

## Cover Letter

Since physicist Dr.Schrödinger published the book ‘What is life?’ in 1944, the proposition ‘what is life?’ has been one of the most important propositions in the field of life science. In other words, ‘Do really exist the systems or the principles which fundamentally control or manage life phenomena?’ I set the proposition 20 years ago. Do really the systems or the principles which totally control or manage replication of DNA, gene expression, translation into amino acids, pathways of protein interactions and pathways of signal transduction exist all together? I finally came up with the idea which the systems fundamentally control or manage life phenomena do not exist, but ‘the principle of fluctuations’ control or manage life phenomena as the result of 20 years thinking. I declare that the phenomena ‘fluctuations’ fundamentally exist on the basis of the systems which control or manage the life. This manuscript proves my idea. Living bodies maintain homeostasis under the steady state, but if once those conditions are damaged by some kinds of stresses, the homeostasis brake and other life phenomena set in motion. Since living bodies are constructed by molecules, living bodies must be accepted the uncertainty principle in the field of physics. Living bodies are not machines. Therefore, I logically proved that ‘fluctuations’ which exist firmly on the

basis of unsteady states, fundamentally control or manage life phenomena in this manuscript. I suppose that life is the states of operation of life phenomena on the basis of 'fluctuations', because the boundary line between living conditions and dead conditions is not able to be defined. The data of gene expression patterns, interactions of proteins, pathways of signal transductions, phenotypes of knock-out mice and so on are publicly opened in such as National Center for Biotechnology information (NCBI) <http://www.ncbi.nlm.nih.gov/>. I think that biology must divide into experimental biology and theoretical biology such as experimental physics and theoretical physics. I have been especially interested in human beings and majored in human molecular biology. That is why I advocate theoretical molecular biology not theoretical biology and I want to contribute to treat human diseases. I thought that it was extraordinary significant to elucidate the principle which control or manage life phenomena to accomplish my aim. I do devote my life to medicine to treat human diseases.