Table S1: Hydrogen Bonding Interactions Extracted from the MD Simulations

| Molecule Type | Residue i | Residue j | Regions | Occupancy | Comments |
|---|---|---|---|---|---|
| P38, peptide, C-tail | R70 | D328 | αC helix and L16 3/10 helix | 95% | MAPK-specific salt bridge interactions |
| | K66 | D328 | αC helix and L16 3/10 helix | 66% | C-capping interaction of L16 3/10 helix |
| | F99 | K338 | β4- β5 and L16 helix | 12% | β4- β5 Insert interactions |
| | K139 | P318 | αE helix and L16 loop | 11% | |
| | A144 | Y323 | αE helix and L16 loop | 73% | MAPK-specific alanine (see Fig. 2) |
| | S143 | P318 | αE helix and L16 loop | 9% | |
| | K76 | E344 | αC helix and L16 loop | 90% | |
| | R173 | Q325 | A-loop and L16 loop | 19% | |
| P38, no peptide, C-tail | R70 | D328 | αC helix and L16 3/10 helix | 91% | MAPK-specific salt bridge interactions |
| | K66 | D328 | αC helix and L16 3/10 helix | 76% | C-capping interaction of L16 3/10 helix |
| | F99 | K338 | β4- β5 and L16 helix | 12% | β4- β5 Insert interactions |

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|---|---|---|---|---|---|
| | K139 | P318 | αE helix and L16 loop | 10% | |
| | A144 | Y323 | αE helix and L16 loop | 6% | MAPK-specific alanine (see Fig. 2) |
| | S143 | P318 | αE helix and L16 loop | ~0% | |
| | K76 | E344 | αC helix and L16 loop | 92% | |
| | R173 | Q325 | A-loop and L16 loop | ~0% | |
| ERK2, peptide, C-tail | R68 | D334 | αC helix and L16 3/10 helix | 65% | MAPK-specific salt bridge interactions |
| | M96 | K342 | β4- β5 and L16 helix | 22% | β4- β5 Insert interactions |
| | I93 | K342 | β4- β5 and L16 helix | 10% | β4- β5 Insert interactions |
| | K71 | E348 | αC helix and L16 loop | 77% | |
| | A141 | F327 | αE helix and L16 loop | 85% | MAPK-specific alanine (see Fig. 2) |
| | S140 | A323 | αE helix and L16 loop | 79% | |
| | D175 | K328 | A-loop and L16 loop | 40% | |
| | H178 | D335 | A-loop and L16 loop | 21% | |

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| ERK2, no peptide, C-tail | R68 | D330 | αC helix and L16 3/10 helix | 99% | MAPK-specific salt bridge interactions |
| | M96 | K342 | β4- β5 and L16 helix | 18% | β4- β5 Insert interactions |
| | I93 | K342 | β4- β5 and L16 helix | 11% | β4- β5 Insert interactions |
| | K71 | E348 | αC helix and L16 loop | 67% | |
| | A141 | F327 | αE helix and L16 loop | 93% | MAPK-specific alanine (see Fig. 2) |
| | S140 | A323 | αE helix and L16 loop | 7% | |
| | D175 | K328 | A-loop and L16 loop | ~0% | |
| | H178 | D335 | A-loop and L16 loop | ~0% | |