disesuaikan dengan atom penyusun tulang punggung adalah 0,36 nm , sedangkan rata-rata untuk atom penyusun tulang punggung saja adalah 0,34 nm.Potensial flooding tidak memberikan efek yang signifikan pada struktur meski memberikan perubahan namun saat energi potensial dihilangkan struktur secara keseluruhan dapat kembali seperti semula. Residu R42 yang tidak terlibat aktif dalam interaksi ikatan hidrogen dan memiliki fleksibilitas tinggi dapat membantu menstabilkan residu R42 yang terlibat aktif dalam inteaksi.

### 5.2. Saran

Penelitian Simulasi dinamika molekul protein FKB12 ini dapat dilanjutkan dengan diganti ligan yang lain.

# DAFTAR PUSTAKA

Abdul, K.A., Andrew, H.L., and Shiv P.2007, 'Introduction to the Immune System' , in Elsevier, Basic Imumunology : Fungtion and Disorders of the Immune System, $5^{th}$ ed.,Catherine Jackson,Canada,pp 1-25

Abraham, M.J., van der Spoel, D., Lindahl, E., and Hess, B. 2018, GROMACS User Manual version 2018.2, *www.gromacs.org*.

Aghdasi, B., Ye, K., Resnick, A., Huang, A., Ha, H, 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.

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.

Bussi, G., Donadio, D. and Parrinello, M. 2008, Canonical Sampling through Velocity-Rescaling, *The Journal of Chemical Physics*, **126(1)**: 014101-1– 014101-7.

Childers, M. and Daggett, V. 2018, Validating Molecular Dynamics Simulations Against Experimental Observables in Light of Underlying Conformational Ensembles, *The Journal of Physical Chemistry B*, **122(26)**: 6673-6689.

Darden, T., York, D. and Pedersen, L. 1993, Particle mesh Ewald: An N - log(N) Method for Ewald Sums in Large Systems, *The Journal of Chemical Physics*, **98(12)**: 10089-10092.

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

Hess, B., Bekker, H., Berendsen, H.J.C. and Fraaije, J.G.E.M. 1997, LINCS: A Linear Constraint Solver for Molecular Simulations, *Journal of Computational Chemistry*, **18**: 1463–1472.

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

Hünenberger, P. H., Mark, A. E., & Van Gunsteren, W. F. 1995. Fluctuation and cross-correlation analysis of protein motions observed in nanosecond molecular dynamics simulations. *Journal Of Molecular Biology*, **252(4)**: 492-503.sssss

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

Karin, C. 2021, 'Simulasi Dinamika Molekul Bentuk Apo dari Imunofilin FKBP12', *Skripsi*, Sarjana Farmasi, Universitas Katolik Widya Mandala,Surabaya.

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.*

Li, J., Kim, S.G., &Blenis, J. (2014). Rapamycin : One drug, many effects. *Cell Metabolism*, **19(3)**:373-379.

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

Maiorov, V. N., & Crippen, G. M. 1995. Size-independent comparison of protein three-dimensional structures. *Proteins: Structure, Function, and Bioinformatics*, **22(3)**: 273-283.

Miyamoto, S and Kollman P.A. 1992, SETTLE: An Analytical Version of the SHAKE and RATTLE Algorithm for Rigid Water Models. *Journal of Computational Chemistry*, **13(8)**: 952-962

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

Prananto, Y. P. (2013). Ikatan Hidrogen. In Universitas Brawijaya,pp 1-4

Schneider, G., Baringhaus, K. 2008, *Molecular Design*: Concepts and Applications. Jerman: Wiley.

Szep,S., Park, S., Boder, E.T., Van Duyne, G.D., & Saven, J.G. (2009). Structural Coupling between FKBP12 and buried water. *Proteins: Structure, Function and Bioinformatics*, **74(3):** 603-611.

van Gunsteren, W. F. & Mark, A. E. 1998. Validation of molecular dynamics simulation. *Journal of Chemical Physics*, **108(15)**: 6109- 6116.Lange, O. F., Schäfer, L. V., & Grubmüller, H. (2006). Flooding in GROMACS: accelerated barrier crossings in molecular dynamics. *Journal of computational chemistry*, **27(14)**, 1693-1702.

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

Wande,I. N., Herawati, S., Widhiartini,I. A.A., Yasa,I. W. P. S., Oka, T.G., & Linawati, N. M.(2014). *Indonesian Journal of Cliical Pathology and Medical Laboratory*,**3(1):**219-223.

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.