BAB 5
KESIMPULAN DAN SARAN

5.1 Kesimpulan

Berdasarkan penelitian perhitungan energi bebas menggunakan metode *Umbrella Sampling* dari protein MIP dan ligan Rapamycin memberikan kesimpulan sebagai berikut:

1. Perubahan energi bebas dengan menggunakan tiga variasi jumlah trayektori 35, 40 dan 45 dengan hasil yang diperoleh masing-masing yaitu -39,918 kJ/mol, -38,413 kJ/mol dan -38,802 kJ/mol.
2. Semakin sedikit jumlah trayektori yang digunakan, maka perubahan energi bebasnya meningkat. Pada trayektori 35 memperoleh hasil dengan nilai ΔG yang lebih tinggi seharusnya hasil yang baik terdapat pada trayektori 45.

5.2 Saran

Untuk mengetahui dengan detail penyebabnya perlu dilakukan penelitian lebih lanjut dengan melihat interaksi yang terjadi.

DAFTAR PUSTAKA

Abraham, M.J., Murtola, T., Schulz, R., Páll, S., Smith, J.C., Hess, B., Lindah, E. 2015, GROMACS: High performance molecular simulations through multi-level parallelism from laptops to supercomputers, *Software X*, 1-25.

Adini, L. 2024, Pengaruh pemilihan jumlah trayektori terhadap perubahan energi bebas pengikatan protein FKBP12-Rapamycin dengan metode Umbrella Sampling, *Skripsi*, Sarjana Farmasi, Universitas Katolik Widya Mandala, Surabaya.

Aliev, A.E., Kulke, M., Khaneja, H.S., Chudasama, V., Sheppard, T.D. and Lanigan, R.M. 2014, Motional timescale predictions by molecular dynamics simulations: Case study using proline and hydroxyproline sidechain dynamics, *Protein*: *Structure*, *Function* and *Bioinformatics*, **82(2)**: 195-215.

Berendsen, H.J.C., Postma, J.P.M., Van Gunsteren, W.F., Dinola, A. and Haak, J.R. 1984, Molecular dynamics with coupling to an external bath, *The Journal of Chemical Physics*, **81(8)**.

Ceymann, A., Horstmann, M., Ehses, P., Schweimer, K., Paschke, A.K., Steinert, M. and Faber, C. 2008, Solution structure of the Legionella pneumophila MIP-Rapamycin complex, *BMC Structural Biology*, **8**: 1-12.

Clarence, A. 2025, Simulasi pendahuluan protein FKBP12-Ligan S35D untuk persiapan Umbrella Sampling, *Skripsi*, Sarjana Farmasi, Universitas Katolik Widya Mandala, Surabaya.

Ferreira De Freitas, R. and Schapira, M. 2017, A systematic analysis of atomic protein-ligand interactions in the PDB, *MedChemComm*, **8(10)**.

Fu, H., Zu, Y. and Chen, Q. 2024, Free energy calculations in biomolecule-nanomaterial interactions, *Frontiers in Physics*, **12**: 1–8.

Gattuso, G., Rizzo, R., Lavoro, A., Spoto, V., Porciello, G., Montagnese, C., Cinà, D., Cosentino, A., Lombardo, C., Mezzatesta, M. L. and Salmeri, M. 2022, Overview of the Clinical and Molecular Features of Legionella pneumophila: focus on novel surveillance and diagnostic strategies, *Antibiotics*, **11(3)**: 370.

Heldiandri, A.E. 2024, Simulasi pendahuluan protein MIP dengan ligan Rapamycin untuk persiapan Umbrella Sampling, *Skripsi*, Sarjana Farmasi, Universitas Katolik Widya Mandala, Surabaya.

Hollingsworth, S.A. and Dror, R.O. 2018, Molecular Dynamics Simulation for all, *In Neuron* , **99(6)**: 1129-1143.

Humphrey, W., Dalke, A., Schulten, K. 1996, VMD: Visual molecular dynamics, *Journal of Molecular Graphics*, **14(1)**: 33-38.

Iliadi, V., Staykova, J., Iliadis, S., Konstantinidou, I., Sivykh, P., Romanidou, G., Vardikov, D. F., Cassimos, D. and Konstantinidis, T. G. 2022, Legionella pneumophila: The Journey from the Environment to the Blood, *Journal of Clinical Medicine*, **11(6126)**: 1-18.

Jomehzadeh, N., Moosavian, M., Saki, M., and Rashno, M. 2019, Legionella and Legionnaires' disease: An overview, *Journal of Acute Disease*, **8(6)**: 221-232.

Jorgensen, W. L., Chandrasekhar, J., Madura, J. D., Impey, R. W. and Klein, M. L. 1983, Comparison of simple potential functions for simulating liquid water, *The Journal pf Chemical Physics*, **79(2):** 926-935.

Joshi, D. C., Gosse, C., Huang, S. Y., and Lin, J. H. 2022, A Curvilinear-Path Umbrella Sampling Approach to Characterizing the Interactions Between Rapamycin and Three FKBP12 Variants, *Frontiers in Molecular Biosciences*, **9**: 1–12.

Juli, C., Sippel, M., Jäger, J., Thiele, A., Weiwad, M., Schweimer, K., Rösch, P., Steinert, M., Sotriffer, C.A. and Holzgrabe, U. 2011, Pipecolic acid derivatives as small-molecule inhibitors of the Legionella MIP protein, *Journal of Medicinal Chemistry*, **54(1)**: 277–283.

Kaisani, O.D. 2024, Simulasi dinamika molekul klasik dari kompleks Macrophage Infectivity Potentiator-Rapamycin (PDB-2VCD) dengan ukuran kotak 580 nm^3, *Skripsi*, Sarjana Farmasi, Universitas Katolik Widya Mandala, Surabaya.

Kästner, J. 2011, Umbrella Sampling, *Wiley Interdisciplinary Reviews: Computational Molecular Science*, **1(6)**: 932–942.

Khorida, M. 2024, Pengaruh pemilihan jumlah trayektori hasil simulasi dinamika molekul yang dilanjutkan dengan Umbrella Sampling terhadap perubahan energi bebas pengikatan protein MIP-Rapamycin, *Skripsi*, Sarjana Farmasi, Universitas Katolik Widya Mandala, Surabaya.

Lindorff-Larsen, K., Piana, S., Palmo, K., Maragakis, P., Klepeis, J. L., Dror, R. O. and Shaw, D. E. 2010, Improved side-chain torsion potentials for the Amber ff99SB protein force field, *Proteins,* **78(8)**: 1950–1958.

Liu, Y., Yang, F., Zou, Sili and Qu, Lefeng. 2019, Rapamycin: A bacteria-derived immunosuppressant that has anti-atherosclerotic effects and its clinical application, *Frontiers in Pharmacology*, **9**: 1–15.

Makowski, M. and Bogunia, M. 2020, Influence of ionic strength on hydrophobic interactions in water: Dependence on solute size and shape, *Journal of Physical Chemistry B*, **124(46)**.

Meo, C.T. 2025, Pengaruh pemilihan jumlah trayektori terhadap perubahan energi bebas FKBP12-Rapamycin menggunakan metode Umbrella Sampling dengan kecepatan tarikan 0,005 nm ps^{-1}, *Skripsi*, Sarjana Farmasi, Universitas Katolik Widya Mandala, Surabaya.

Rasch, J., Theuerkorn, M., Ünal, C., Heinsohn, N., Tran, S., Fischer, G., Weiwad, M. and Steinert, M. 2015, Novel cycloheximide derivatives targeting the moonlighting protein Mip exhibit specific antimicrobial activity against Legionella pneumophila, *Frontiers in Bioengineering and Biotechnology*, **3**: 1–8.

Utami, A.S. 2025, Pengaruh pemilihan jumlah trayektori terhadap perubahan energi bebas pengikatan FKBP12-Rapamycin menggunakan metode Umbrella Sampling dengan kecepatan tarikan 0,001 nm ps^{-1}, *Skrispsi*, Sarjana Farmasi, Universitas Katolik Widya Mandala, Surabaya.

Ünal, C.M. and Steinert, M. 2014, Microbial Peptidyl-Prolyl cis / trans Isomerases (PPIases): Virulence Factors and Potential Alternative Drug Targets, *Microbiology and Molecular Biology Reviews*, **78(3)**: 544–571.

Yong, S. 2025, Pengaruh pemilihan jumlah trayektori terhadap perubahan energi bebas pengikatan protein FKBP12-S35D dengan metode Umbrella Sampling, *Skripsi*, Sarjana Farmasi, Universitas Katolik Widya Mandala, Surabaya.

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

Viasus, D., Gaia, V., Manzur-Barbur, C. and Carratalà, J. 2022, Legionnaires' Disease: Update on Diagnosis and Treatment, *Infectious Diseases and Therapy*, **11(3)**: 973–986.

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, *In J Comput Chem*, **25**.

Widjajakusuma, E. C., Frederica, M. and Kaweono, K. 2023, Combined Classical and Flooding Molecular Dynamics Simulations of The Mip-Rapamycin and FKBP12-Rapamycin Complexes, *Jurnal Kimia Sains Dan Aplikasi*, **26(8)**: 300–309.

You, W., Tang, Z. and Chang, C.E.A. 2019. Potential mean force from Umbrella Sampling simulations: what can we learn and what is missed?, *Journal of chemical theory and computation*, **15(4)**: 2433-2443.