EVALUATING THE ASYMPTOTIC LIMITS OF THE DELETE-A-GROUP JACKKNIFE FOR MODEL ANALYSES. Phillip S. Kott, National Agricultural Statistics Service, Department of Agriculture, Fairfax VA 22030 & Steven T. Garren, Department of Mathematics and Statistics, James Madison University, Harrisonburg VA 22807. The delete-a-group jackknife can be e ectively used when estimating the variances of statistics based on a large sample. The theory supporting its use is asymptotic, however. Consequently, analysts have questioned its e ectiveness when estimating parameters for a small domain computed using only a fraction of the large sample at hand. We investigate this issue empirically by focusing on heavily poststrati ed estimators for a population mean and a simple regression coe cient, where the poststrati cation take place at the full-sample level. Samples are chosen using di erentially-weighted Poisson sampling. The bias and stability of delete-a-group jackknife employing either 15 of 30 replicates are evaluated and compared with the behavior of linearization variance estimators.

INFORMATION REDUCTION FOR BIAS AND VARIANCE ESTIMATION. Leonard A. Stefanski, Dept. of Stat., N.C. State Univ., Raleigh, NC 27696-8203. The jackknife and bootstrap are two well-known methods of reducing bias and estimating variance. Simulation-extrapolation is a method of reducing bias and estimating variance in measurement error models that works by adding more error to the observed data. Omitting an observation (jackknife), sampling from the observed data (bootstrap), and adding noise to data (simulation-extrapolation) are all ways of reducing information in a data set. In this talk I show that all three methods are conceptually similar when viewed in terms of information reduction, and argue that doing so is sometimes advantageous.

Structural Biology, Biochemistry and Biophysics

NEUROSTEROID REGULATION OF IONOTROPIC GLUTAMATE RECEPTORS. Sarah Rhoads & Lisa Gentile, University of Richmond. AMPA, NMDA and kainate receptors belong to the ionotropic glutamate receptor (iGluR) family. As binding to glutamate, a major fast excitatory neurotransmitter, causes activation of these channels, they play an important role in synaptic plasticity, memory and learning. Our research focuses on understanding how these receptors are regulated binding for potential applications in conditions such as Alzheimer's and Parkinson's disease. The data presented here is aimed at understanding the differential regulation of NMDA receptors by the endogenous neurosteroids pregnenolone sulfate (PS) and 3α-hydroxy-5β-pregnan-20-one sulfate (PREGAS). PS potentiates the activity of NMDA receptors containing an NR2B subunit while it inhibits those containing an NR2D subunit. PREGAS negatively regulates all iGluRs. Intrinsic and extrinsic fluorescence studies will be presented that confirm the binding of the NMDA NR2B S1S2 and amino terminal domain (ATD) to both PS and PREGAS. Unlike the NR2B subunit, the NR2D S1S2 domain does not bind to PS and PREGAS, however the NR2D ATD does bind to both neurosteroids. Data from isothermal titration calorimetry and Stern-Volmer

analysis will be presented to help differentiate the binding site of each of these neurosteroids on both the NMDA NR2B and NR2D subunits.

CHARACTERIZATION OF RECOMBINANT ASPERGILLUS FUMIGATUS SIDA: A FLAVIN-DEPENDENT N-HYDROXYLASE WITH BOUND FLAVIN COFACTOR. Samuel W. Chocklett & Pablo Sobrado Department of Biochemistry, Virginia Tech, Blacksburg, VA 24060. *Aspergullus fumigatus* (*Af*) SidA, is the flavin-dependent enzyme that catalysis the NADPH-dependent hydroxylation of L-ornithine in ferrichrome biosynthesis. *Af* SidA was recombinantly expressed and purified as a soluble tetramer with a bound FAD cofactor. *Af* SidA is the first member of this class of flavin monooxygenases to be isolated with a tightly bound flavin cofactor. The enzyme showed typical saturation kinetics with respect to L-ornithine, while substrate inhibition was observed at high concentrations of reduced coenzyme. Increasing concentrations of hydrogen peroxide were measured as a function of coenzyme concentration, indicating that inhibition was caused by an increase in uncoupling. *Af* SidA is highly specific for its amino acid substrate, only hydroxylating L-ornithine. In contrast, an 8-fold preference in the catalytic efficiency was determined for NADPH as compared to NADH. In the absence of substrate, *Af* SidA can be reduced by NADPH and a stable C4a-(hydro)peroxyflavin intermediate is observed. The decay of this intermediate is accelerated by L-ornithine binding, and was only stabilized by NADPH and not by NADH, suggesting a role for $NADP^+$ in the stabilization of intermediates in the reaction of *Af* SidA. $NADP^+$ is a competitive inhibitor with respect to NADPH, demonstrating that *Af* SidA forms a ternary complex with $NADP^+$ and L-ornithine for catalysis. These data indicates that *Af* SidA likely proceeds by a sequential kinetic mechanism. Supported in part by the Allan T. Gwathmey Chemistry award from the Virginia Academy of Sciences and Ralph Powe award from ORAU.

ADVANCING THERAPEUTICS FOR ALZHEIMER'S DISEASE WITH MOLECULAR DYNAMICS SIMULATIONS. Justin A. Lemkul & David R. Bevan, Department of Biochemistry, Virginia Polytechnic Institute and State University, Blacksburg, Virginia. Neuronal deposition of the amyloid β-peptide (Aβ) is believed to trigger the symptoms of Alzheimer's disease, the leading cause of senile dementia that afflicts over 5 million Americans. *In vitro* and *in vivo* studies suggest that natural products, such as flavonoids, may be effective in preventing and reversing this protein aggregation, but their mechanism of action is unknown. We conducted molecular dynamics (MD) simulations on a model of the Aβ protofibril in the presence of the flavonoid morin to understand how this compound, one of the most potent anti-aggregation flavonoids, may function in destabilizing pre-formed Aβ aggregates. Our results indicate that morin principally binds to the end of the protofibril, occupying backbone hydrogen bonds that are exposed to solvent and would otherwise be accessible to an incoming peptide. We call this binding mode a "capping network," and we have demonstrated that this configuration effectively blocks the attachment of an incoming peptide. Morin can also penetrate into the hydrophobic core of the protofibril structure, where it associates with the Asp23-Lys28 salt bridges and interferes with backbone hydrogen bonding to destabilize the native structure. The material is based

upon work supported by the Macromolecular Interfaces with Life Sciences (MILES) Integrative Graduate Education and Research Traineeship (IGERT) of the National Science Foundation under Agreement No. DGE-0333378, and by the Institute for Critical Technology and Applied Science (ICTAS) at Virginia Tech.