The MATLAB codes here are required to perform the hidden-Markov modeling described in

Yongli Zhang, Junyi Jiao, and Aleksander A. Rebane. 2016. Hidden Markov modeling with detailed balance and its application to single protein folding. *Biophys J.* 111: 2110-2124.

The main programs are hmm\_sim\_grad\_em\_error.m and hmm\_sim\_grad\_skew.m. The former simulates an extension-time trajectory based on a hidden-Markov model with a normal noise distribution, analyzes the trajectory using the hidden-Markov modeling with detailed balance (HMM-DB) and the HMM with the traditional expectation-maximization (HMM-EM), and compares the results obtained from both HMM methods and the model inputs. The latter simulates an extension-time trajectory based on a hidden-Markov model with a skew-normal noise distribution, analyzes the trajectory using HMM-DB, and compares the best-fit parameter values with the model input. Other programs are required by the two programs.

The following codes are directly extracted from the Hidden Markov Model toolbox, which are downloaded from <http://www.cs.ubc.ca/~murphyk/Software/HMM/hmm.html> and distributed under the [MIT License](http://www.opensource.org/licenses/mit-license.php):

em\_converged.m

fwback.m

logdet.m

mc\_sample.m

mhmm\_em.m

mhmm\_logprob.m

mk\_stochastic.m

normalize.m

process\_options.m

sample\_discrete.m

sqdist.m

viterbi\_path.m.

The following codes are modified from the above codes by Dr. Yongli Zhang (YZ):

fwdback\_YZ.m

fwdback\_YZ\_skew.m

mhmm\_sample\_YZ.m

mhmm\_sample\_YZ\_skew.m.

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