Support Information for:

Processive Binding Mechanism of Cel9G from *Clostridium cellulovorans*: Molecular Dynamics and Free Energy Landscape Investigations

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Table S1. Some basic terminologies involved in this work.

Terminologies	Definition
Processivity	The ability of the enzyme to continuously reaction without releasing the template/substrate strand.
Processive binding	The process for the substrate to fill the active site of a processive enzyme after one catalytic reaction.
Pucker conformer	The conformation of a sugar ring resulting from the out-of-plane motions of some atoms.
Multimodular enzyme	The enzyme containing multiple functional modules.
CBM3c	Carbohydrate-Binding Module family 3c
GH9	Glycoside Hydrolase family 9

Table S2. Box size and total atom number of each model.

Model	Box Size	Atom Number
Cel9G/G6	$130\ \text{Å} \times 84\ \text{Å} \times 103\ \text{Å}$	93808
Cel9G/G12	$130\ \text{Å} \times 84\ \text{Å} \times 103\ \text{Å}$	93772
Y520A/G12	$89\ \text{Å} \times 87\ \text{Å} \times 137\ \text{Å}$	88442

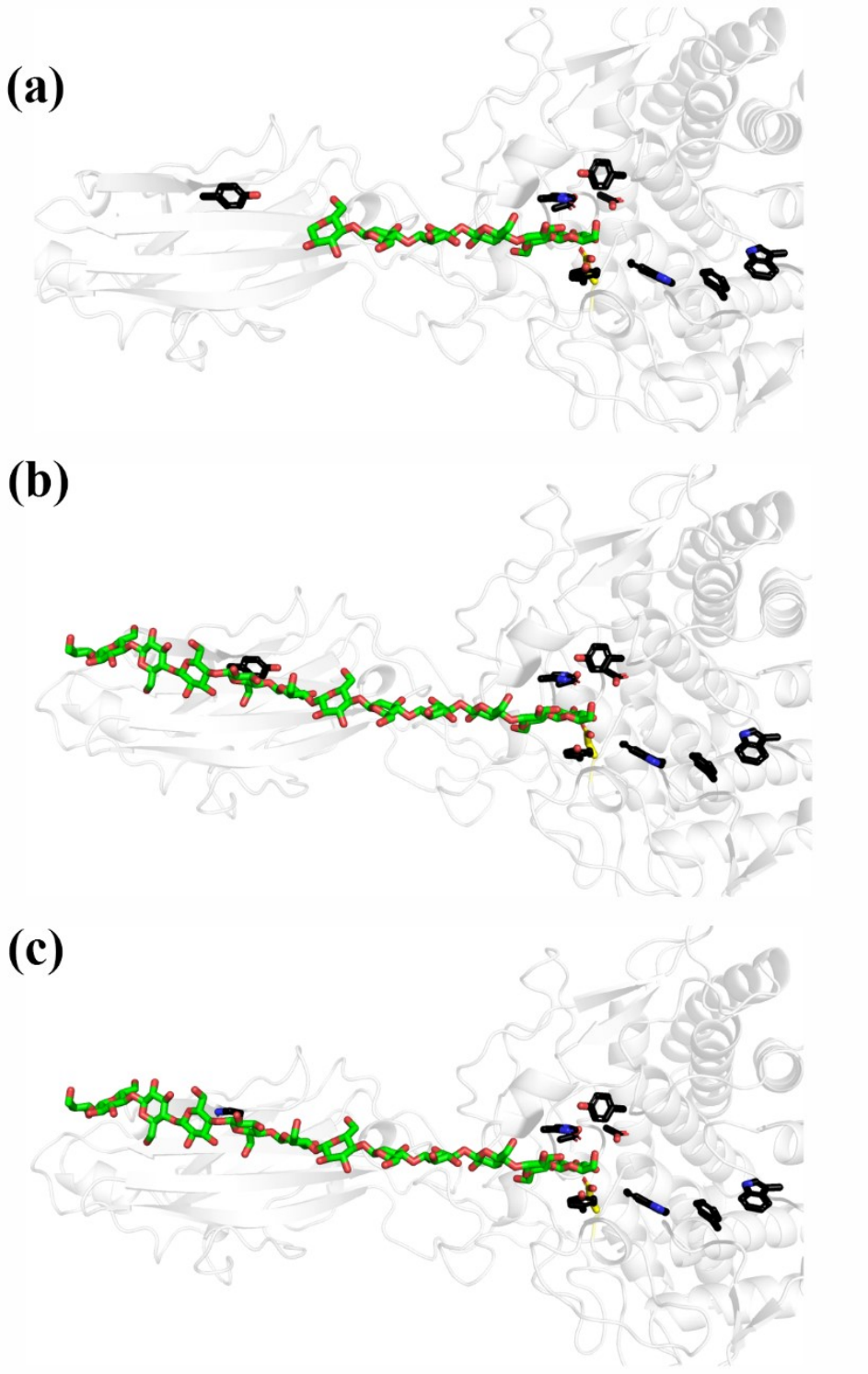

Figure S1. Initial structures for all three systems extracted from Cel9G/G18 model reported in our previous work. (a) Cel9G/G6, (b) Cel9G/G12, (c) Y520A/G12.

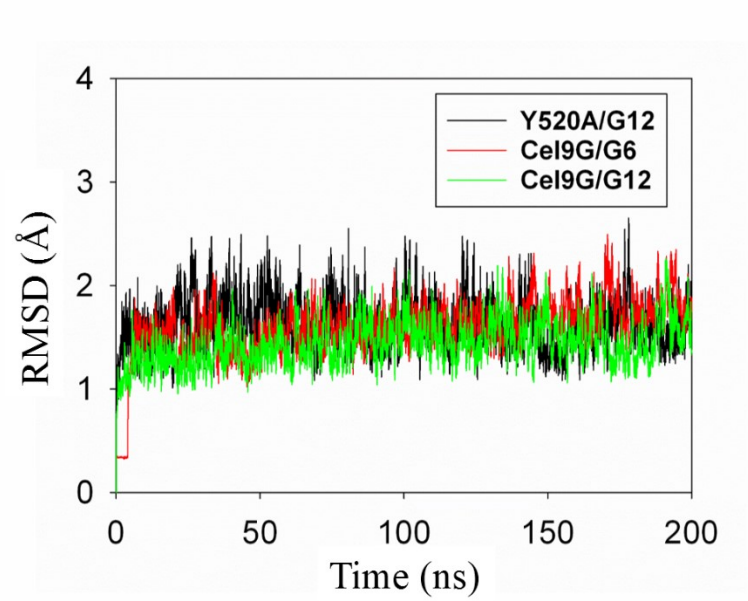

Figure S2. Root-mean-square deviations (RMSD) of backbone atoms compared to the crystal structure (PDB ID: 1KFG) during the 200 ns of classic molecular dynamics of the Pre-Slide mode of each model.

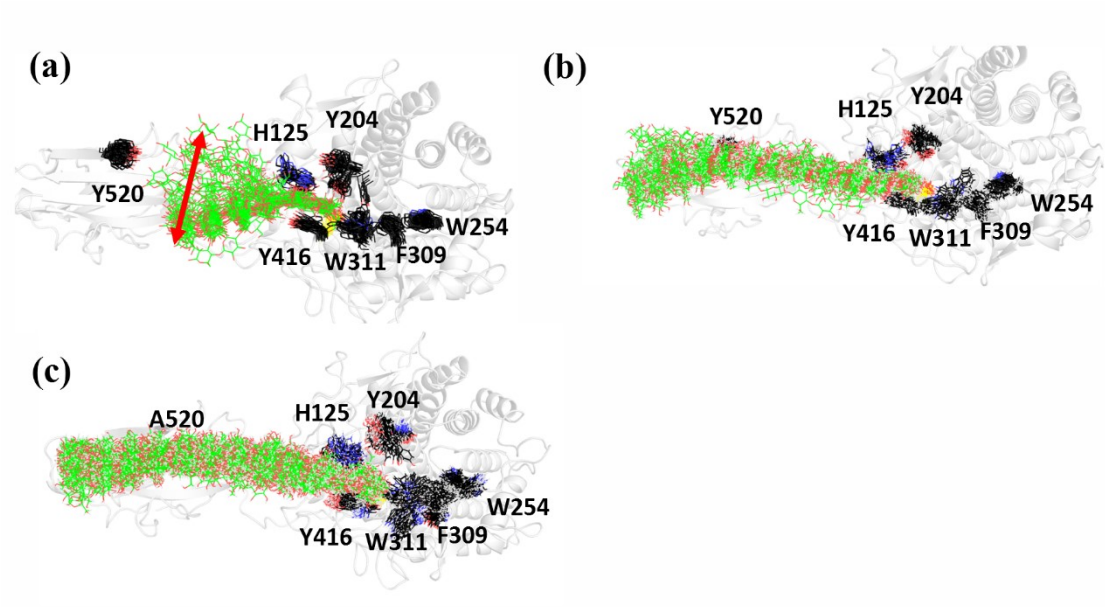

Figure S3. Overlap of 100 snapshots from the 200 ns of classic molecular dynamics of the Pre-Slide modes for each model. The snapshot was saved every 1 ns. The sugar chains were shown in green lines, and the substrate-binding residues were shown in black lines.

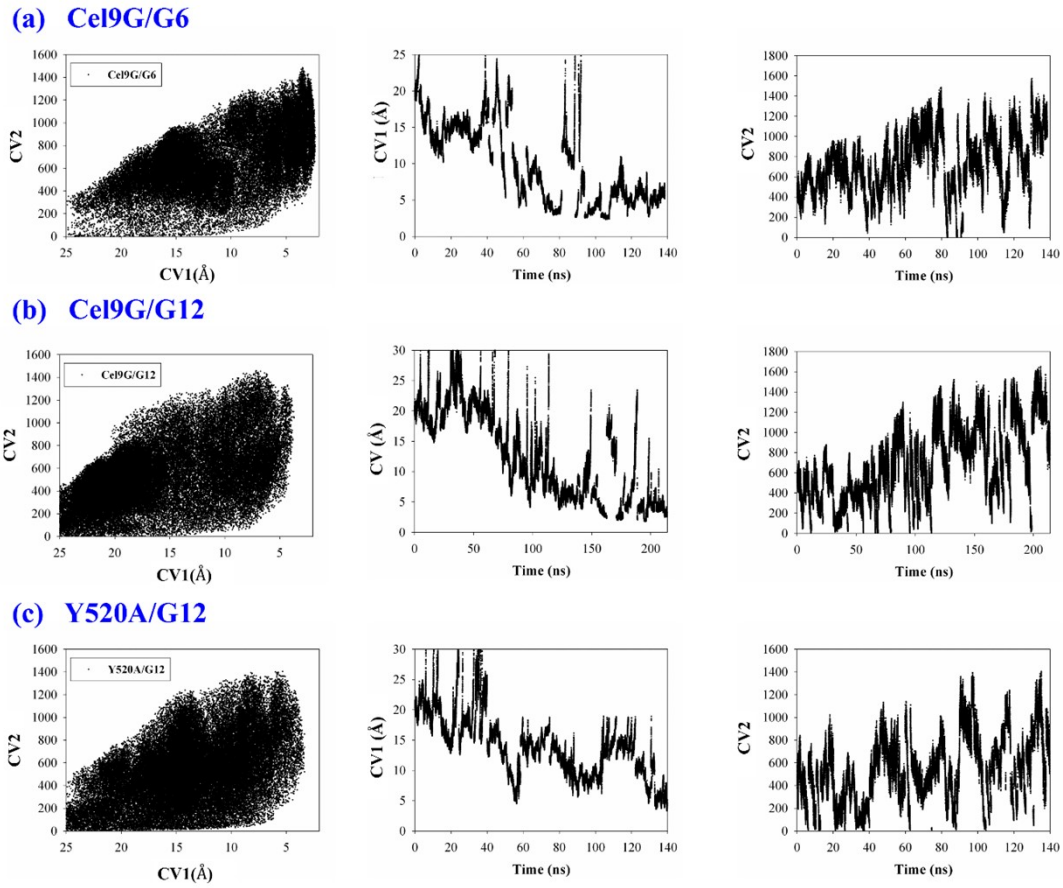

Figure S4. Sampling of the metadynamics (left), time series of CV1 (middle) and CV2 (right).

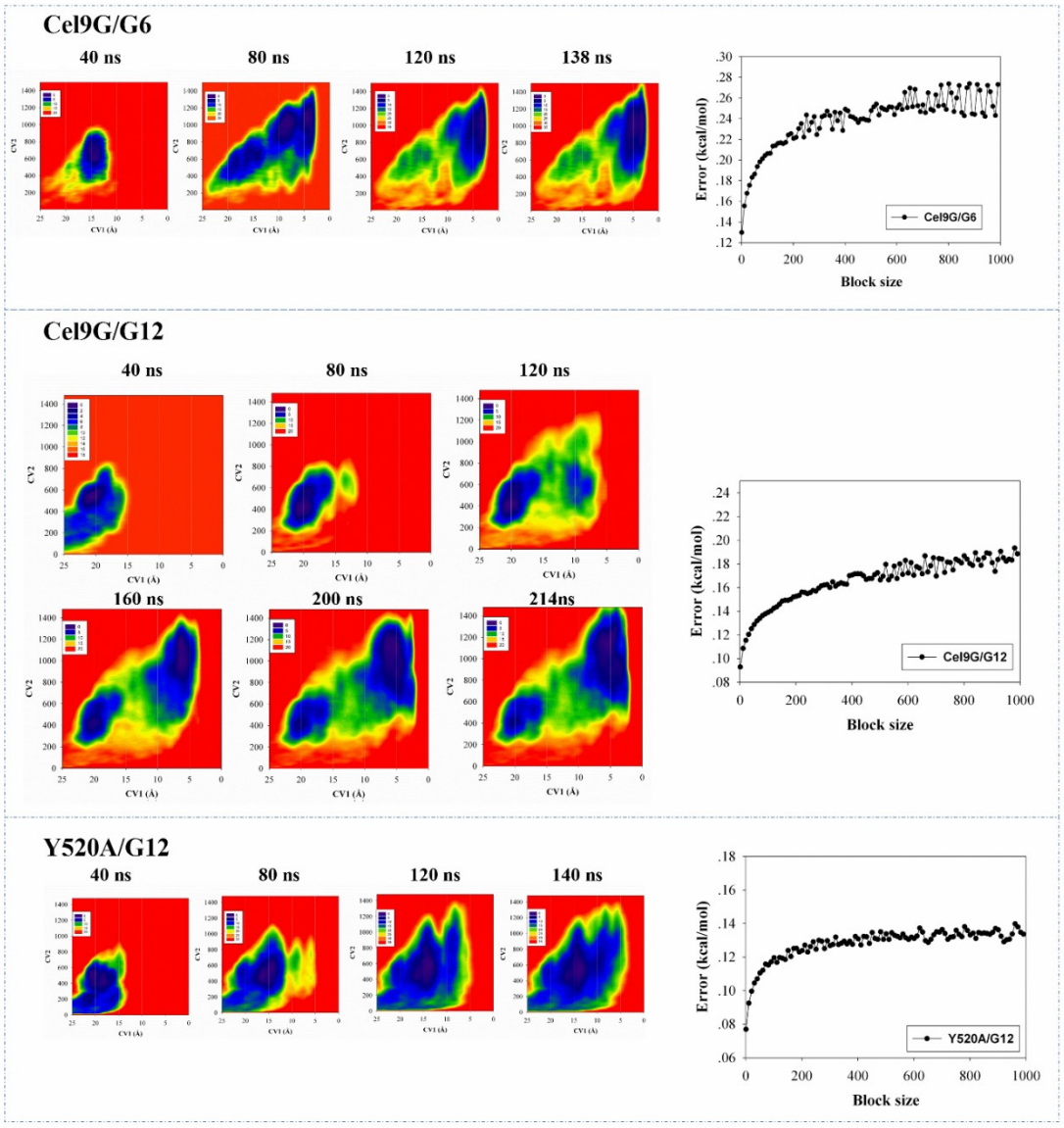

Figure S5. Convergence analyses of the metadynamics simulations, which were characterized by the PMF evolution along the simulation time (left) and the block-analysis (right). The units for energy are in kcal/mol.

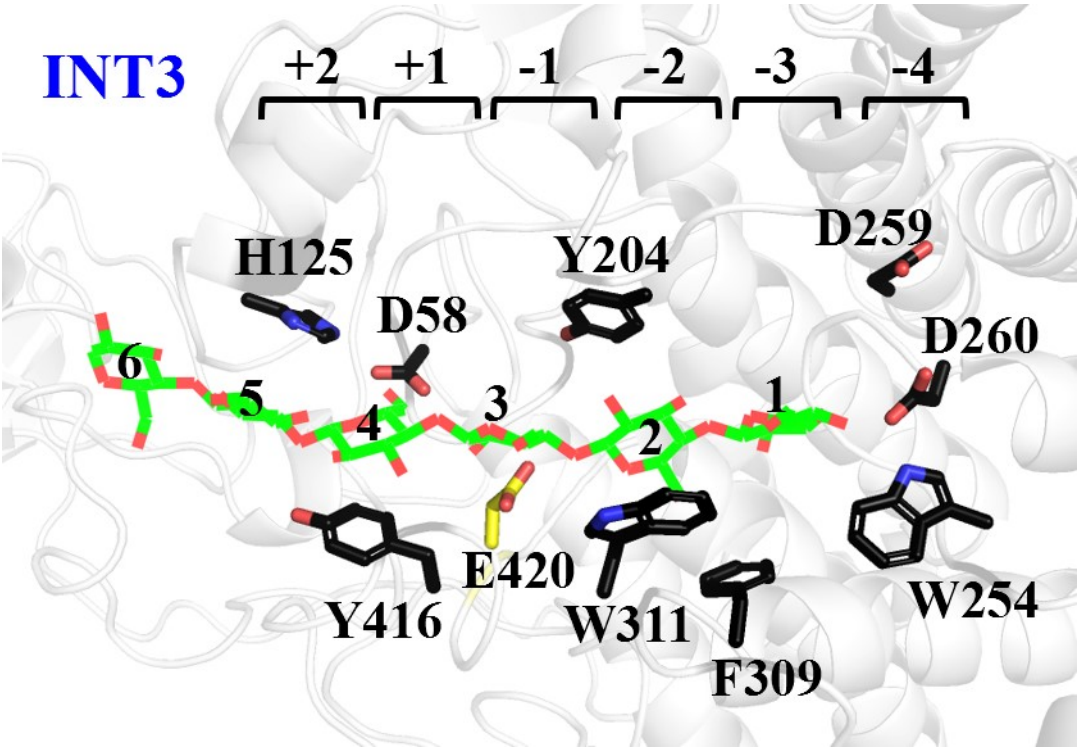

Figure S6. Representative snapshot from metadynamics trajectory of Cel9G/G6 system for third intermediate state (INT3).

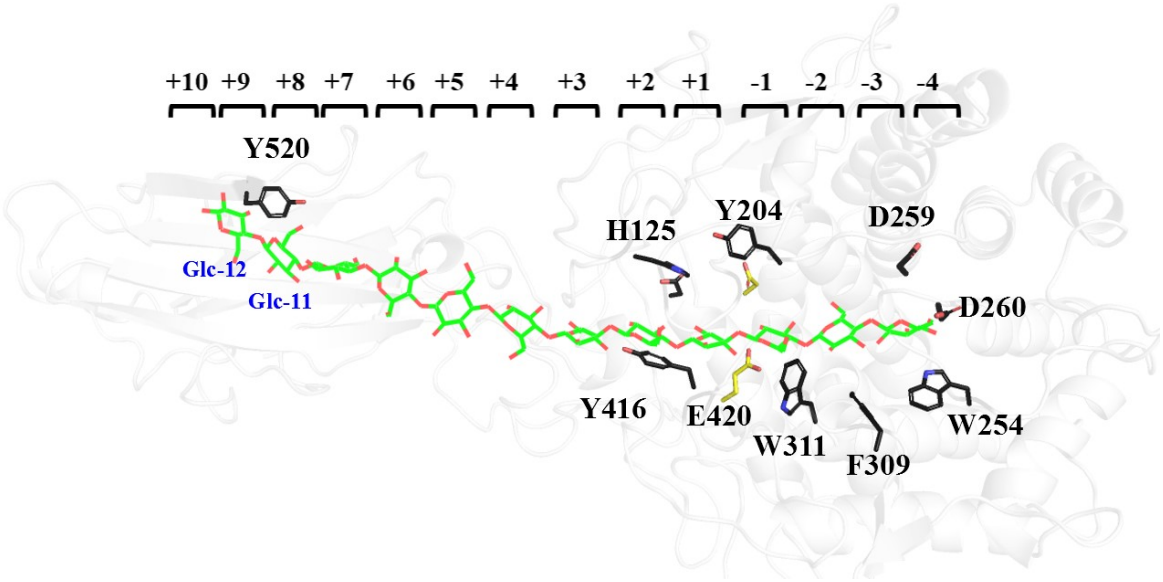

Figure S7. Representative snapshot from metadynamics trajectory of Cel9G/G12 system for slide mode which shows the entire complex structure.

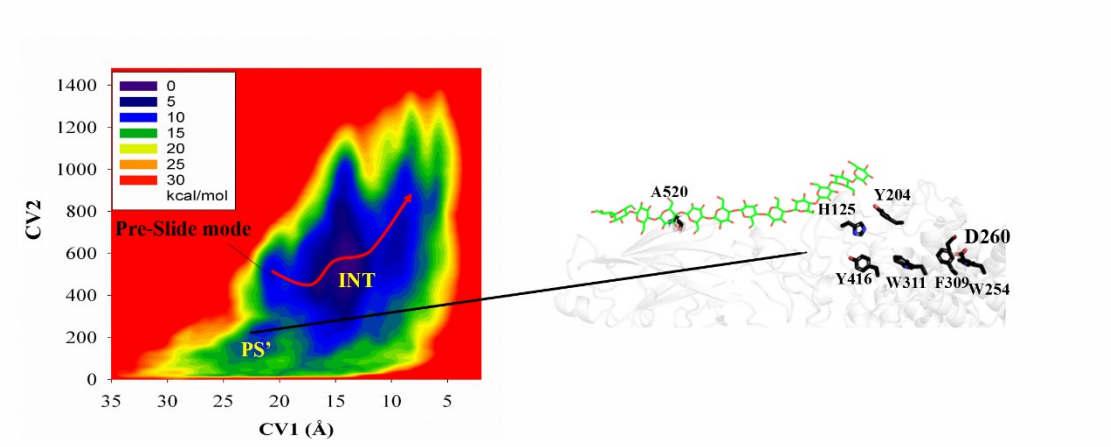

Figure S8. The representative snapshot for PS' state during the metadynamic of Y520A/G12 system.