Energy landscapes and heat capacity signatures for monomers and dimers of amyloid forming hexapeptides

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SUPPLEMENTARY INFORMATION

- Table S1 contains the details of sequence numbers for the hexapeptides.
- Tables S2, S3, and S4 contain the details of temperatures at which features are observed in the C_V.
- Figure S1 shows correlation plots between different amyloid predictors.
- Figures S2–S31 show disconnectivity graphs for all the hexapeptides.

UniProt Identifier	Hexapeptide	Sequence
P10997 IAPP HUMAN	NFGAIL	55–60
	GAILSS	57–62
	SSTNVG	61-66
P12969 IAPP RAT	NLGPVL	59–64
P10636 TAU HUMAN	VQIVYK	623–628
P01308 INS HUMAN	LYQLEN	102–107
	YQLENY	103–108
P61769 B2MG HUMAN	LLYYTE	84–89
	YYTEFT	86–91
	EVDLLK	56–61
	LSFSKD	74–79
	NGERIE	62–67
P05067 A4 HUMAN	KLVFFA	687–692
	GAIIGL	700–705
	MVGGVV	706–711
	GGVVIA	708–713
P02649 APOE HUMAN	SSQVTQ	71–76
P04156 PRIO HUMAN	SNQNNF	170–175
P02743 SAMP HUMAN	GYVIIK	213–218

Table S1: Sequence numbers of hexapeptides in their respective proteins as obtained from the UniProt database.

Hexapeptide	Peak/Inflection(*) temperatures			
	Feature 1	Feature 2	Feature 3	Feature 4
NFGAIL	0.076*	0.364*	0.701	-
NAGAIL	0.167*	0.524	-	-
LIAGFN	0.043	0.223*	0.392	0.962
NLGPVL	0.055	0.456	-	-
STVIIE	0.248	0.564	-	-
STVIIP	0.012	0.157	0.390	0.945
SPVIIE	0.030	0.295	-	-
STVVIE	0.101	0.235	0.947	-
VQIVYK	0.089	0.518	0.891	-
VQIVEK	0.011	0.131*	0.269	1.031
NAEVYK	0.047	0.216	0.898	-
LYQLEN	0.079*	0.227	0.385	0.802
YQLENY	0.024	0.281	-	-
LLYYTE	0.041	0.178	0.316	-
YYTEFT	0.017	0.242	0.427*	1.145

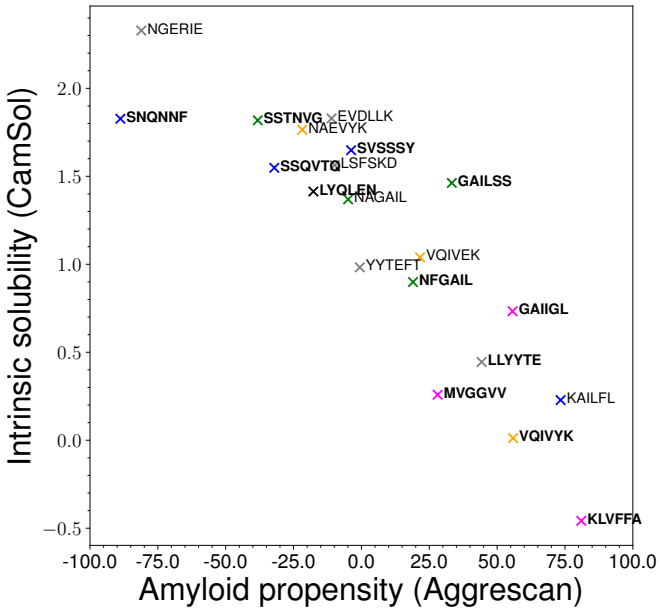
Table S2: Hexapeptides, and $k_{\mathrm{B}}T$ (kcal mol^{-1}) at which peaks or distinct inflection points are observed. The features are labelled as 1, 2, 3, and 4 from low temperature to high temperature. The inflection points are marked with an asterisk (*).

Hexapeptide	Peak/Inflection(*) temperatures			
	Feature 1	Feature 2	Feature 3	Feature 4
GAIIGL	0.219*	0.598	-	-
GGVVIA	0.034	0.377*	0.582	-
MVGGVV	0.037	0.213	0.630	-
GAILSS	0.179	0.310	-	-
SSQVTQ	0.218	0.426	-	-
SSTNVG	0.054	0.241	-	-
SNQNNF	0.016	0.199	0.312	1.011
SVSSSY	0.039	0.240	0.514	-
GYVIIK	0.016	0.437	-	-
KLVFFA	0.150	0.439	-	-
KAFIIQ	0.259	-	-	-
KAILFL	0.112	0.309	-	-
EVDLLK	0.021	0.204*	0.417	-
LSFSKD	0.011	0.101*	0.368	0.860
NGERIE	0.155	0.404	-	-

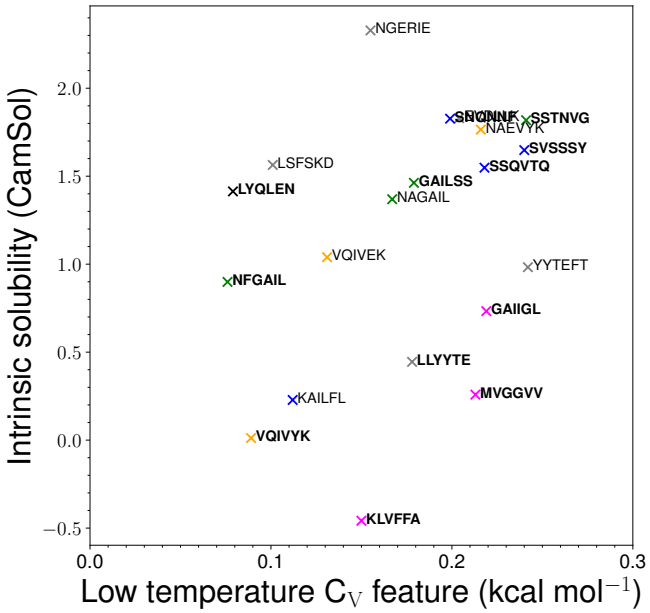
Table S3: Hexapeptides, and $k_{\mathrm{B}}T$ (kcal mol^{-1}) at which peaks or distinct inflection points are observed. The features are labelled as 1, 2, 3, and 4 from low temperature to high temperature. The inflection points are marked with an asterisk (*).

Hexapeptide	Peak/Inflection(*) temperatures			
	Feature 1	Feature 2	Feature 3	Feature 4
NFGAIL	0.060	0.432*	0.859	-
NAGAIL	0.016	0.107	1.148	-
LIAGFN	0.167	0.294*	1.080	-
NLGPVL	0.100	0.458^{i}	1.095	-
STVIIE	0.122	0.540	1.096^{i}	-
STVIIP	0.036	0.547	1.051	-
SPVIIE	0.023	0.229	0.400	-
STVVIE	0.043	0.354	0.667	-
VQIVYK	0.081*	0.268	1.123	-
VQIVEK	0.061	0.420	0.891	-
NAEVYK	0.107	0.718	-	-
LYQLEN	0.042	0.173*	0.600	0.888
YQLENY	0.271*	0.408	-	-
LLYYTE	0.021^{i}	0.281	0.902	-
YYTEFT	0.057	0.215	0.418	1.156^{i}

Table S4: Dimers of hexapeptides, and $k_{\mathrm{B}}T$ (kcal mol^{-1}) at which peaks or distinct inflection points are observed. The features are labelled as 1, 2, 3, and 4 from low temperature to high temperature. The inflection points are marked with an asterisk (*) and very small peaks are marked with 'i' (^{i}).



(a) Correlation plot between amyloid predictor Aggrescan and intrinsic solubility predictor CamSol.



(b) Correlation plot between low temperature heat capacity feature and intrinsic solubility as predicted using CamSol.

Figure S1: Correlation plots between different amyloid predictors.

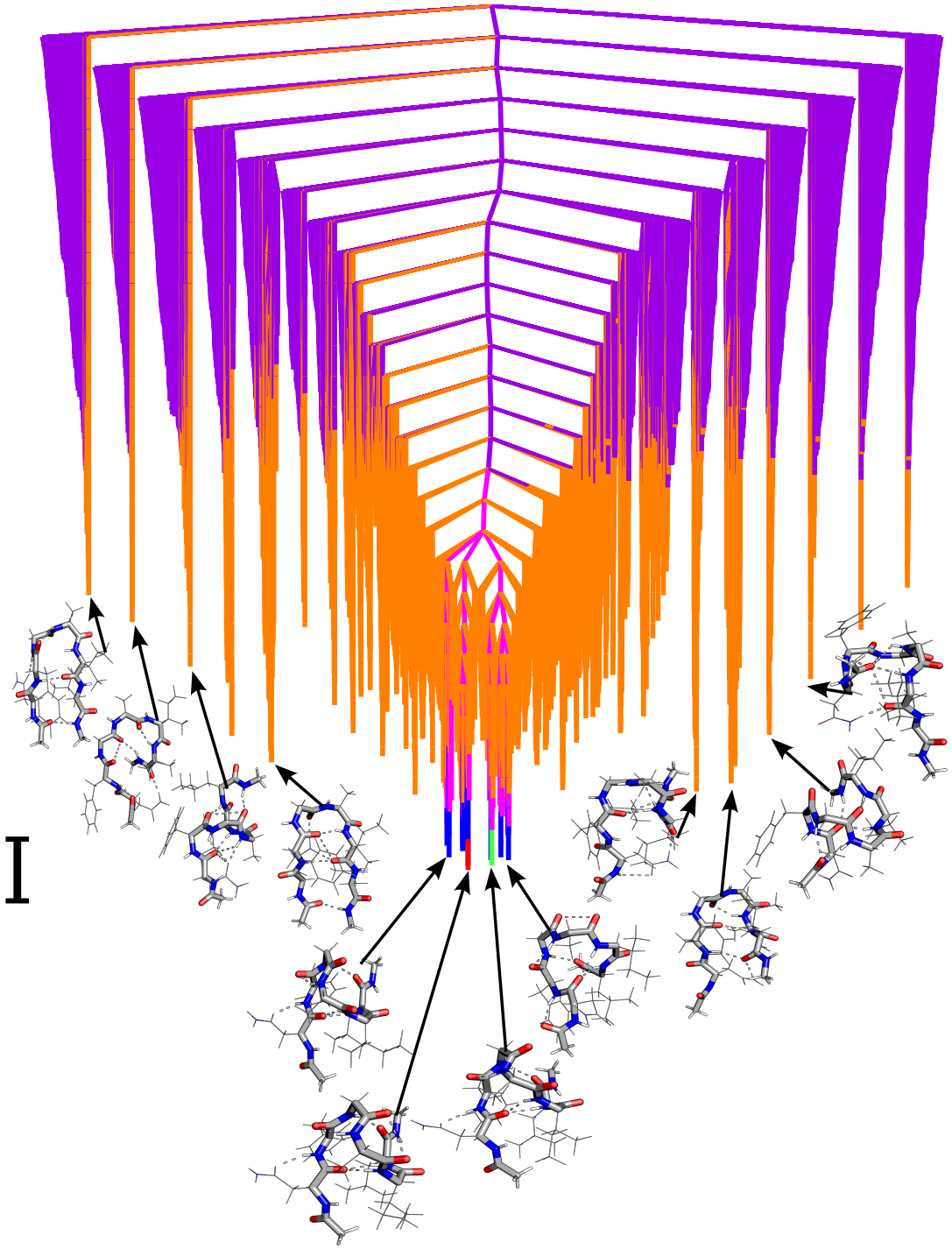


Figure S2: Disconnectivity graphs for **NFGAIL** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

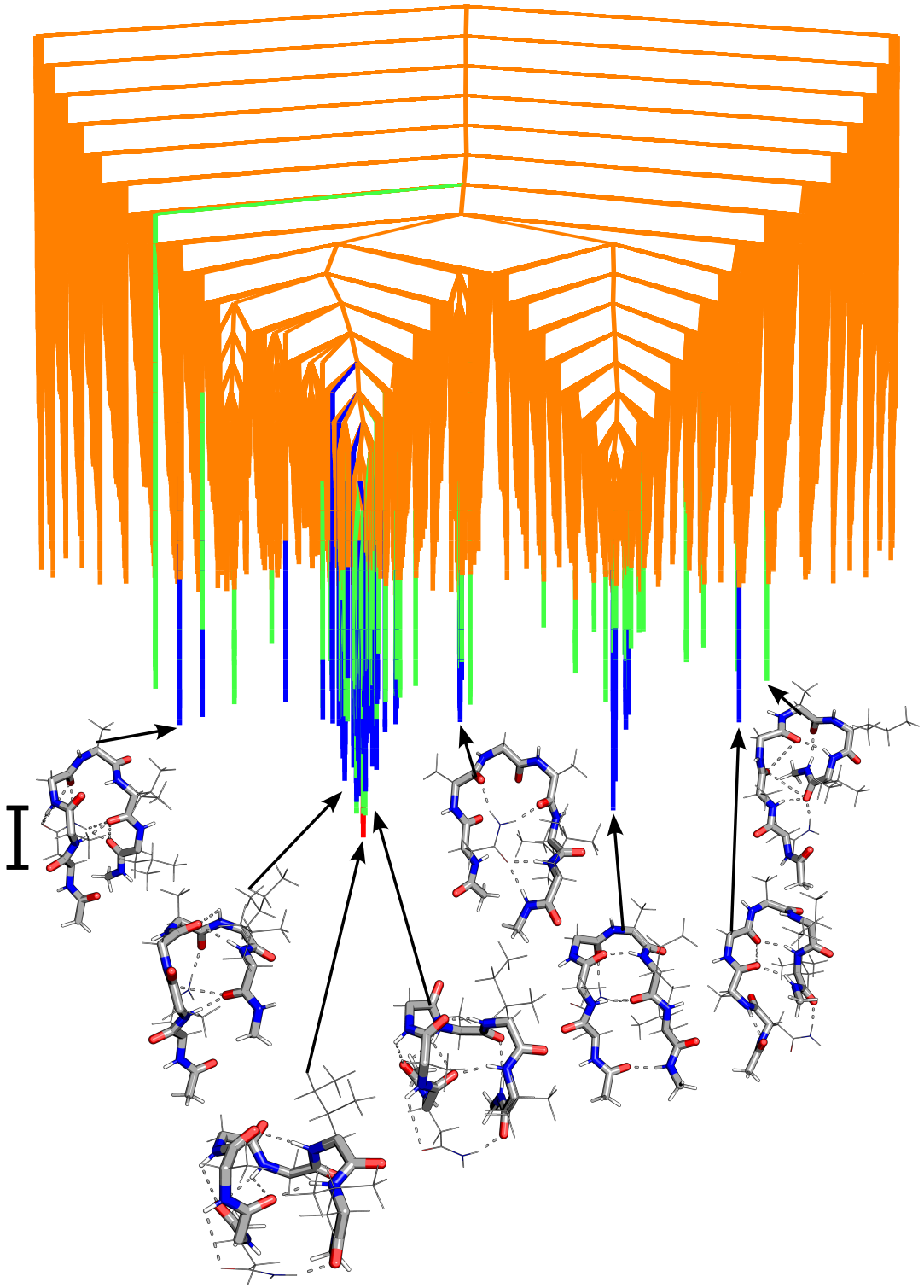


Figure S3: Disconnectivity graphs for NAGAIL monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

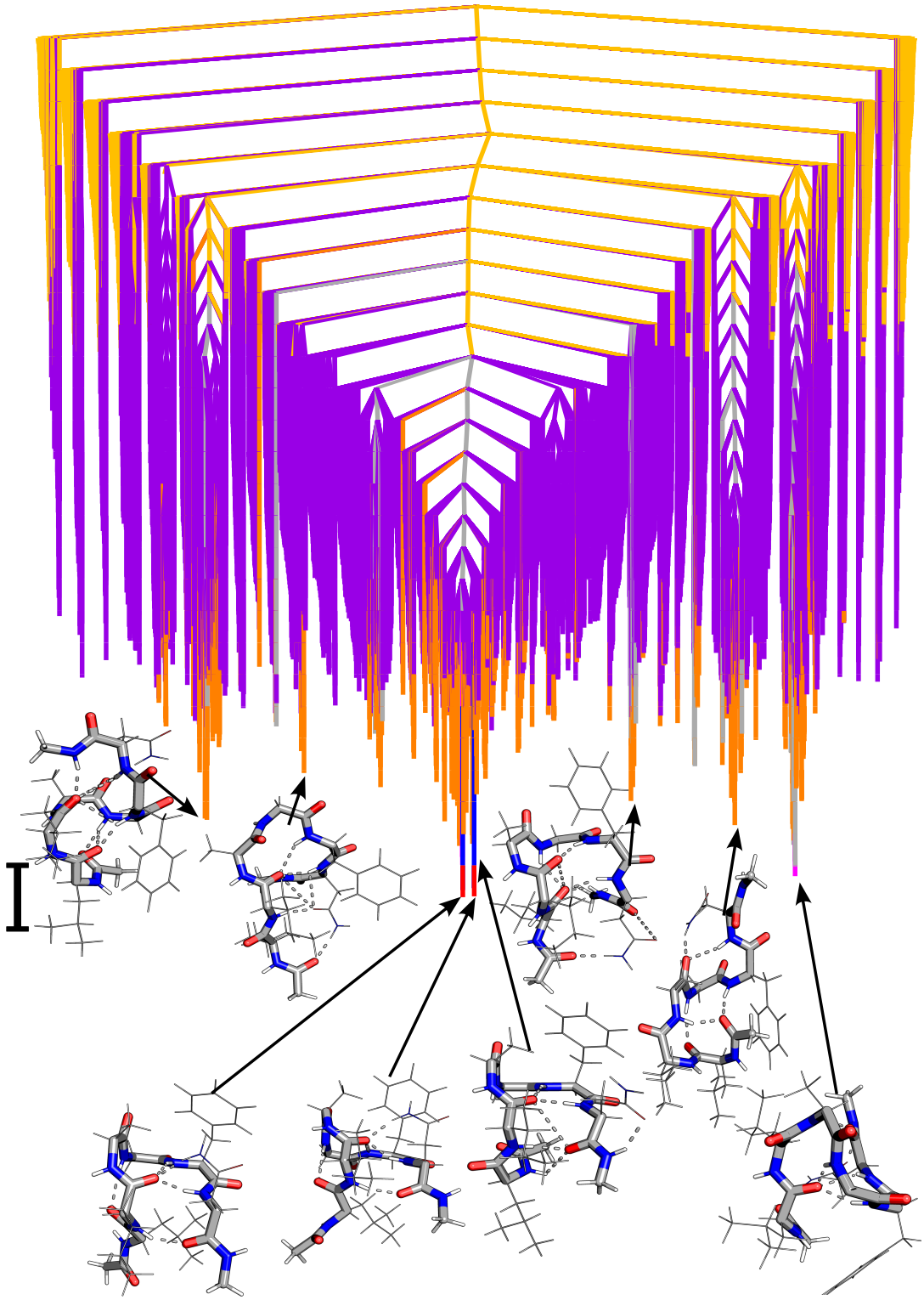


Figure S4: Disconnectivity graphs for LIAGFN monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

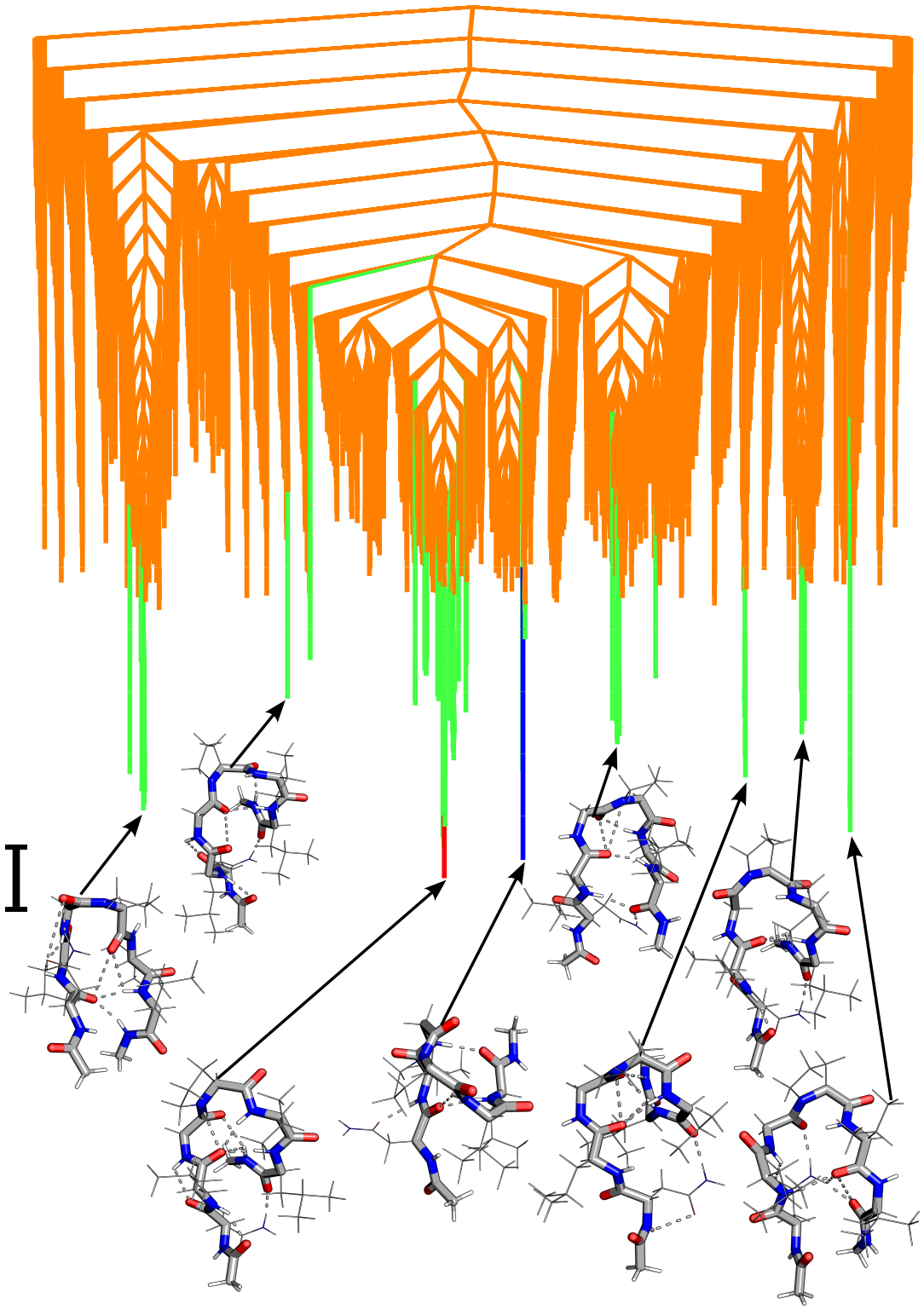


Figure S5: Disconnectivity graphs for NLGPVL monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

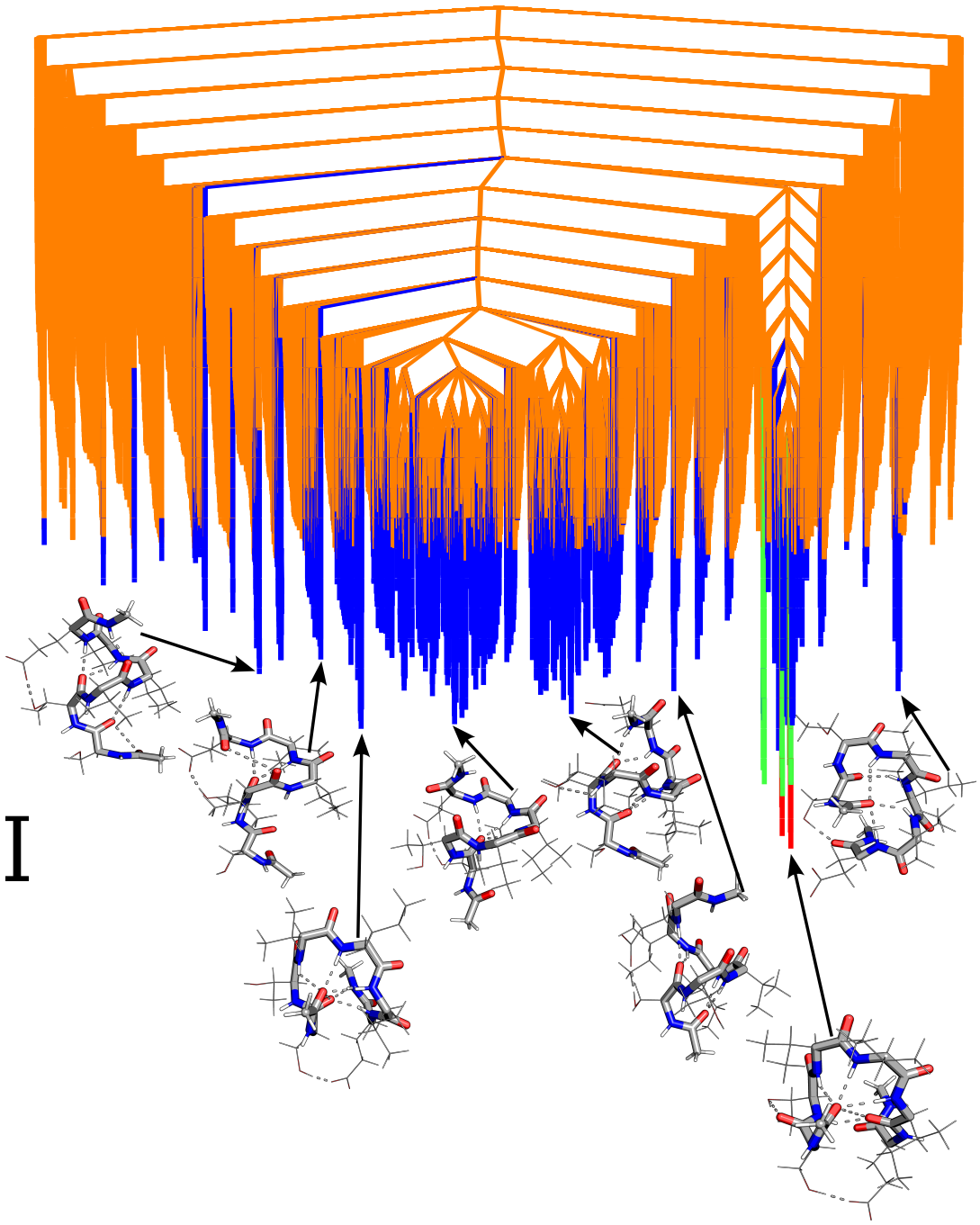


Figure S6: Disconnectivity graphs for **STVIIE** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

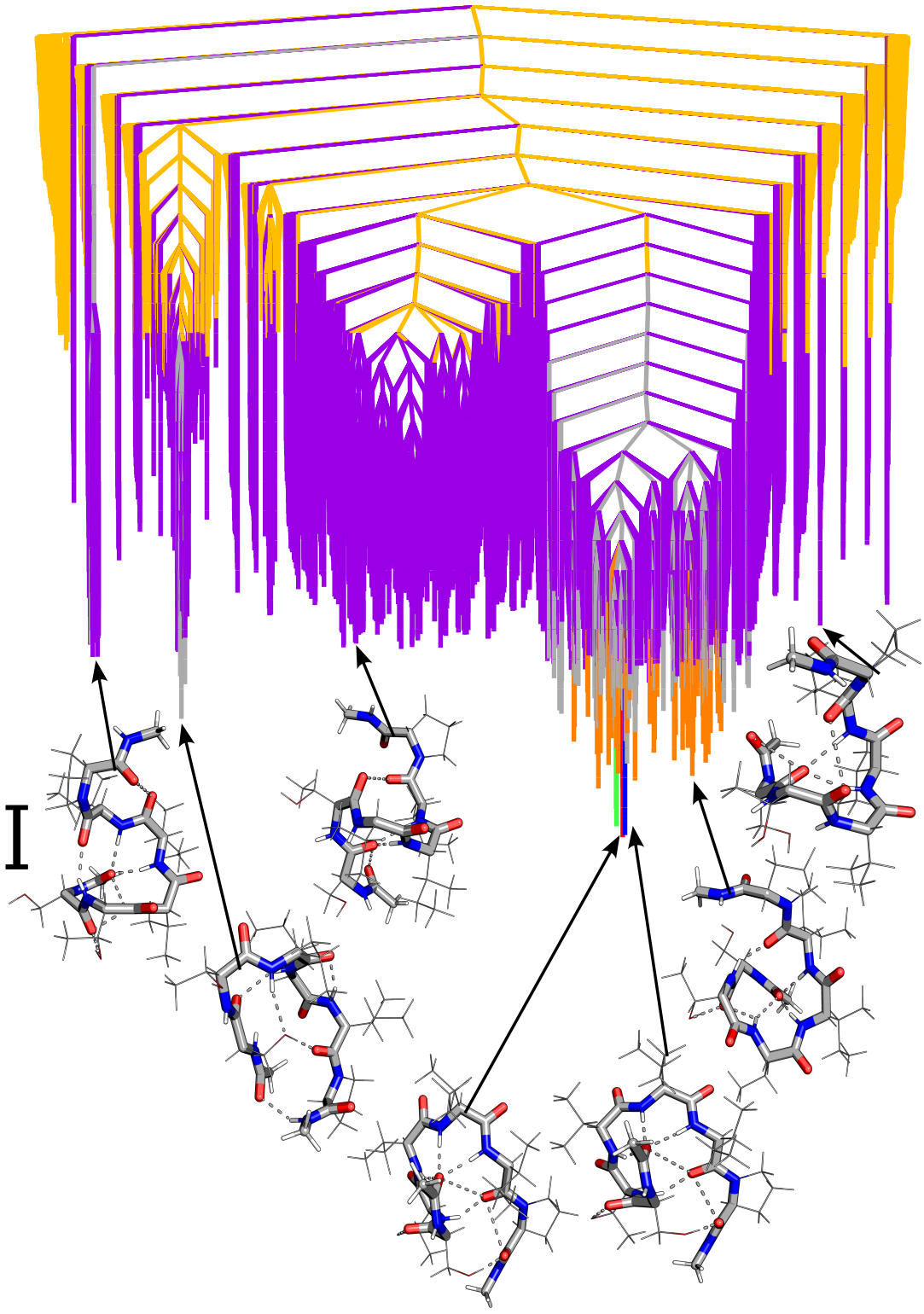


Figure S7: Disconnectivity graphs for STVIIP monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

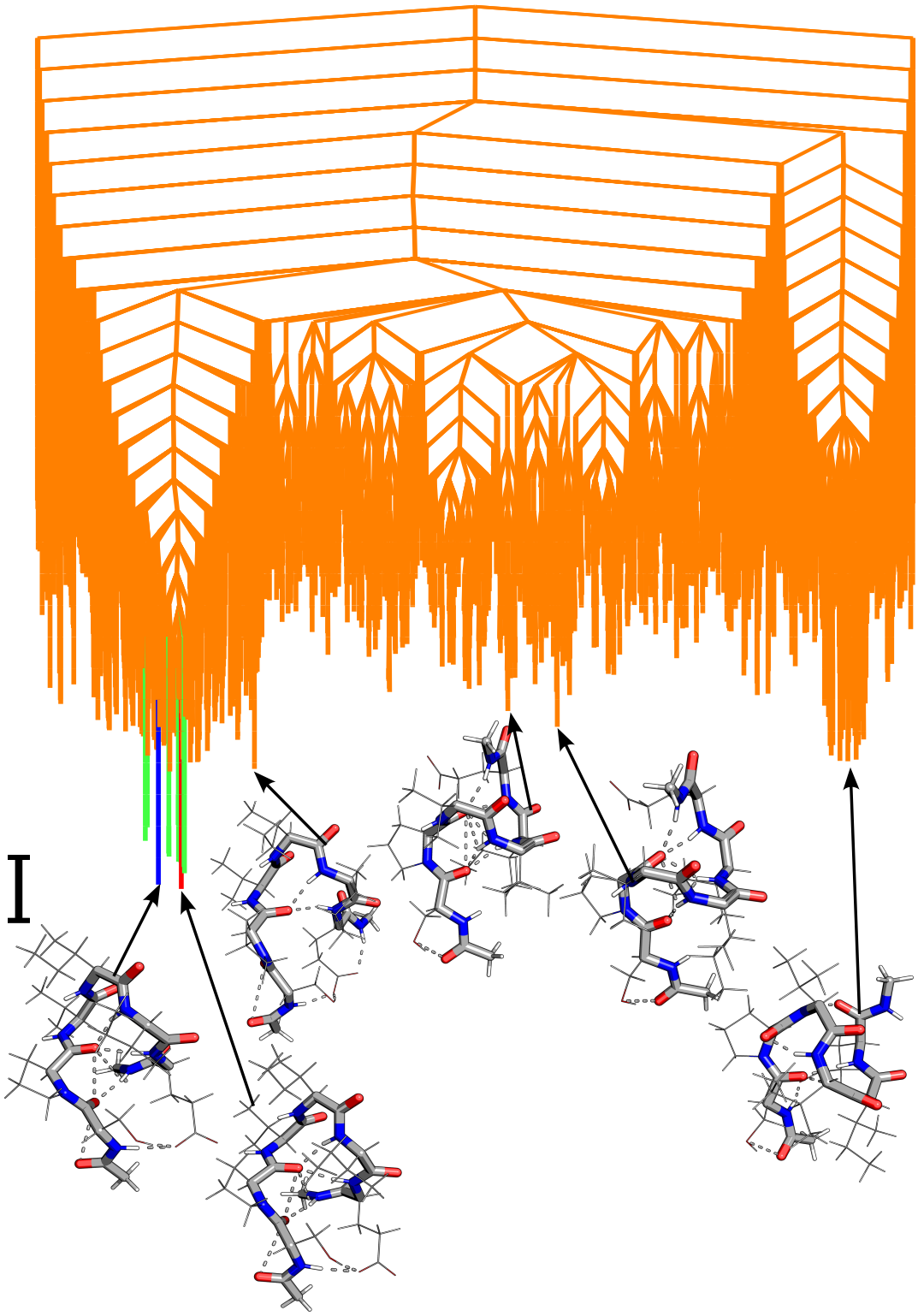


Figure S8: Disconnectivity graphs for SPVIIE monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

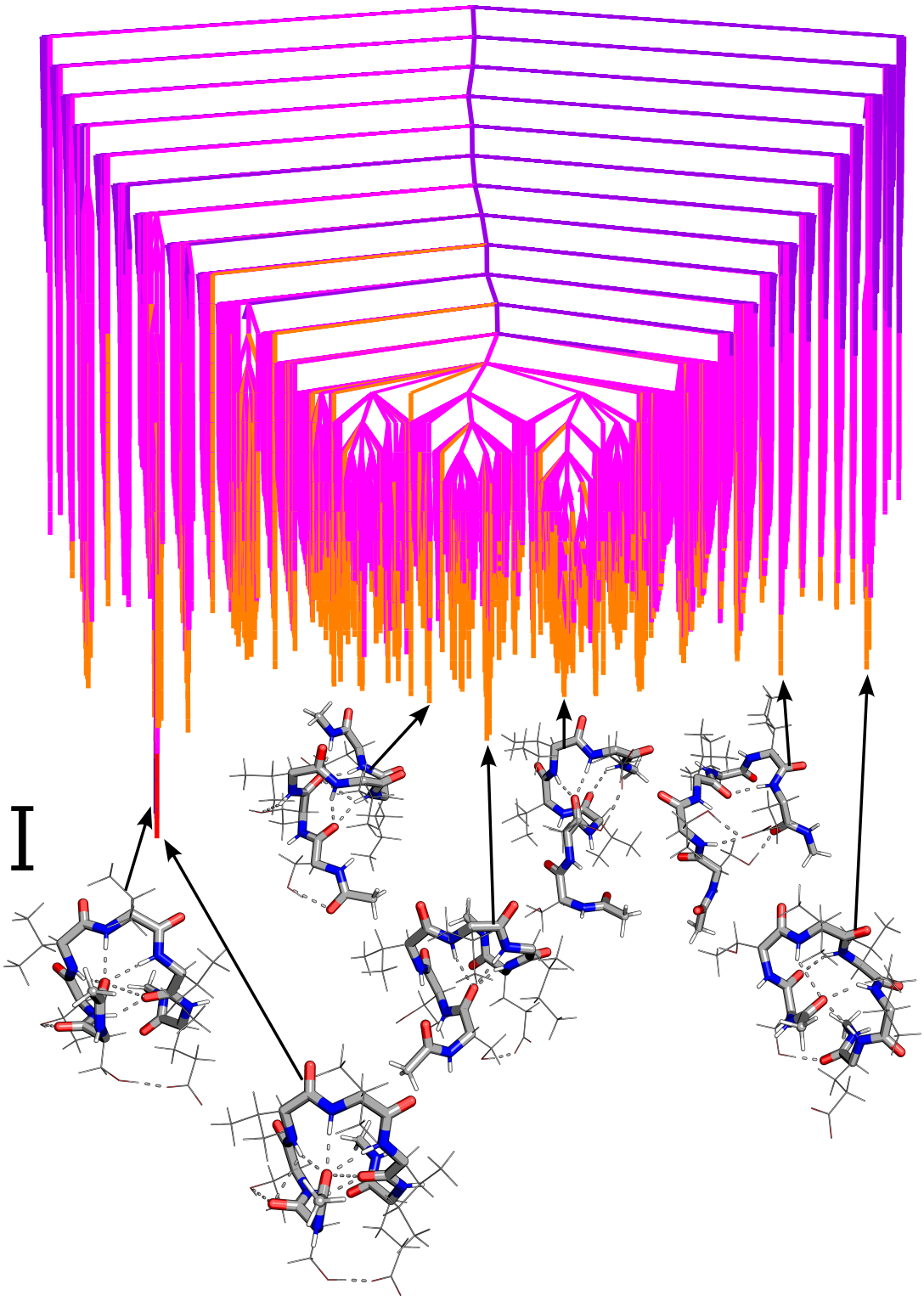


Figure S9: Disconnectivity graphs for STVVIE monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

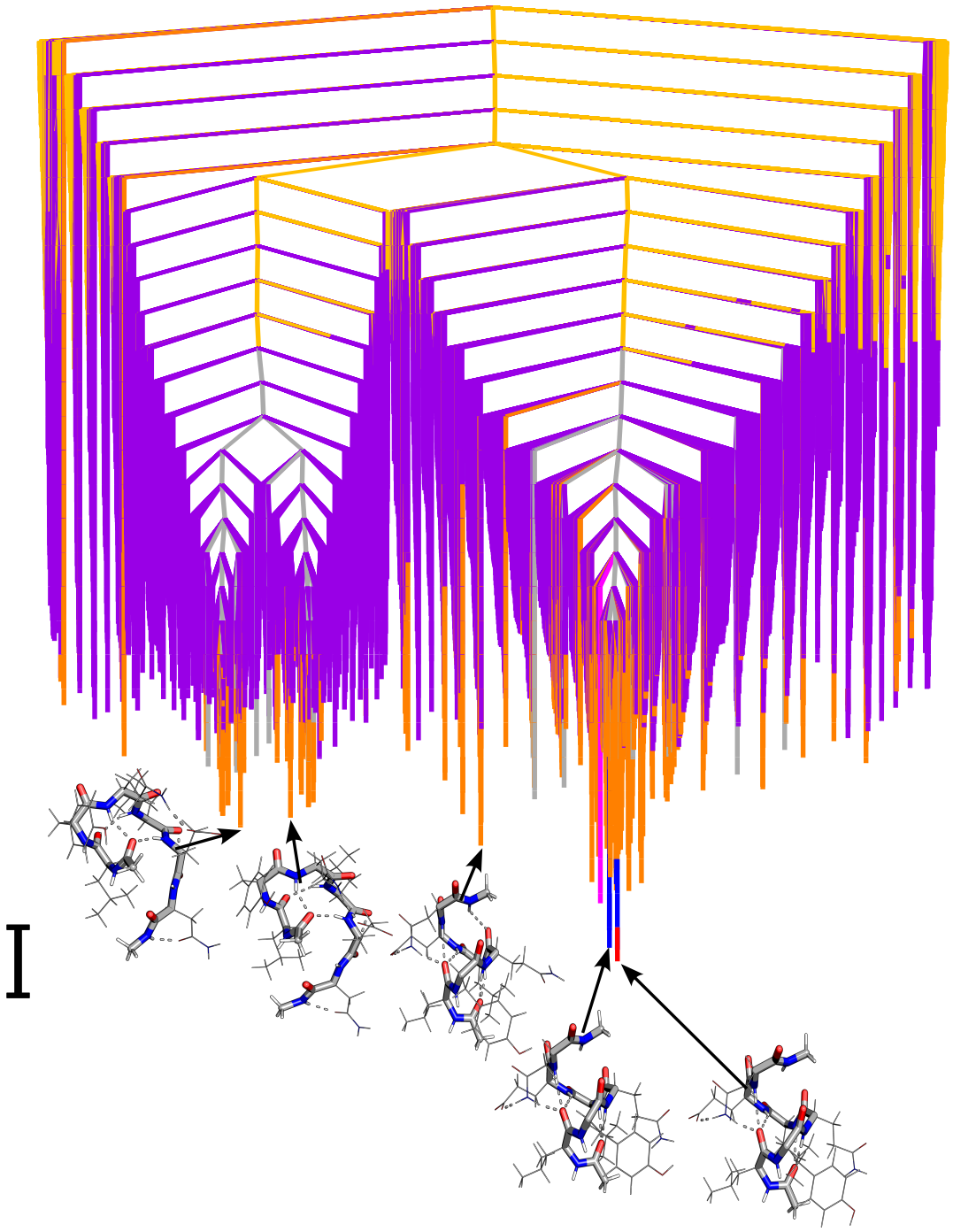


Figure S10: Disconnectivity graphs for **LYQLEN** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

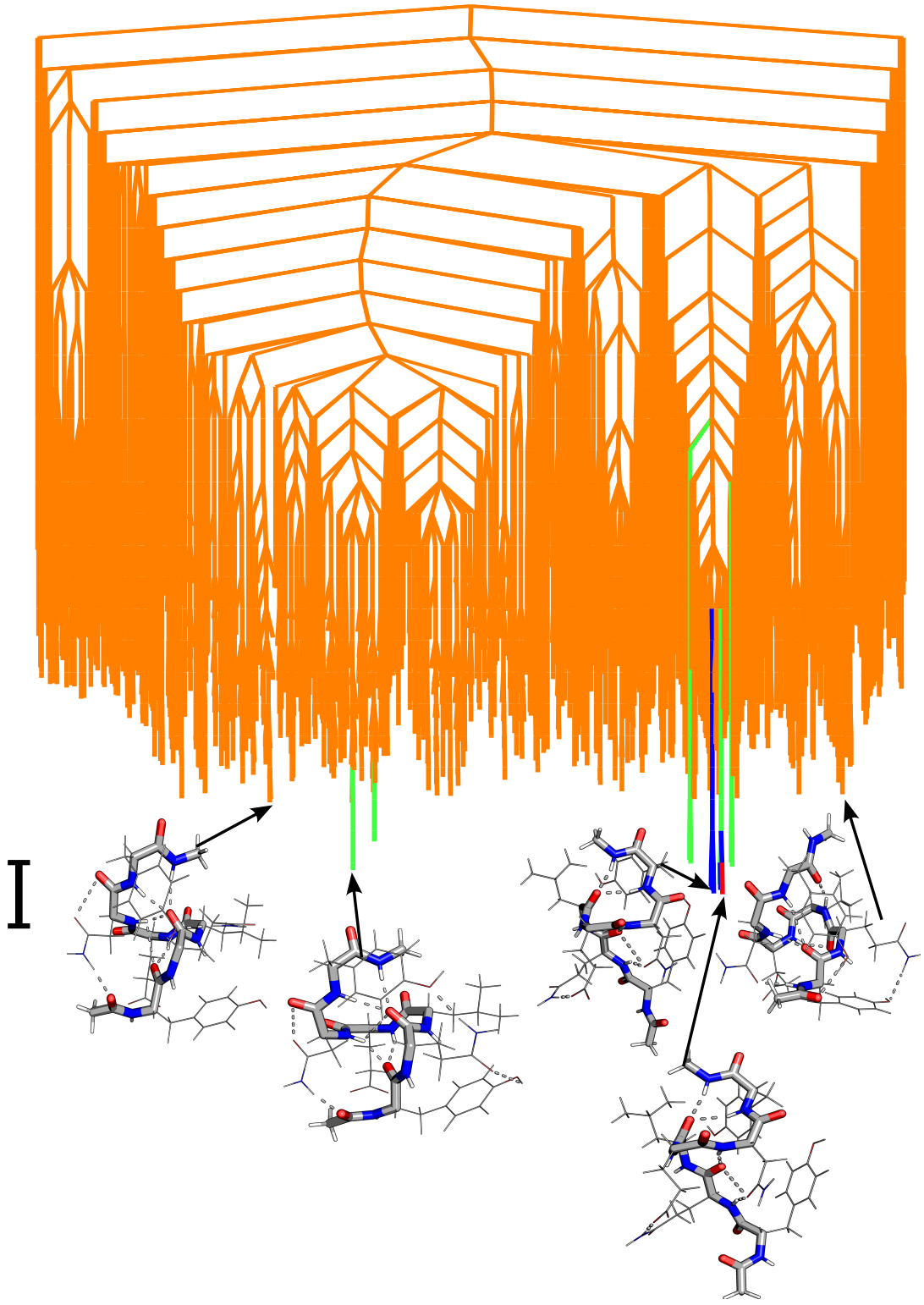


Figure S11: Disconnectivity graphs for YQLENY monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

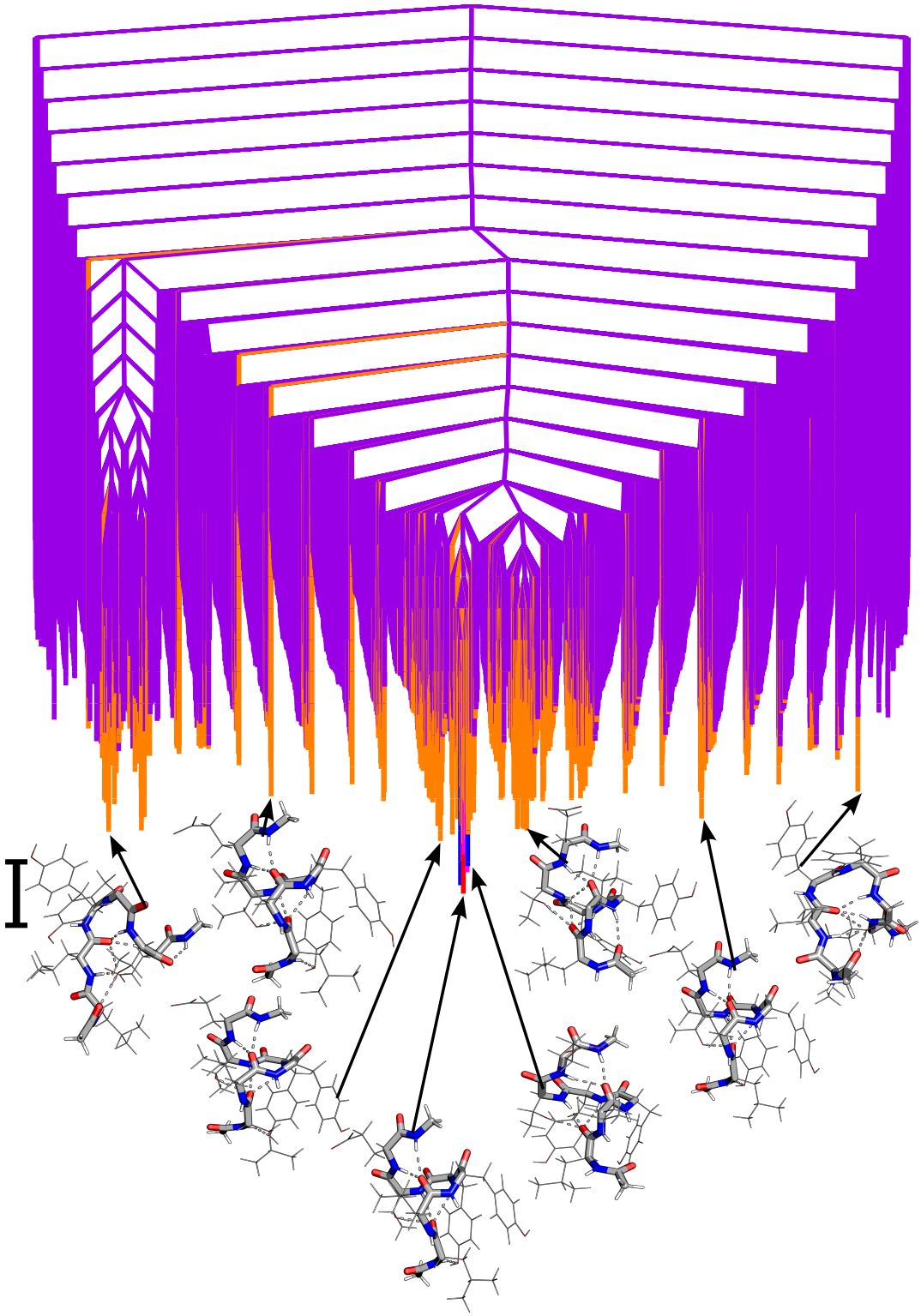


Figure S12: Disconnectivity graphs for **LLYYTE** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

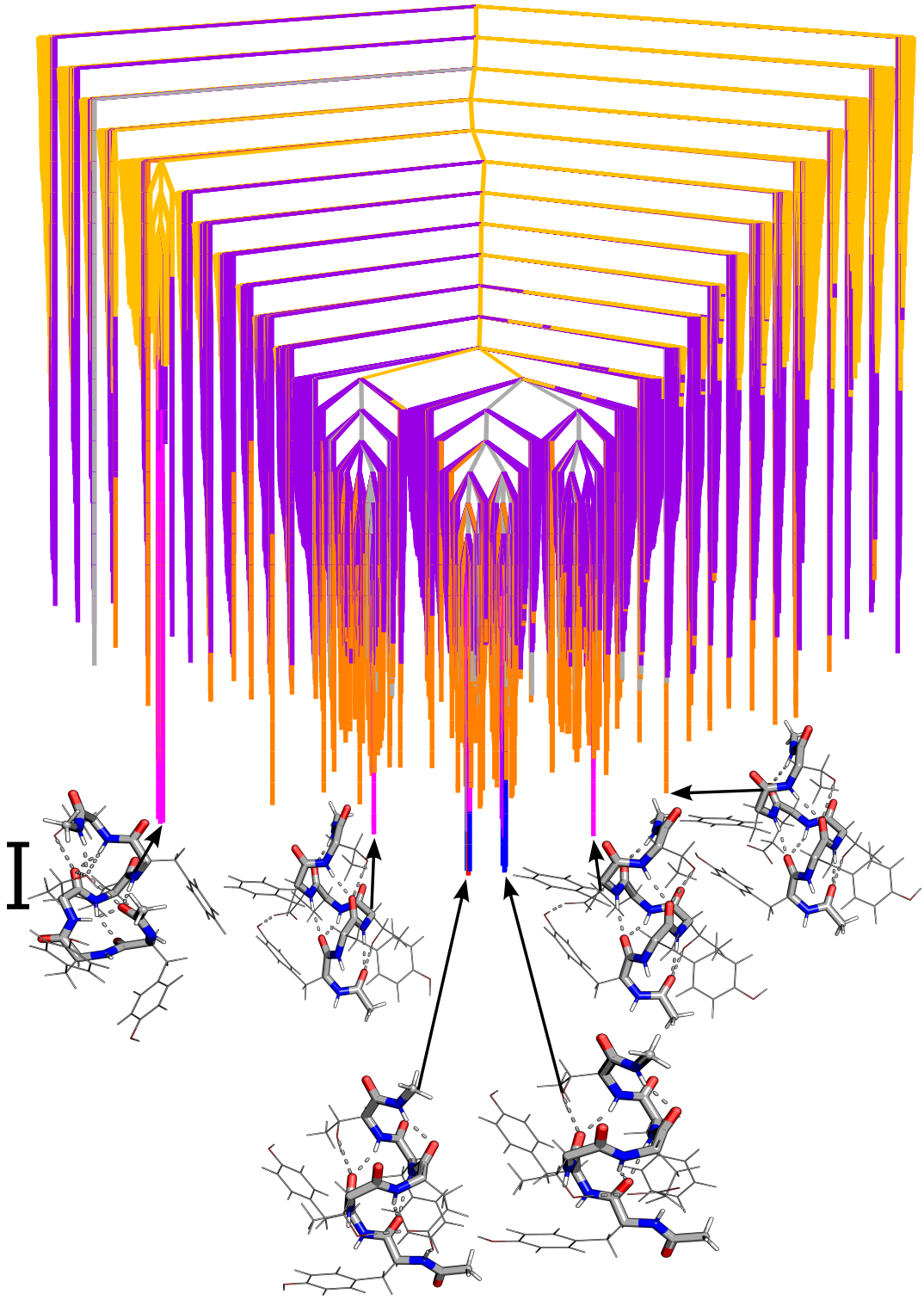


Figure S13: Disconnectivity graphs for YYTEFT monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

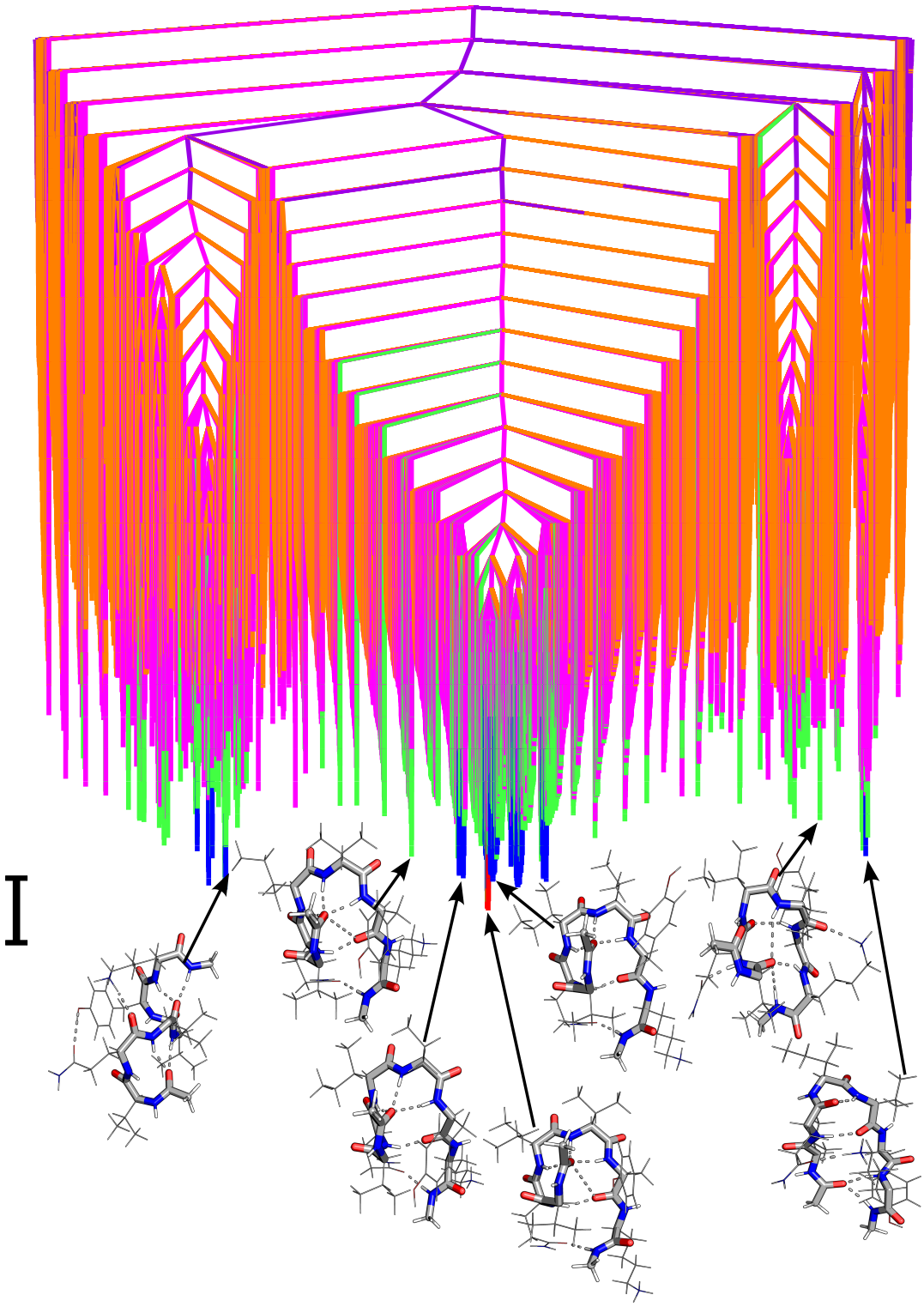


Figure S14: Disconnectivity graphs for **VQIVYK** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

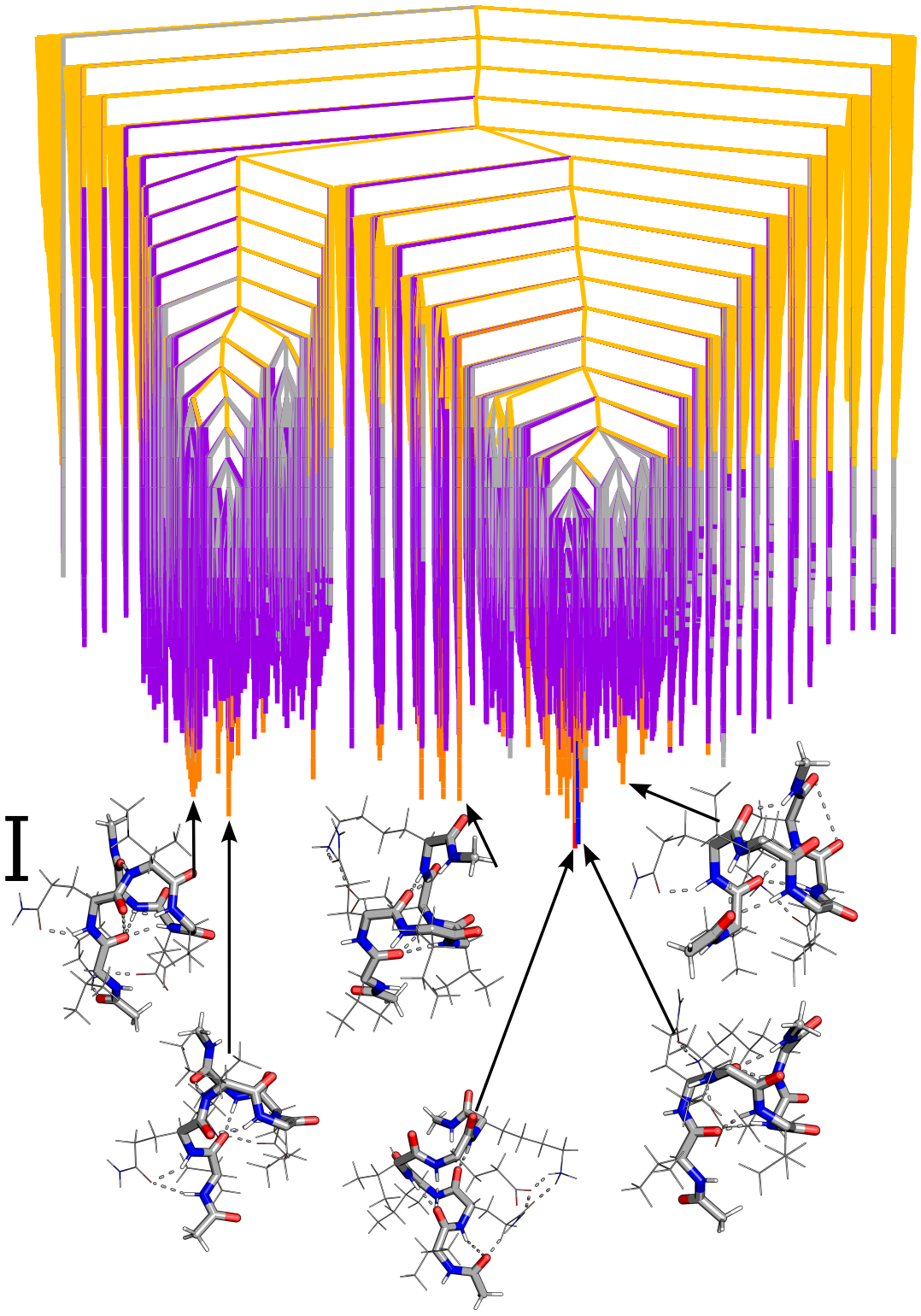


Figure S15: Disconnectivity graphs for VQIVEK monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

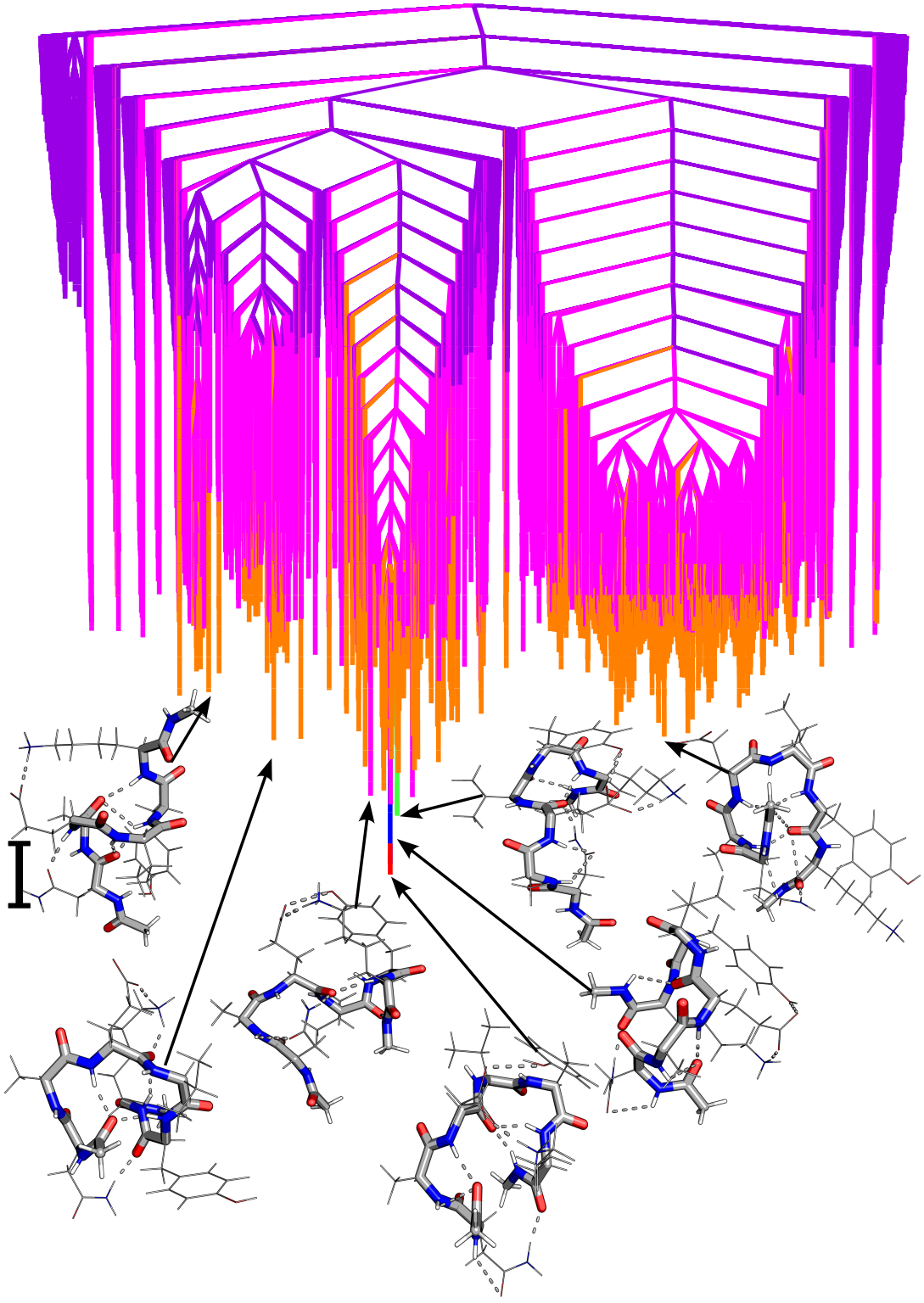


Figure S16: Disconnectivity graphs for NAEVYK monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

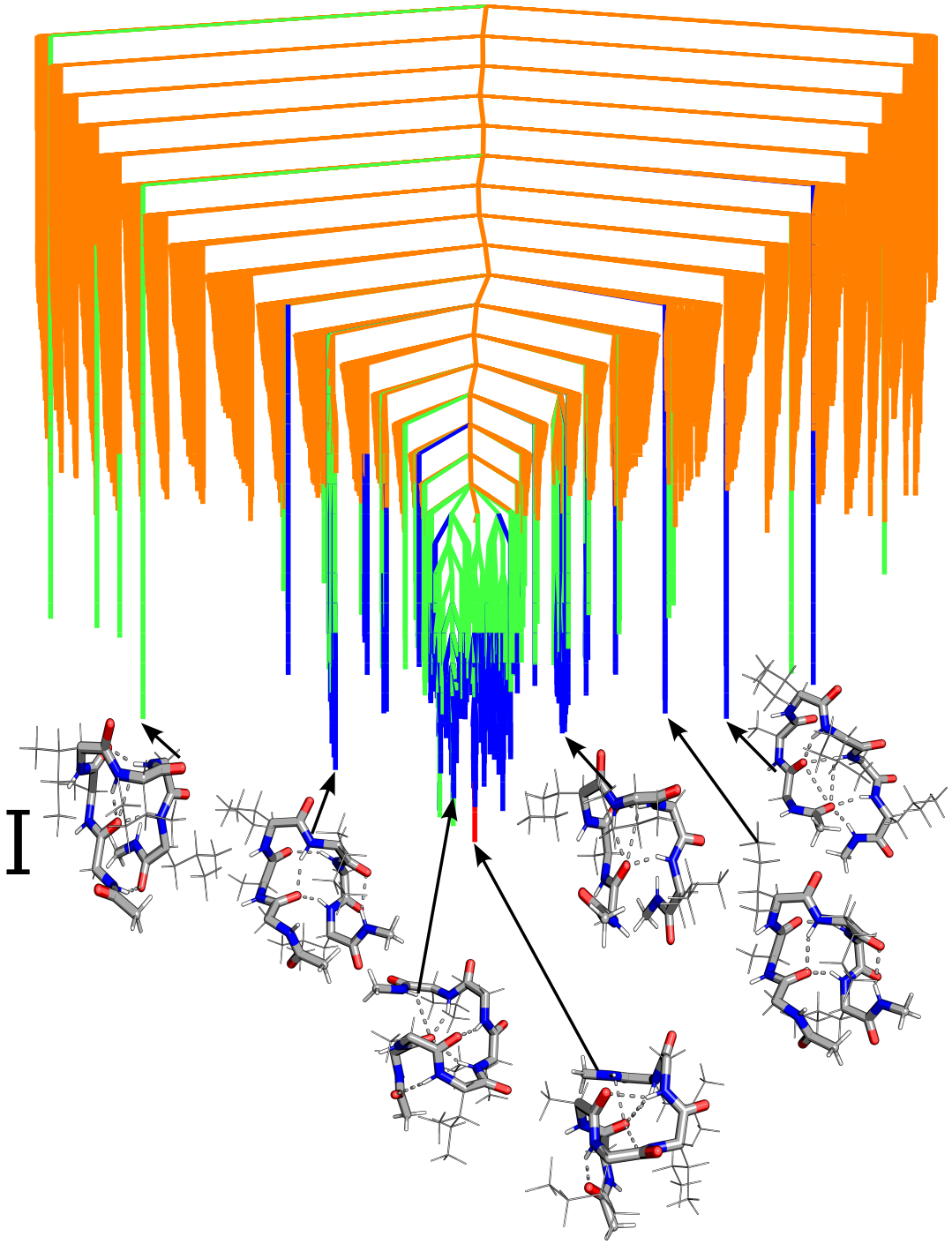


Figure S17: Disconnectivity graphs for **GAIIGL** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

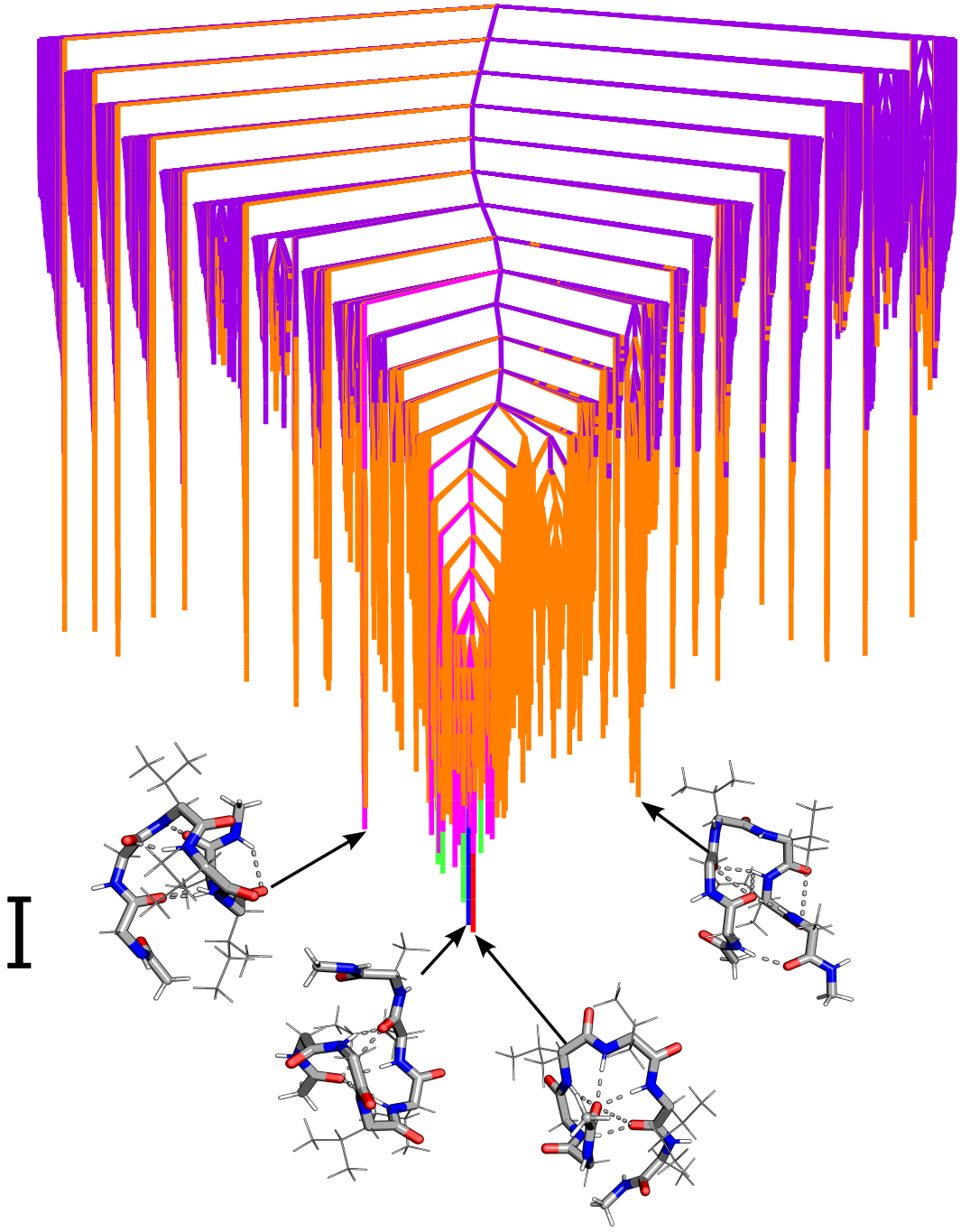


Figure S18: Disconnectivity graphs for **GGVVIA** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

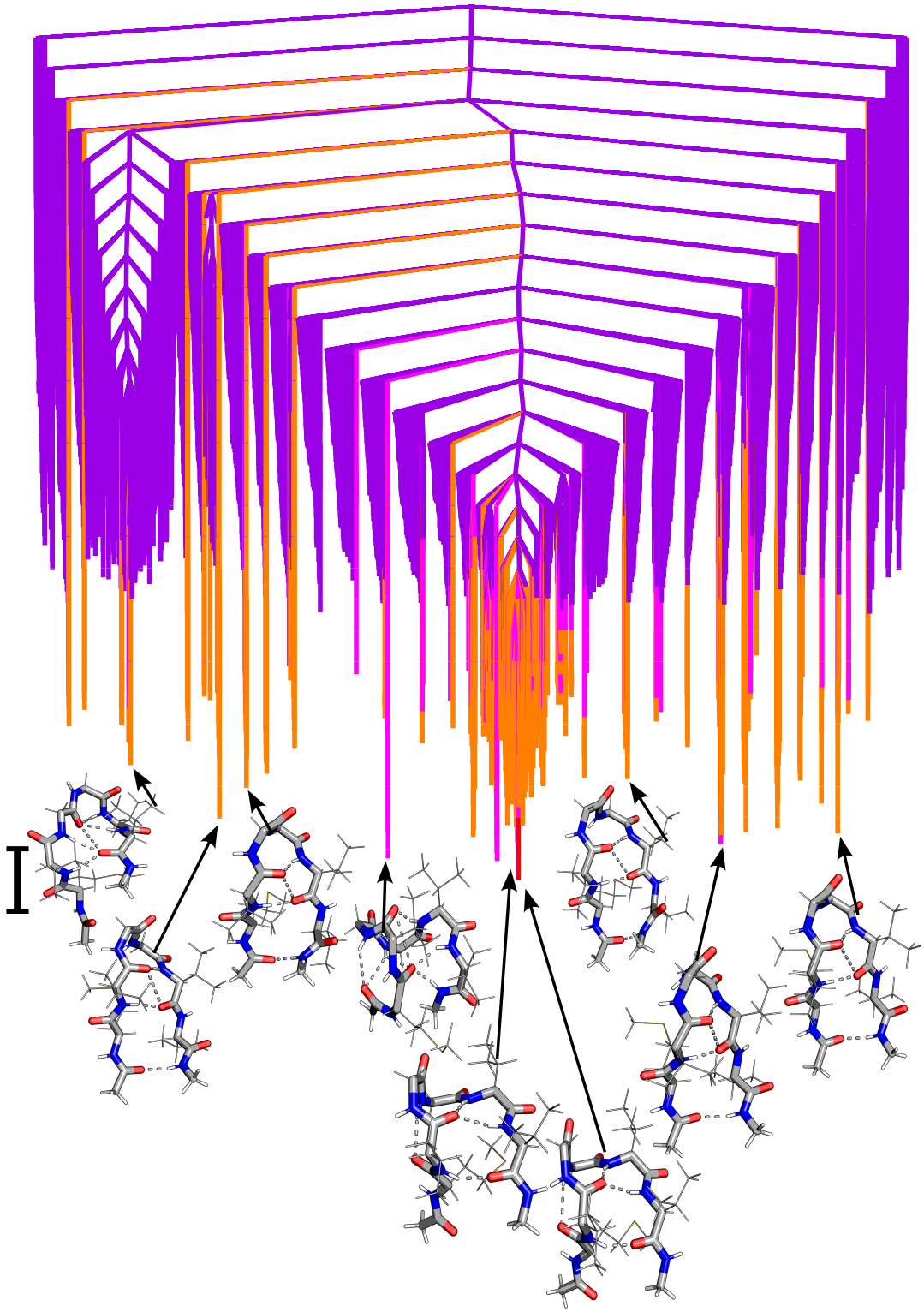


Figure S19: Disconnectivity graphs for **MVGGVV** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

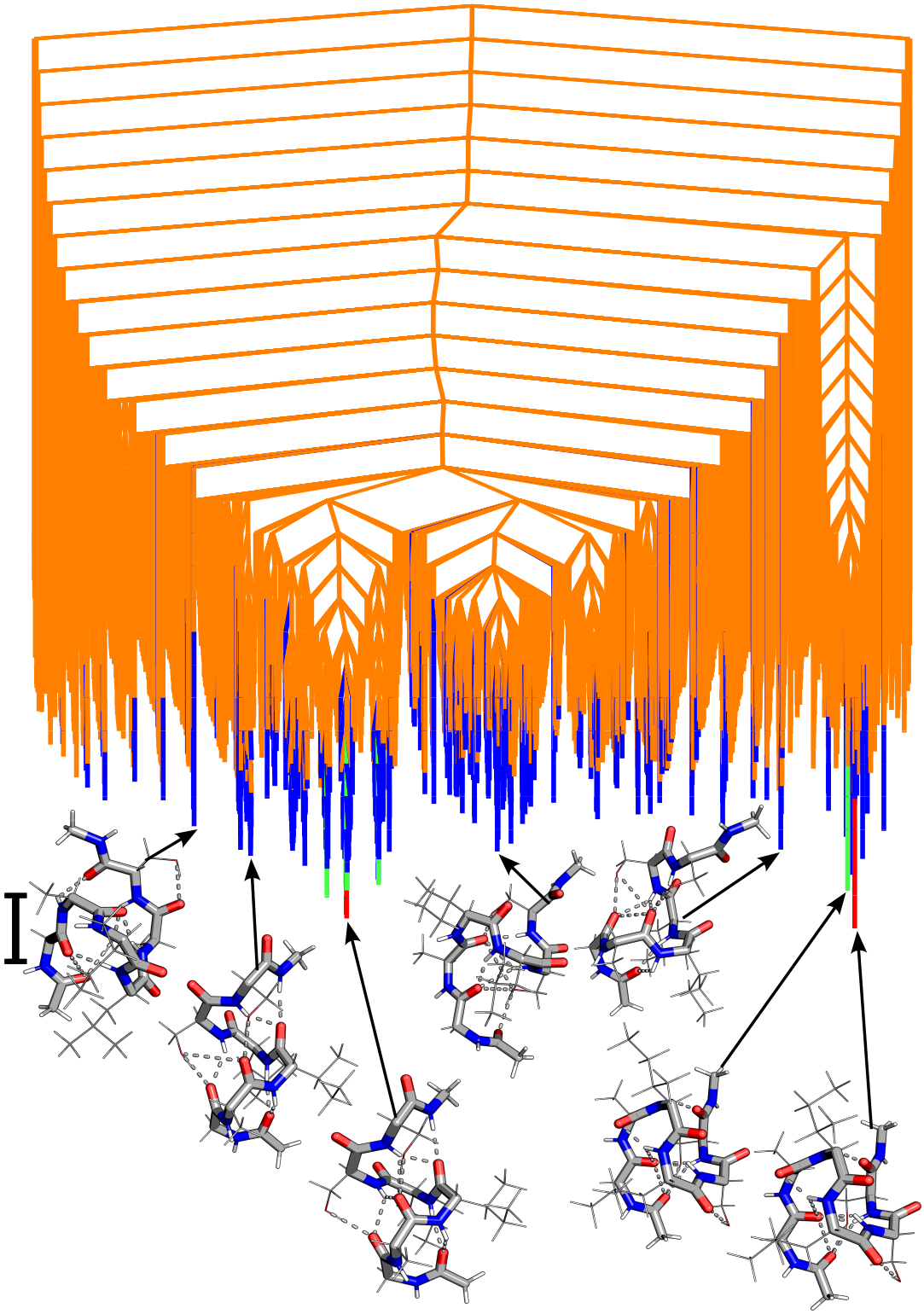


Figure S20: Disconnectivity graphs for **GAILSS** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

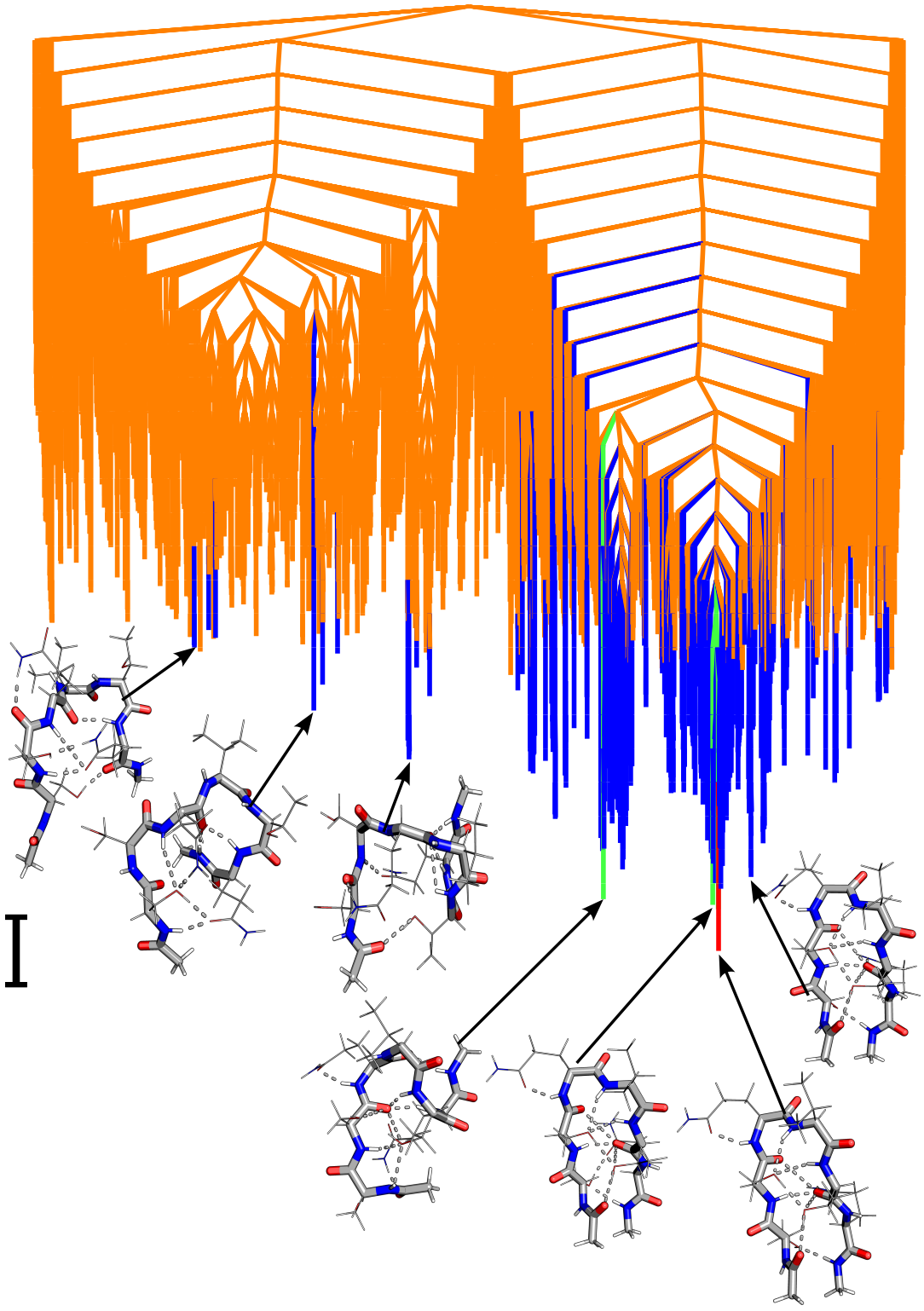


Figure S21: Disconnectivity graphs for **SSQVTQ** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

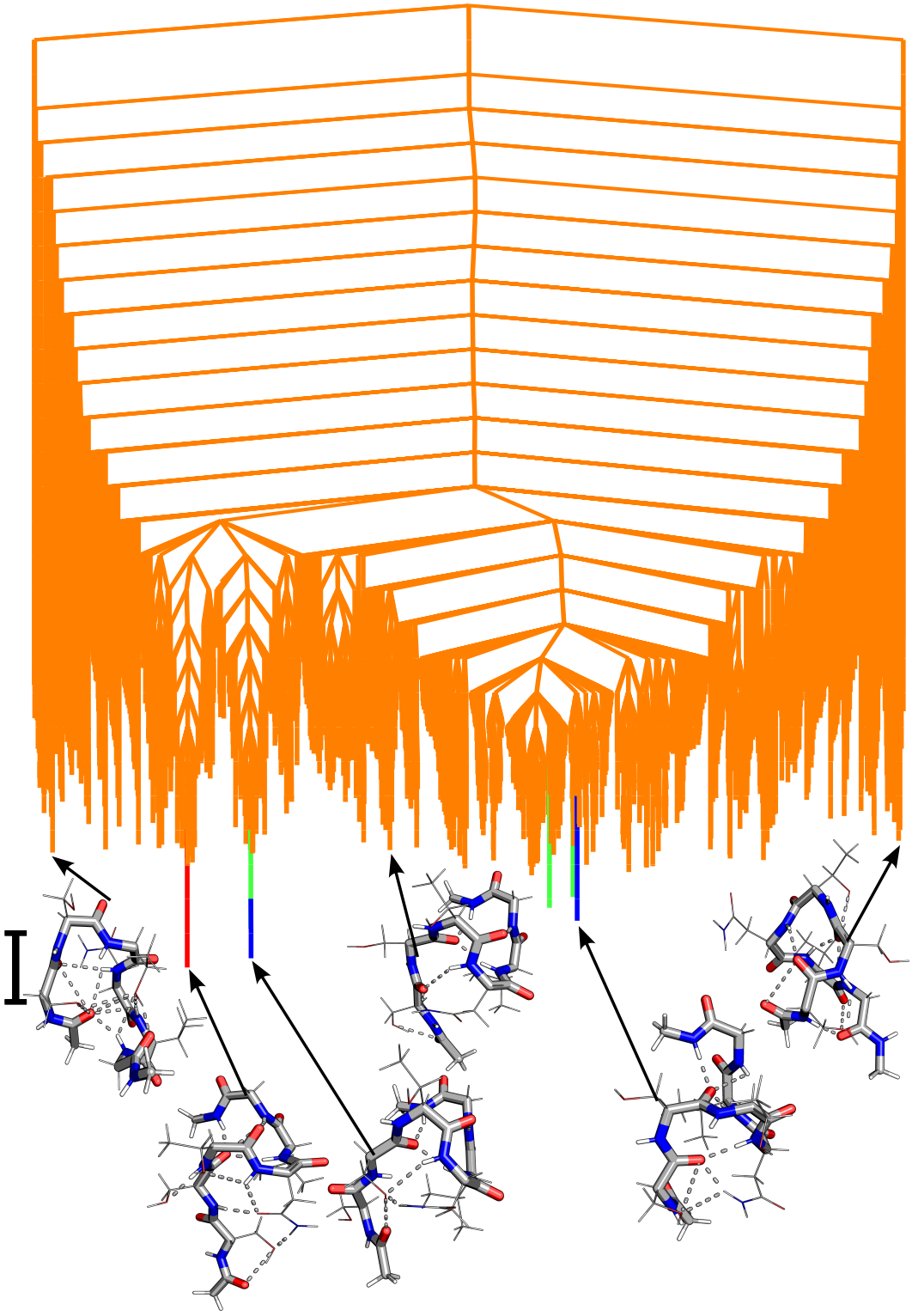


Figure S22: Disconnectivity graphs for **SSTNVG** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

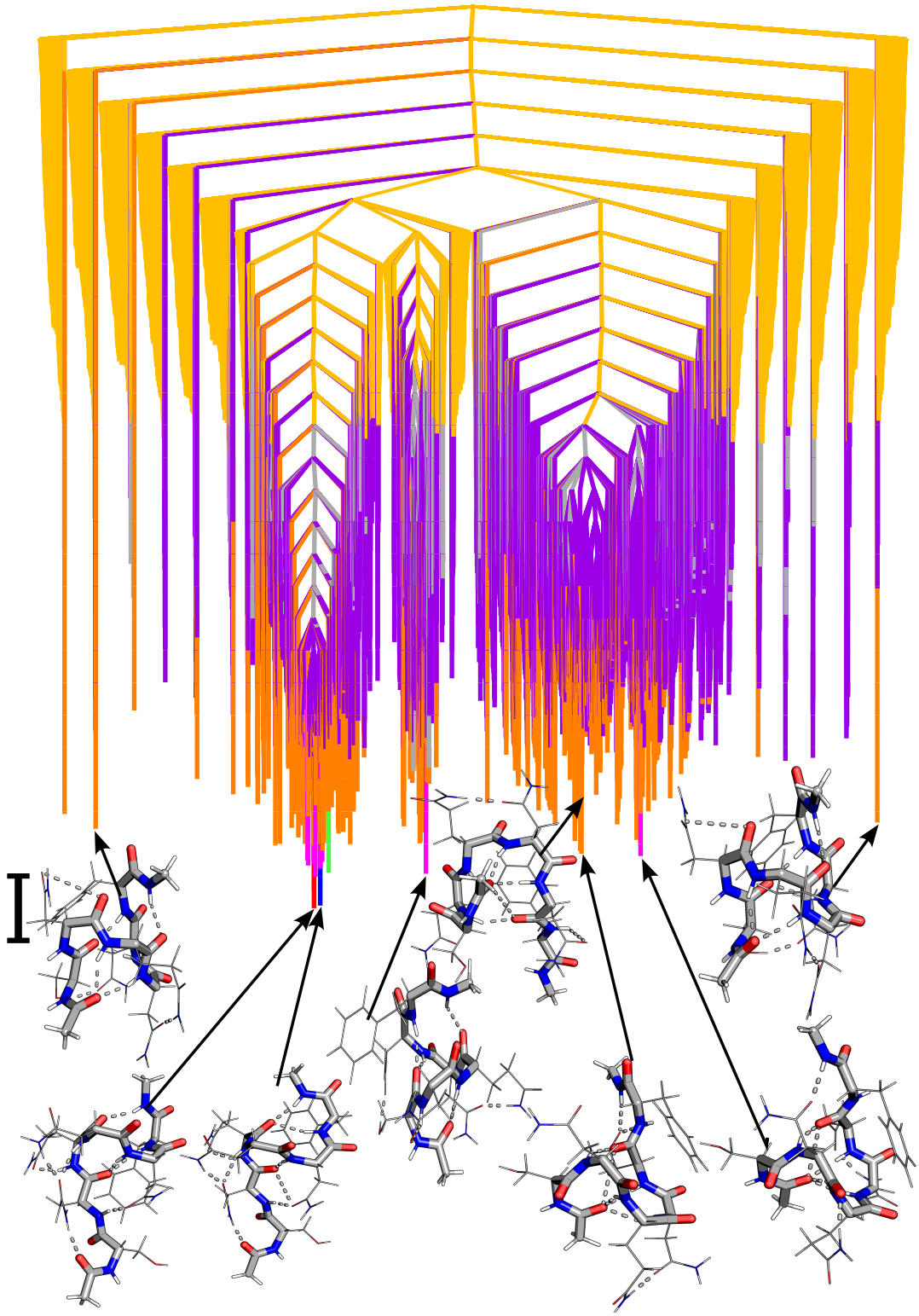


Figure S23: Disconnectivity graphs for **SNQNNF** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

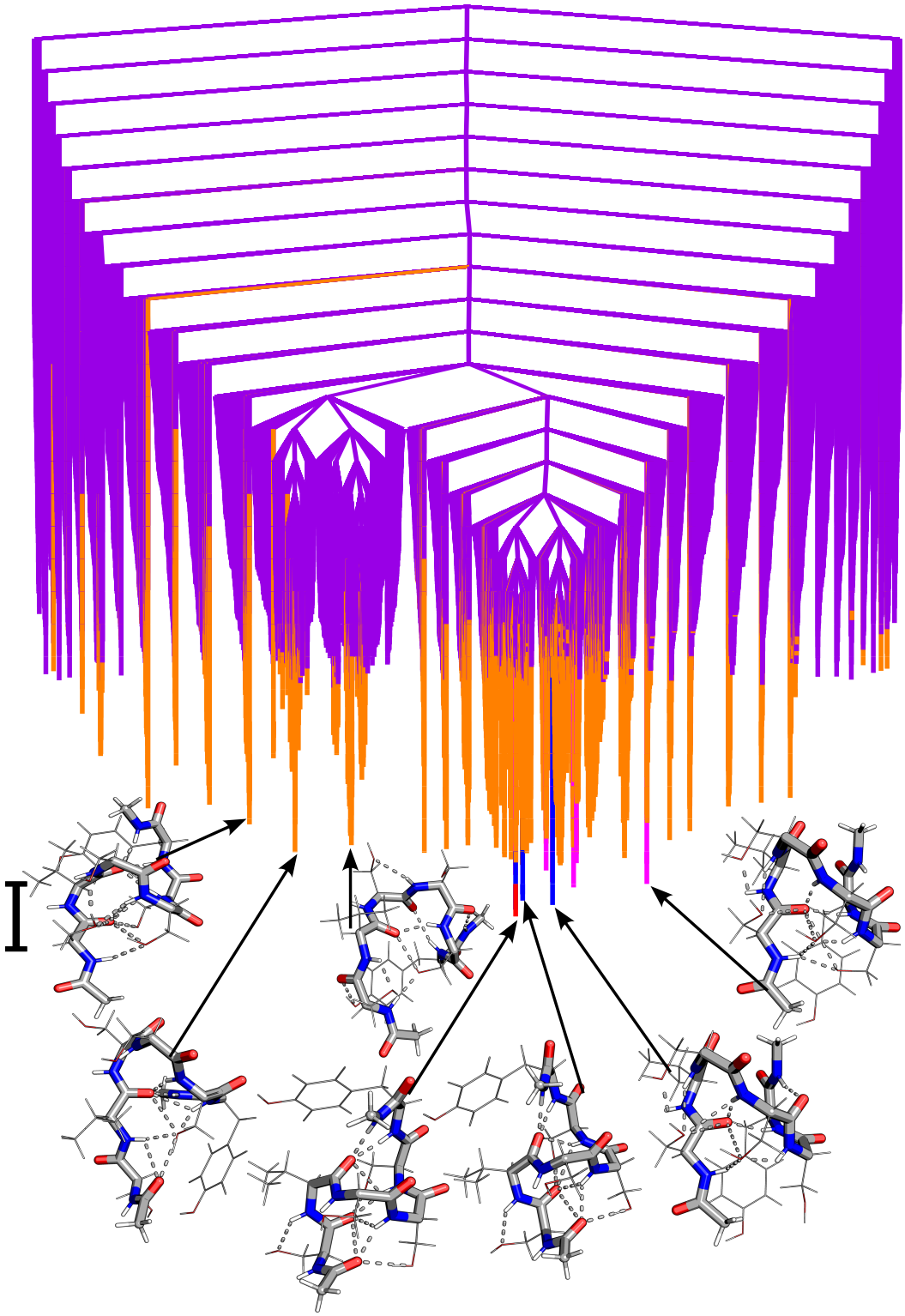


Figure S24: Disconnectivity graphs for **SVSSSY** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

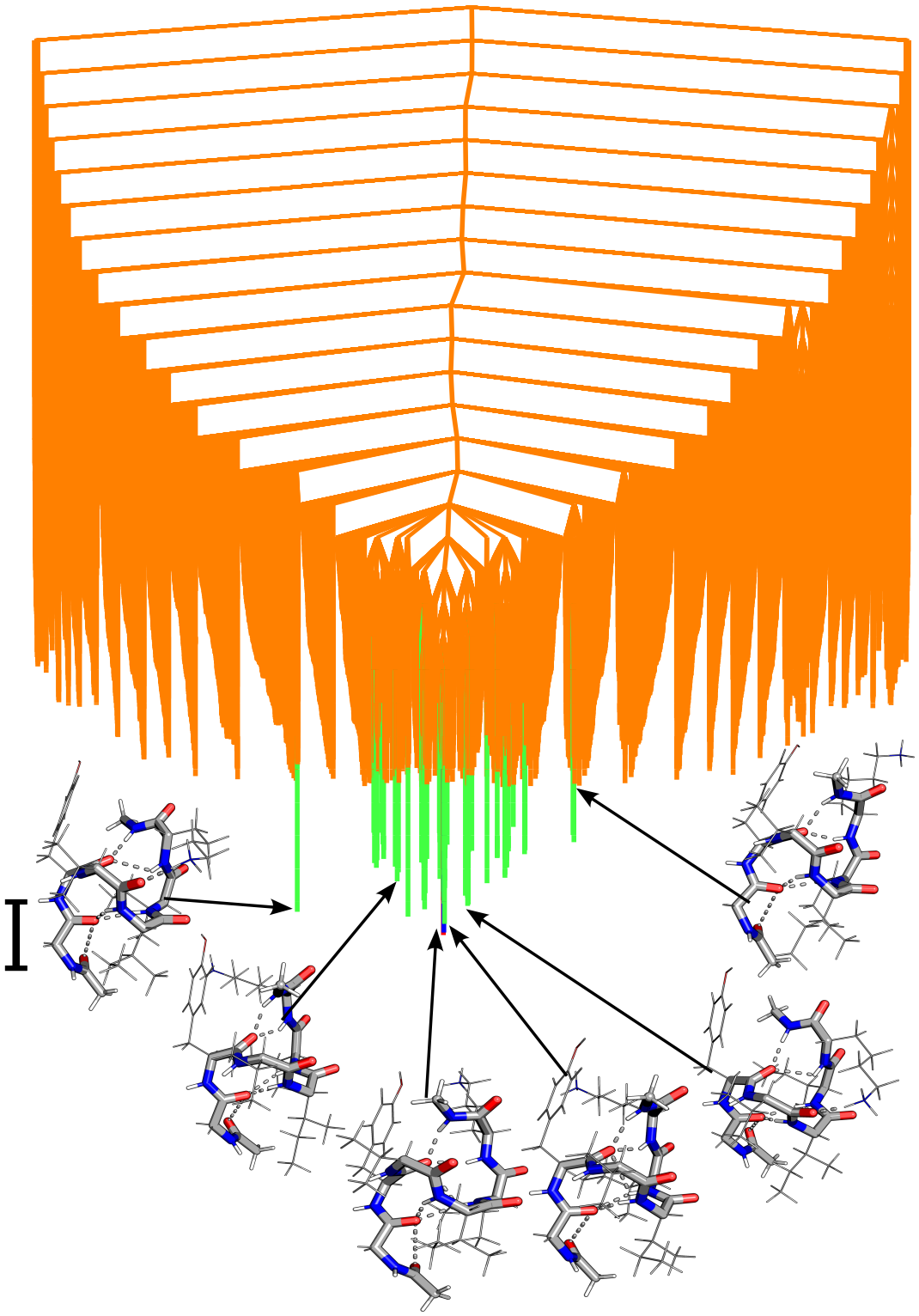


Figure S25: Disconnectivity graphs for **GYVIIK** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

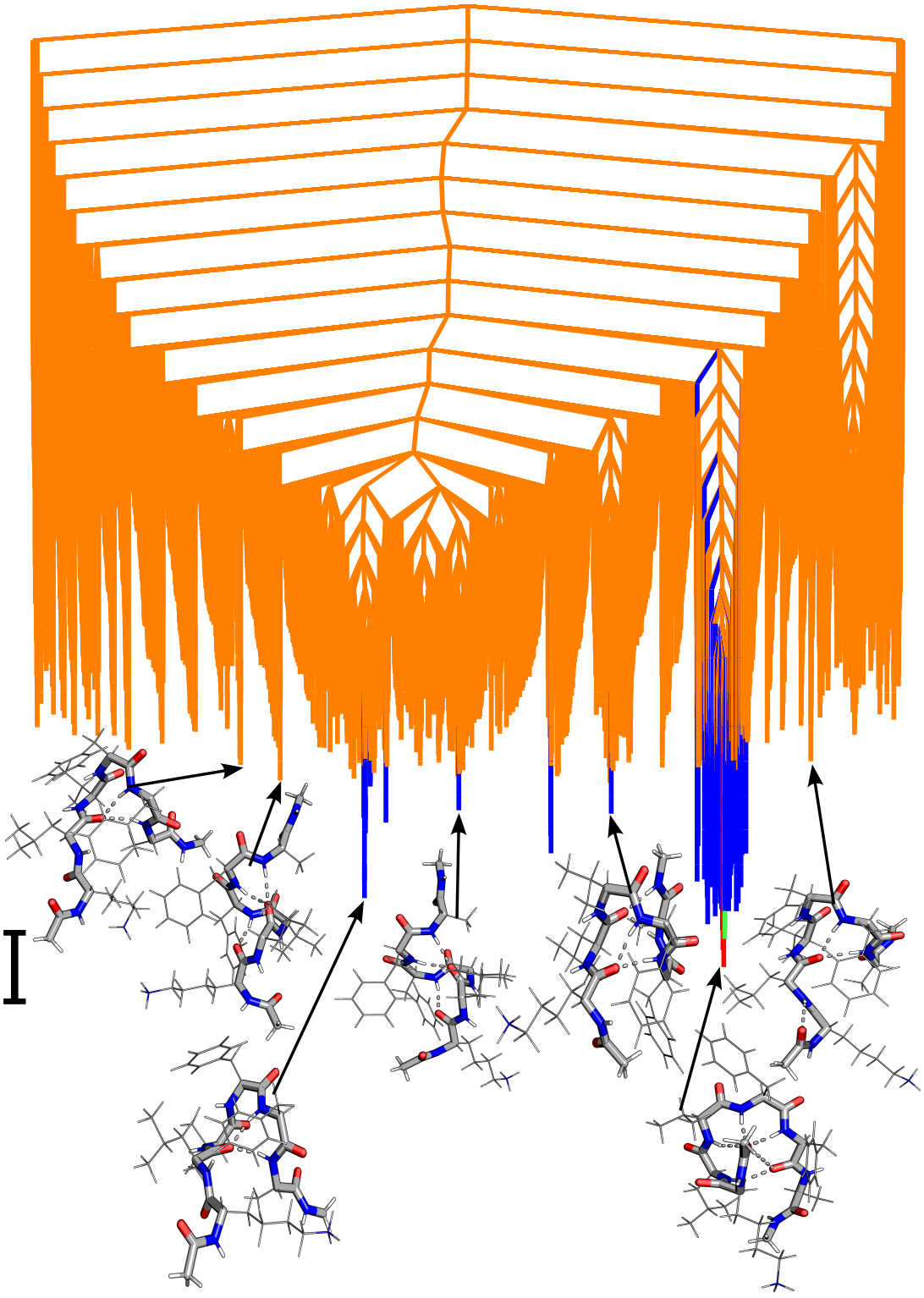


Figure S26: Disconnectivity graphs for **KLVFFA** monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

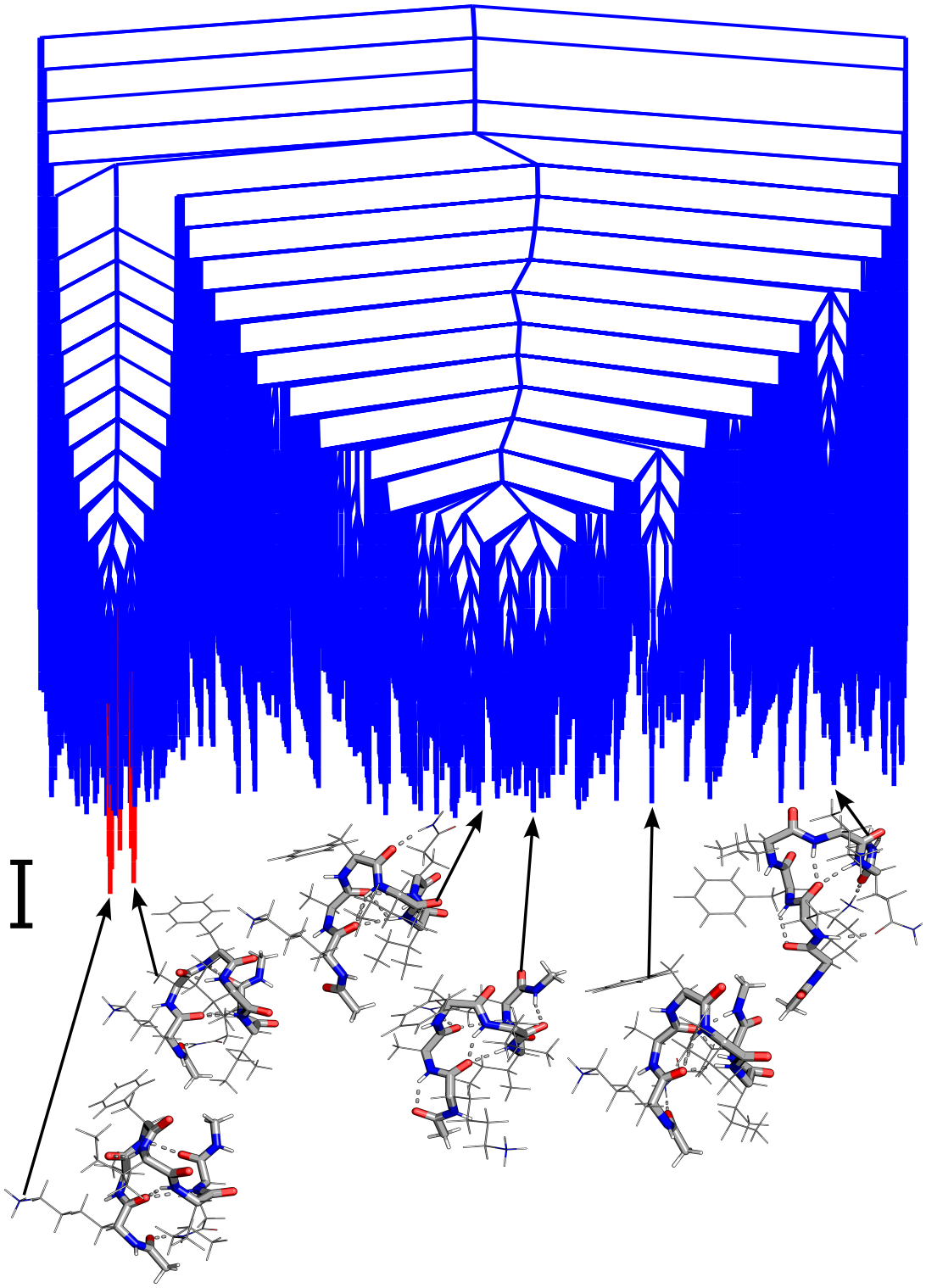


Figure S27: Disconnectivity graphs for KAFIIQ monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

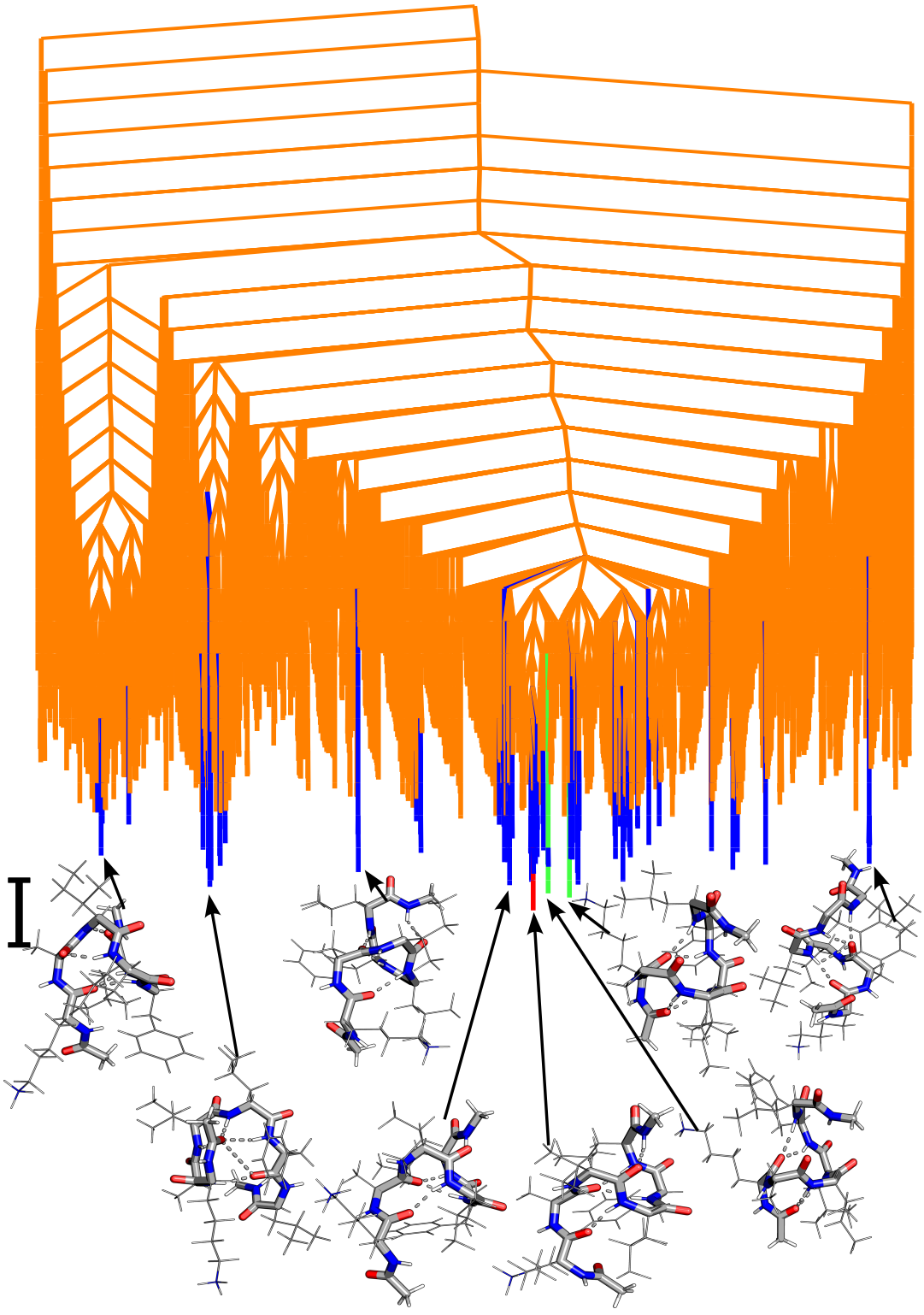


Figure S28: Disconnectivity graphs for KAILFL monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

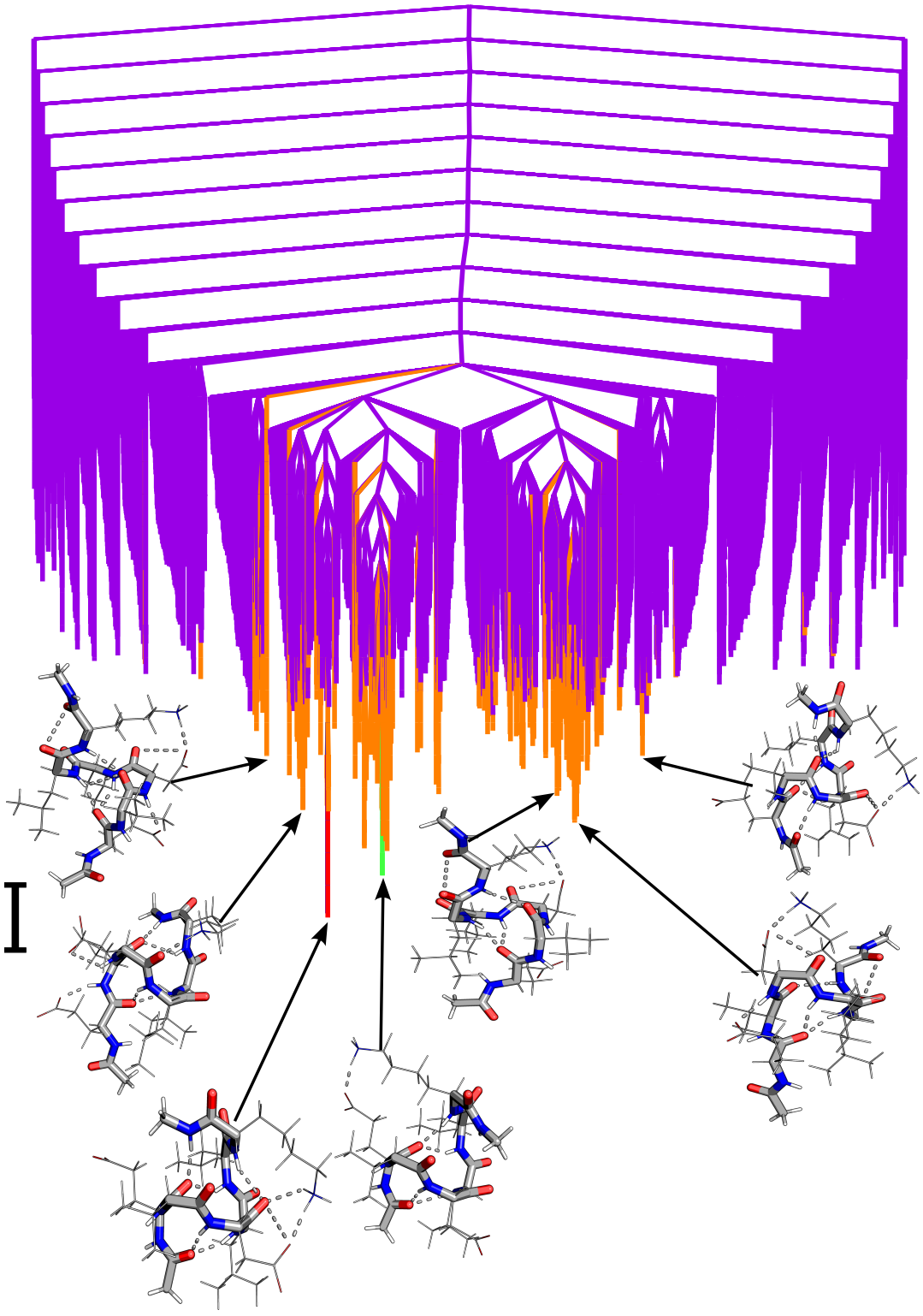


Figure S29: Disconnectivity graphs for EVDLLK monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

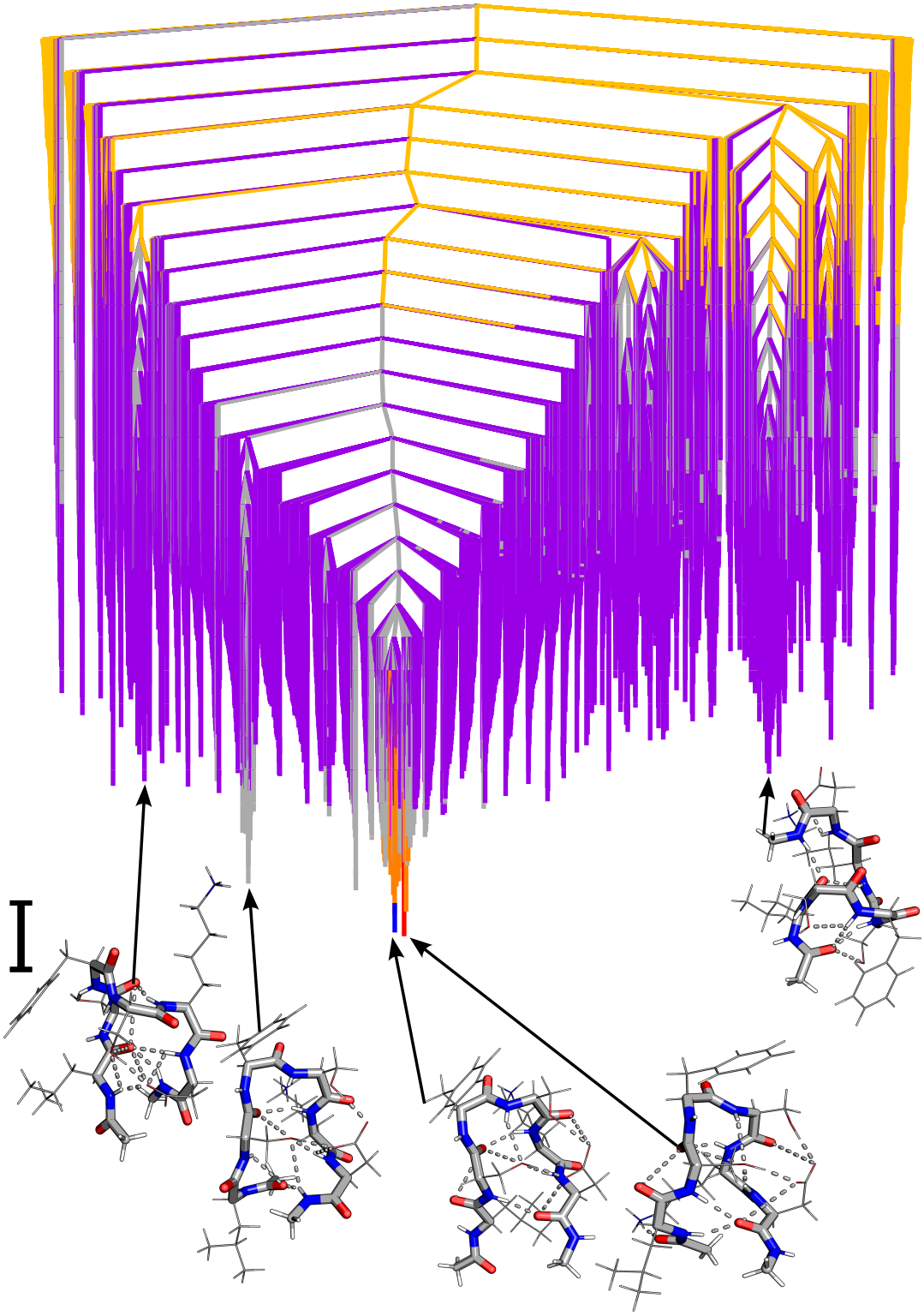


Figure S30: Disconnectivity graphs for LSFSKD monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.

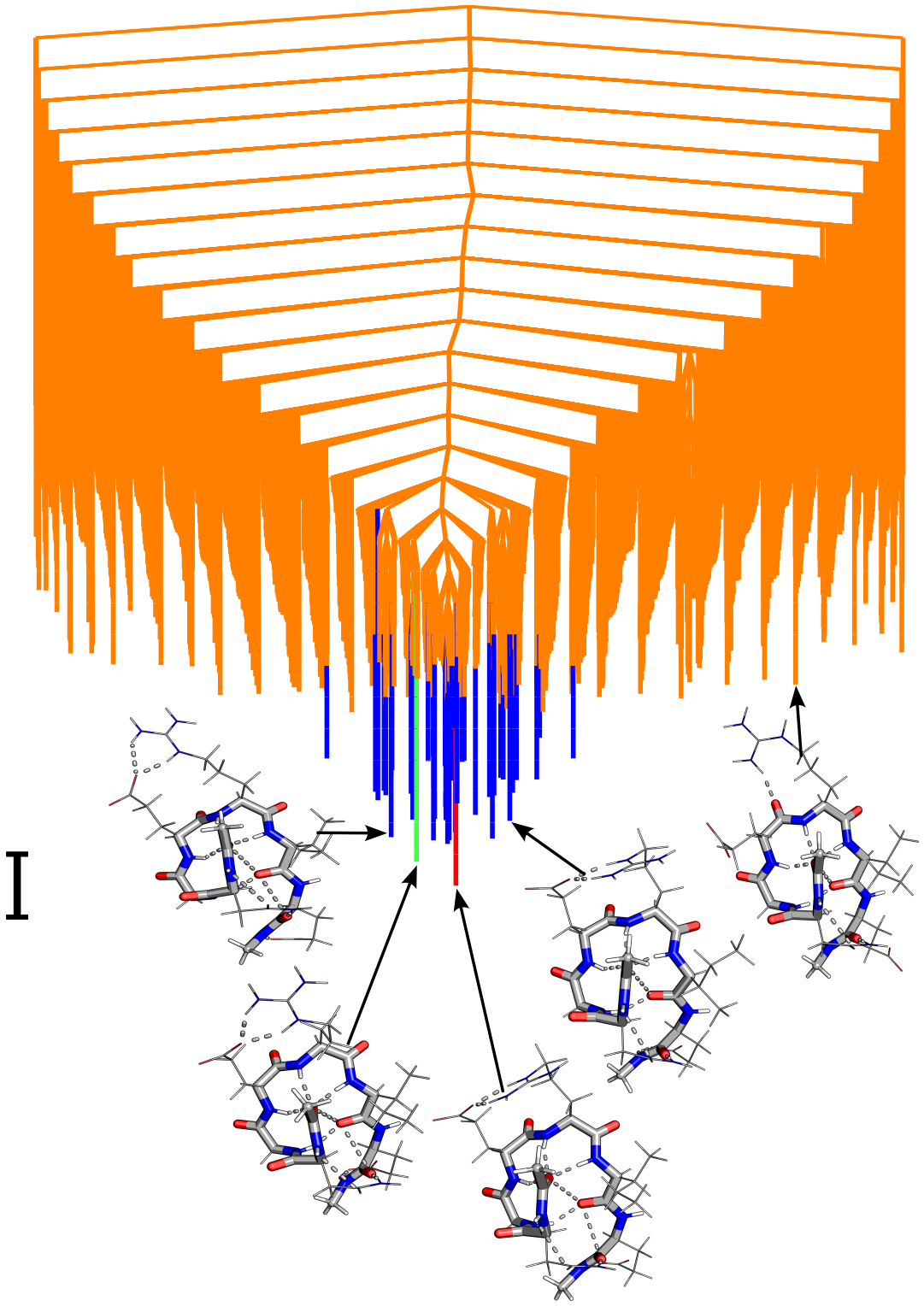


Figure S31: Disconnectivity graphs for NGERIE monomer. Local minima representing transition for peaks/inflection points are represented by red to blue (peak 1), green to orange (peak 2), pink to purple (peak 3) and grey to yellow (peak 4). The scalebar represents 1 kcal mol^{-1}.