



# Granule and mossy cell gene expression study: single cell sequence and alignment monitored by electroencephalography scans with Markov Chain and Bayes Hierarchical Model

**Abstract:** Modern evidence show the importance of the genetics changing the clinical practice in developing new drugs and therapies for epilepsy. Through the study of epilepsy with hippocampus mice clinical data, mossy cells(MC) and granule cells(GCs) especially contributes to the normal memory function in dentate gyrus. Compared to control group, seizure patients suffering memory loss and deficits syndrome can be diagnosed with not only abnormal EEG spikes but also differentially RNA-edited genes detected(KCNQ2, CDKL5, STXBP1, SCN1A, PCDH19 and GRIN1 etc.).

The basic problem of sequencing and alignment can be considered as a mixed linear model, composed by the phenotypic observations  $y$ , associated by incidence matrices  $X$  inverted with  $\beta$ , genetical incidences  $F1$  and  $F2$  inverted by  $d$  and  $s$  respectively, In addition to the field data, the model also consider the inevitable noise which can be simulated with Gaussian white noise[2]. Single cell sequencing with the whole genome transcription factors(TF) is easy to be implemented, regarded as a simple supervised classification problem. Due to the large size of the protein sequences database and TF matrices, Bayes model[1] is chosen for its robustness with high dimension data. In addition, with the inverse matrices, TF being unique, the Bayes estimator is sampled with Gibbs sampler to raise the randomness against the possible redundancy (might lead to overfitting) brought up by such high dimension. Furthermore, it is conducted with hierarchical modeling utilizing maximum a prior(MAP) similar as maximum likelihood(MLE) but adapted in every gradient descending search dynamically.  $X$  here is solved with the inverse of TF. In case of memory out GPU is suggested in computation as well. On contrast, given more genetics, the sequencing of  $X$  can be calculated with next generation(NGs) through Markov Chain[5]sequentially. That is, Hidden Markov Model is combined with the Indel Model in calculating the numerator. In each iteration, the insertion and deletion of the protein can be associated with DNA genomes as well which makes the hidden vector shorter and faster for calculation. The guarantee of convergence of this hierarchical model is realized through configuration in each iteration step. To be more specific, with the DNA genome given, the simulated equilibrium distribution gives the acceptance ratio directly while without the DNA genome, the configuration has to be made considering the neighbors of the protein denoted as  $F1$  matrix. However, if given structural information, the inference criteria can be improved adding diffusive drift rate[3] for randomness of connected atoms with same ancestor (sequence for deletion and insertion) which simulates the prior with the expectation instead of point-wise estimates only( $F2$ ). Lastly, when it comes to clinical data, the chaos is inevitable problem due to the uncertainty raised with both electrical appliances and human operation.

With such sequencing and alignment of GC and MC cells, the epilepsy further analyzed by pseudo time-analysis and other methods with regards to the expression on population scale[4]. As reference, the traditional EEG potential on time and phase domain is calculated as well. Excitation and Inhibition of the cell can be verified with both expression of the protein and spikes/train/bursts of the cell according to EEG on network[6] scale.

**Keyword:** Epilepsy, hippocampus DG, Bayes Hierarchical Model, MCMC, HMM, Indel Model, Diffusive structure

**References:** [1] Qin He.SOURCE LOCALIZATION APPLYING H(DIV) SOURCEMODEL AND HIERARCHICAL BAYES MODEL IN EEG AND MEGCOM- BINING MACHINE LEARNING. Tampere University and TampereUniversity of Applied Science, 2019. [2] CR. Henderson.Best linear unbiased prediction of nonadditive genetic meritsin nonbred populations. J Anim Sci,1985.[3] Nova k Jotun Hein Scott Schmidler Joseph L. Herman, Christo-pher J.Challis.Simultaneous Bayesian Estimation of Alignment and Phy-logeny under a Joint Model of Protein Sequence and Structure. MBE.[4] Sachin Talathi.Deep Recurrent Neural Networks for seizure detection andearly seizure detection systems. Lawrence Livermore National Lab, 2017.[5] Hoti F Sillanpaa MJ Waldmann P, Hallander J.Efficient MCMC implemen-tation of Bayesian analysis of additive and dominance genetic variance inon-inbred pedigrees. Genetics, 2008. [6] Kapucu F, Vornanen I, Mikkonen J, Leone C, Lenk K, Tanskanen J, Hyttinen J. Spectral entropy based neuronal network synchronicity analysis based on microelectrode array measurements. Frontiers in Computational Neuroscience, 2016