Dynamics and mechanism of amino acid transport

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Amino acid transport across biological membranes is catalyzed by amino acid transporters from several protein families. In our work, we have focused on transporters from the solute carrier 1 (SLC1) family (alanine serine cysteine transporter 2, ASCT2), and SLC38 family, sodium-coupled neutral amino acid transporter 2, SNAT2. While SNATs transport neutral amino acids, such as glutamine, into cells driven by the transmembrane electrochemical concentration gradient of sodium, ASCTs function as exchangers, taking up neutral amino acid in homo- or hetero-exchange with intracellular amino acid in a sodium-dependent manner. Despite these functional differences, and the proposed different structural folds, the kinetic alternating access mechanisms of transmembrane movement of amino acid show many similarities. For example, Na^+/substrate translocation is electrogenic in both transporters and charge balance appears to be a key mechanism of transport. In addition, both transporters display an uncoupled anion conductance activated by sodium binding. Results from rapid kinetic experiments that reveal the time dependence of the translocation process down to the sub-millisecond time range will be presented, demonstrating dynamic behavior that spans 2 orders of magnitude. The results allow the dissection of individual reaction steps in the transport cycle, explaining voltage-dependent behavior with electrostatic calculations based on structural models.