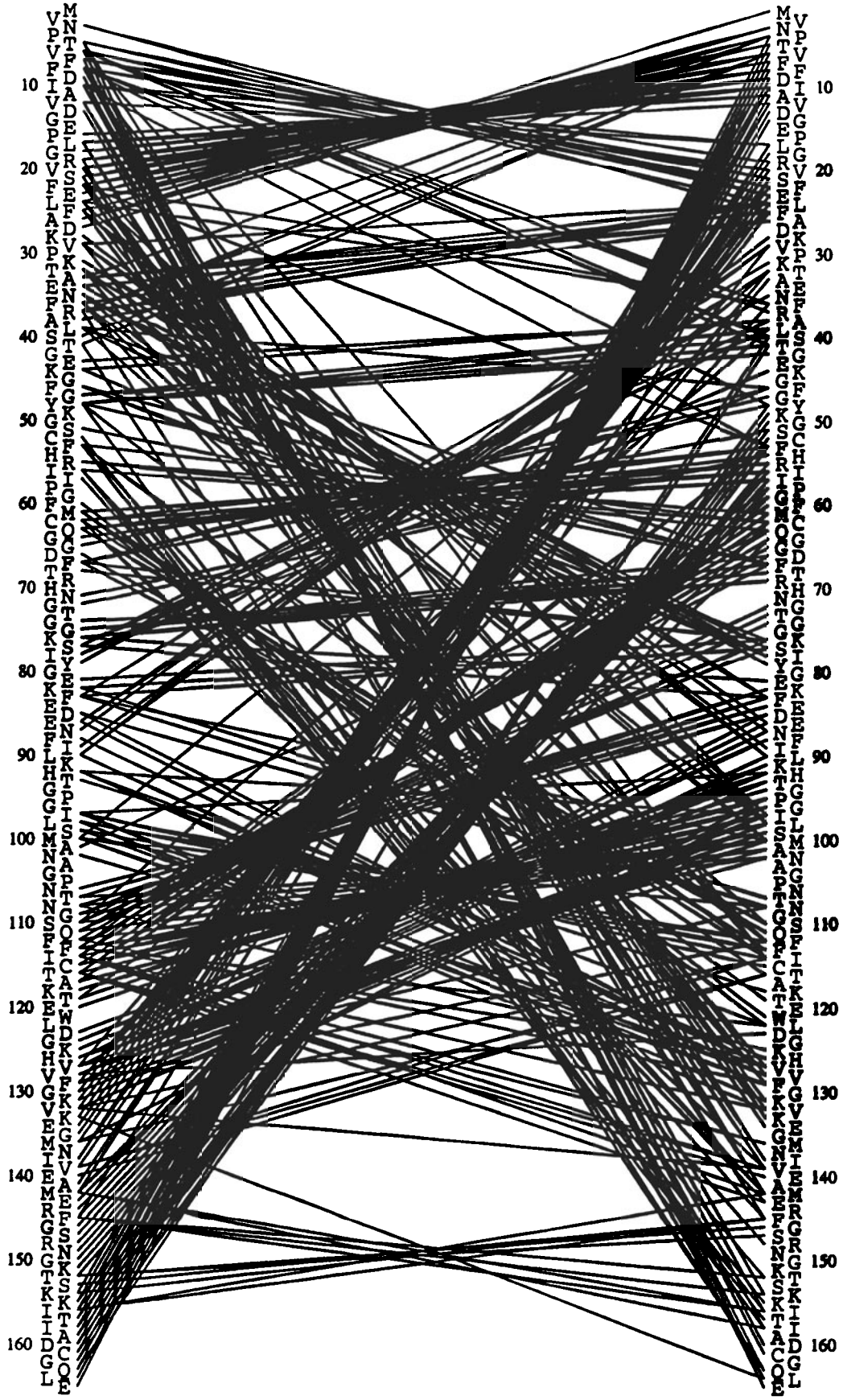


Fig. 5. Long-range distance restraints in the experimental NMR data set for the protein cyclophilin A (Ottiger *et al.* 1997). Restraints between atoms five or more residues apart in the sequence are represented by lines going from upper left to lower right (restraints between side-chain atoms), or from lower left to upper right (restraints involving backbone atoms). On the left and right hand sides the amino acid sequence of cyclophilin A is given.

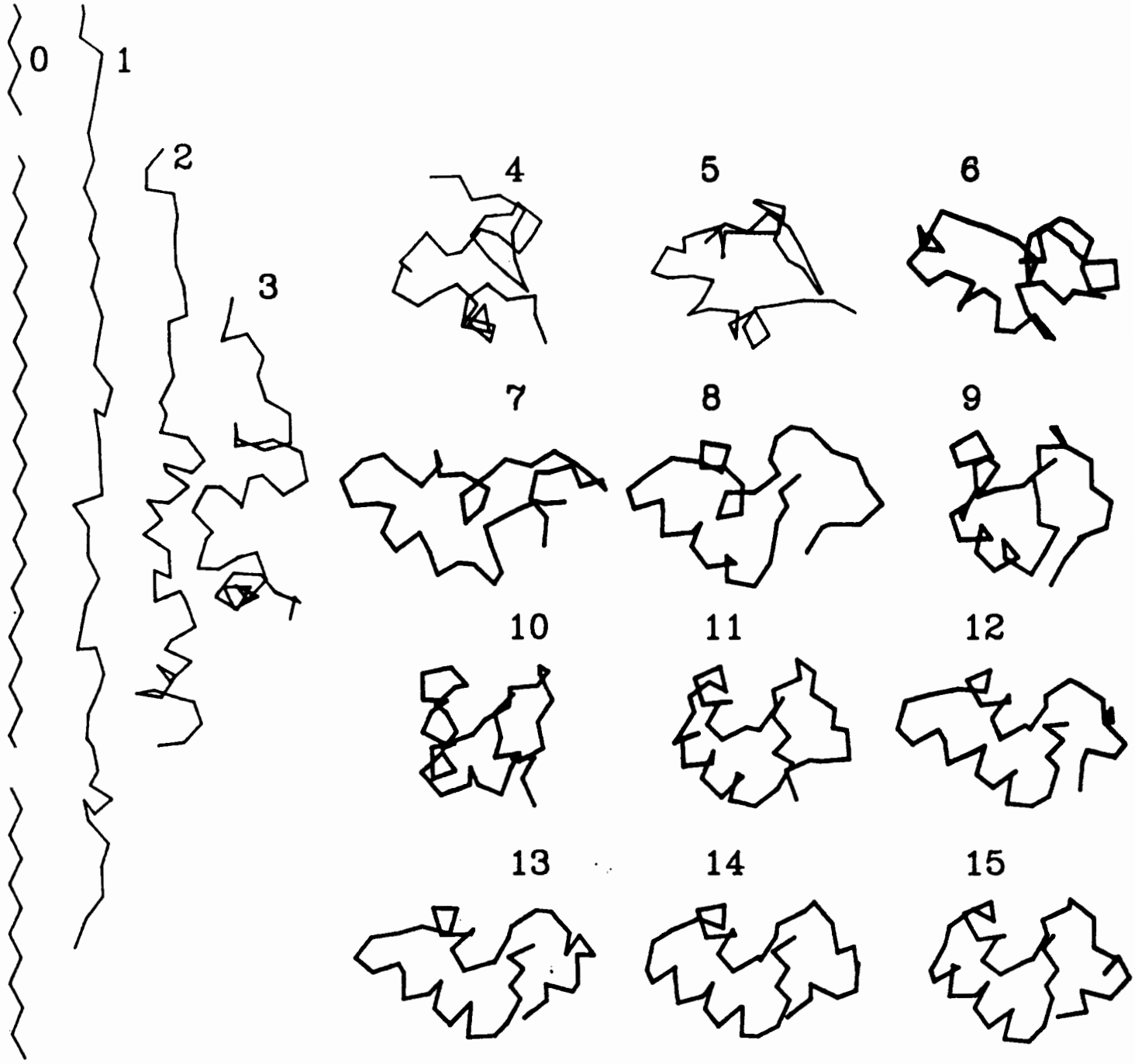
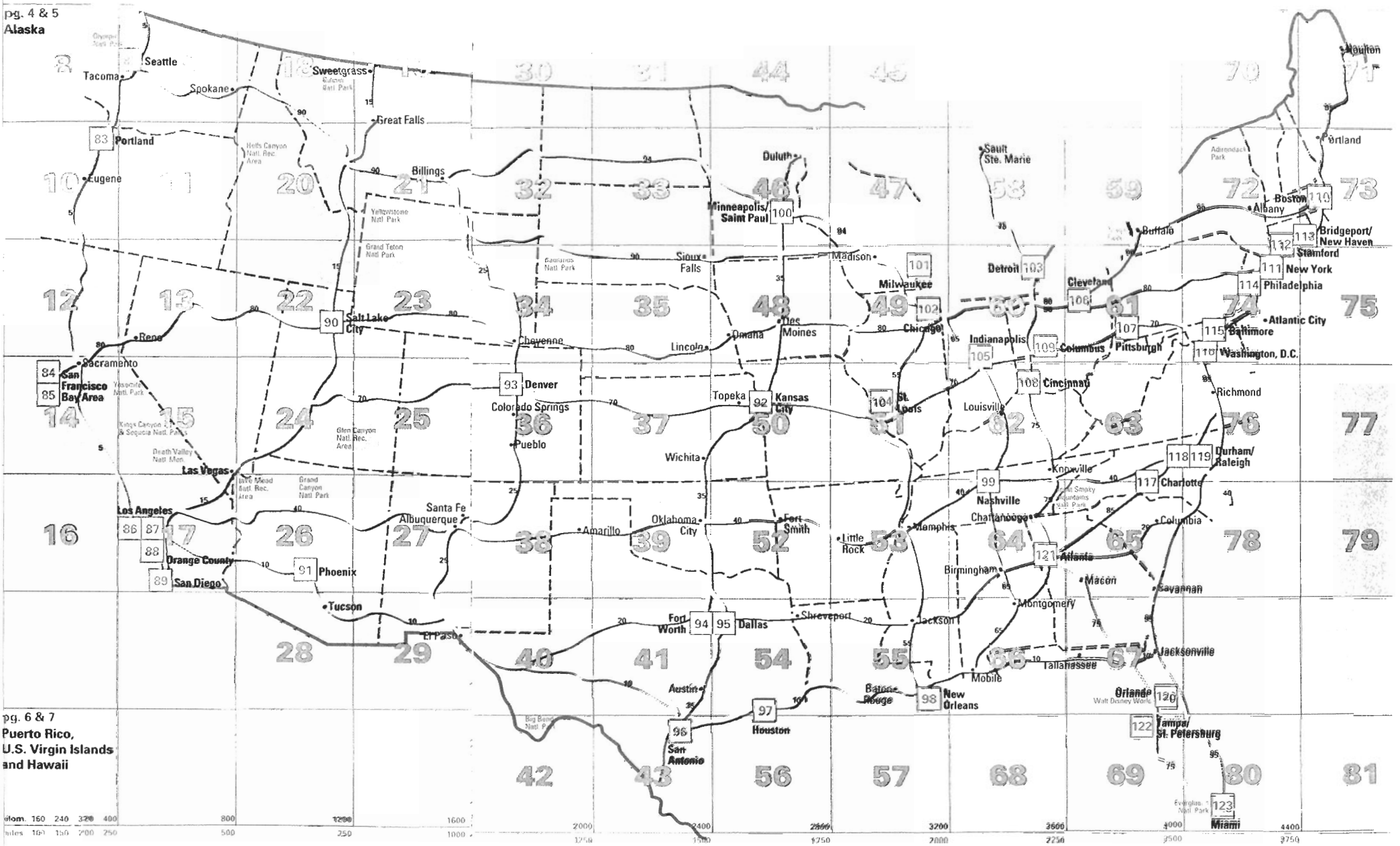


Figure 1. Pathway of SA for the structure determination of crambin starting with an extended β-strand using interproton distance data.[13] Simulated interproton distance data were used that could realistically be obtained by two-dimensional NOE spectroscopy. Snapshots of the C^{α} backbone are shown at 1-ps intervals. During the first 5 ps (thin lines), only interproton distance restraints between residues i, $i \pm 1$, $i \pm 2$, $i \pm 3$, $i \pm 4$, and $i \pm 5$ were taken into account, while all interproton distances were used during the following stages (thick lines).

Mileage Chart

	Atlanta, GA	Atlantic City, NJ	Baltimore, MD	Boston, MA	Charlotte, NC	Chicago, IL	Cincinnati, OH	Cleveland, OH	Columbus, OH	Dallas, TX	Denver, CO	Detroit, MI	Durham, NC	Ft. Worth, TX	Houston, TX	Indianapolis, IN	Kansas City, MO	Las Vegas, NV	Los Angeles, CA	Miami, FL	Milwaukee, WI	Minneapolis, MN	Nashville, TN	New Haven, CT	New Orleans, LA	New York, NY	Orlando, FL	Philadelphia, PA	Phoenix, AZ	Pittsburgh, PA	Portland, OR	Raleigh, NC	St. Louis, MO	Salt Lake City, UT	San Antonio, TX	San Diego, CA	San Francisco, CA	San Jose, CA	Seattle, WA	Stamford, CT	Tampa, FL	Washington, DC
Atlanta, GA		838	680	1084	250	715	481	727	560	826	1519	741	422	860	875	549	882	2004	2252	662	814	1136	250	967	518	863	449	776	1894	741	2873	410	582	1959	1022	2230	2554	2509	2854	908	458	641
Atlantic City, NJ	838		168	370	455	829	640	483	390	1623	1832	670	477	1657	1710	709	1203	2756	2891	1293	911	1241	917	241	1374	165	1069	62	2507	367	2923	480	949	2255	1857	2841	3022	3067	3065	205	1043	202
Baltimore, MD	680	168		404	423	696	493	361	428	1460	1624	524	289	1494	1555	574	1070	2473	2724	1146	783	1106	754	277	1206	191	922	106	2332	232	2892	301	800	2120	1702	2736	2899	2944	2792	251	1189	39
Boston, MA	1084	370	404		835	976	853	643	769	1868	2008	706	728	1902	1961	948	1442	2810	3130	1547	1069	1399	1168	140	1625	215	1323	308	2746	595	3229	731	1188	2431	2108	3285	3198	3243	3163	376	1427	443
Charlotte, NC	250	455	423	835		849	481	728	584	1076	1733	754	120	1110	1114	581	1006	2256	2490	745	961	1283	407	696	736	620	531	524	2091	547	2917	136	740	2149	1307	2480	2801	2756	2873	680	590	384
Chicago, IL	715	829	696	976	849		301	343	316	936	1017	279	813	970	1073	182	505	1866	2189	1386	95	416	442	910	938	818	1162	767	1837	468	2250	825	296	1411	1245	2277	2233	2278	2184	874	1215	696
Cincinnati, OH	481	640	493	853	481	301		247	103	986	1245	273	531	1022	1115	114	604	1972	2292	1143	391	721	291	709	848	623	940	578	1908	292	2495	543	348	1682	1247	2257	2449	2294	2485	673	972	519
Cleveland, OH	727	483	361	643	728	343	247		142	1225	1373	163	590	1259	1358	305	799	2167	2487	1365	439	769	542	565	1132	497	1141	421	2103	128	2599	602	545	1796	1488	2625	2563	2608	2533	529	1209	358
Columbus, OH	560	390	428	769	584	316	103	142		1091	1236	180	464	1125	1212	175	668	2256	2356	1236	403	736	945	612	988	555	1022	473	2112	180	2559	529	408	1746	1405	2317	2526	2571	2500	576	966	389
Dallas, TX	826	1623	1460	1868	1076	936	988	1225	1091		797	1194	1263	34	241	921	505	1453	1431	1394	1030	940	706	1740	495	1649	1170	1561	1015	1282	2145	1219	843	1240	271	1337	1791	1746	2222	1704	1286	1414
Denver, CO	1519	1832	1624	2008	1733	1017	1245	1373	1236	797		1302	1761	763	1038	1047	604	765	1189	2126	1036	871	1205	2033	1292	1852	1902	1770	904	1420	1347	1773	858	497	975	1243	1267	1312	1426	1997	1933	1707
Detroit, MI	741	670	524	706	754	279	273	163	180	1194	1302		677	1228	1328	273	752	2123	2448	1395	383	693	563	606	1143	632	1171	588	2072	294	2523	689	514	1725	1458	2544	2492	2537	2457	570	1224	525
Durham, NC	422	477	289	728	120	813	531	590	464	1263	1761	677		1263	1335	660	1312	2370	2648	854	940	1225	510	575	937	500	630	408	2269	459	3037	20	858	2205	1470	2578	2959	2914	2989	539	1110	249
Ft. Worth, TX	860	1657	1494	1902	1110	970	1022	1259	1125	34	763	1228	1263		236	955	499	1419	1397	1428	1084	934	740	1774	529	1683	1204	1595	981	1316	2111	1297	637	1206	265	1303	1757	1712	2188	1738	1320	1448
Houston, TX	875	1710	1555	1961	1114	1073	1115	1356	1212	241	1038	1326	1335	236		1010	714	1484	1564	1306	1150	1181	814	898	363	1742	1042	1648	1208	1396	2368	1347	780	1502	193	1578	1984	1939	2445	862	1045	1501
Indianapolis, IN	549	709	574	948	581	182	114	305	175	921	1047	273	660	955	1010		503	1910	2182	1219	281	598	293	744	831	729	995	647	1769	356	2385	680	242	1528	1192	2151	2353	2398	2375	708	949	572
Kansas City, MO	882	1203	1070	1442	1006	505	604	799	668	505	604	752	1312	499	714	503		1417	1631	1485	585	435	564	1299	809	1223	1278	1141	1274	856	1953	1132	255	1105	788	1651	1903	1858	1984	1263	1292	1066
Las Vegas, NV	2004	2756	2473	2810	2250	1866	1972	2167	2256	1453	765	2123	2370	1419	1484	1910	1417		288	2582	2038	1688	1843	2667	1740	2591	2328	2509	266	2224	1027	2386	1068	418	1283	330	576	531	1284	2631	2312	2434
Los Angeles, CA	2252	2891	2742	3130	2490	2189	2292	2487	2356	1431	1189	2448	2648	1397	1564	2182	1631	288		2885	2149	2033	2098	2987	1947	2911	2661	2829	379	2944	1016	2868	1942	706	1388	126	377	332	1193	2951	2554	2754
Miami, FL	662	1293	1148	1547	745	1386	1143	1365	1238	1394	2126	1395	854	1428	1308	1219	1485	2582	2885		1476	1786	921	1401	881	1325	224	1231	2417	1261	3438	834	1231	2621	1435	2881	3238	3193	3469	1365	270	1096
Milwaukee, WI	814	911	783	1069	961	95	391	439	403	1030	1036	363	940	1064	1150	281	585	2038	2149	1476		335	554	1000	1018	931	1252	849	1845	333	2130	920	370	1434	1307	2275	2186	2231	2043	964	1206	786
Minneapolis, MN	1136	1241	1106	1399	1283	416	721	769	736	940	871	693	1225	934	1181	598	435	1688	2033	1786	335		876	1337	1228	1261	1562	1179	1869	885	1830	1245	853	1309	1188	2083	2077	2122	1691	1301	1615	1116
Nashville, TN	250	917	754	1168	407	442	291	542	945	706	1205	553	510	740	814	283	564	1843	2098	921	554	876		1025	549	949	697	855	1762	582	2517	530	310	1700	977	2043	2409	2364	2548	989	664	708
New Haven, CT	967	241	277	140	696	910	709	565	612	1740	2033	606	575	1774	1838	744	1299	2667	2987	1401	1000	1337	1025		1482	76	723	184	2603	443	3184	587	1028	2351	1965	2927	3158	3203	3101	36	1293	326
New Orleans, LA	518	1374	1206	1625	736	938	846	1132	988	495	1292	1143	937	529	363	831	809	1740	1947	881	1018	1228	549	1482		1406	657	1312	1553	1172	2654	967	690	1735	874	1934	2300	2255	2731	1446	639	1165
New York, NY	863	165	191	215	620	818	623	497	555	1649	1852	632	500	1683	1742	729	1223	2591	2911	1325	931	1261	949	76	1406		1101	91	2527	376	3088	512	969	2275	1889	2851	3082	3127	3025	40	1208	236
Orlando, FL	449	1069	922	1323	531	1162	940	1141	1022	1170	1902	1171	630	1204	1042	995	1278	2328	2661	224	1252	1562	697	723	657	1101		1007	2193	1037	3214	810	1007	2397	1211	2857	3014	2969	3245	697	78	872
Philadelphia, PA	776	62	106	308	524	767	578	421	473	1561	1770	588	408	1595	1648	647	1141	2509	2829	1231	849	1179	855	184	1312	91	1007		2446	305	3006	418	887	2193	1795	2779	2960	3005	2943	148	1114	140
Phoenix, AZ	1894	2507	2332	2746	2091	1837	1908	2103	2112	1015	904	2072	2269	981	1208	1769	1274	268	379	2417	1845	1669	1762	2603	1553	2527	2193	2446		2180	1382	2288	1543	846	1009	384	606	761	1597	2567	2147	2370
Pittsburgh, PA	741	367	232	595	547	468	292	128	180	1282	1420	294	459	1316	1398	356	856	2224	2544	1261	555	885	582	443	1172	376	1037	305	2160		2712	471	602	1933	1528	2505	2710	2265	2649	407	1123	231
Portland, OR	2873	2923	2892	3229	2917	2250	2495	2599	2559	2145	1347	2523	3037	2111	2368	2385	1953	1027	1018	3438	2130	1830	2517	3184	2654	3088	3214	3006	1383	2712		3638	2207	768	2224	1137	638	683	173	3128	3245	2943
Raleigh, NC	410	480	301	731	136	825	543	602	529	1219	1773	689	20	1297	1347	680	1132	2386	2668	834	920	1245	530	587	957	512	810	418	2289	471	3608		878	2225	1490	2598	2979	2934	3009	551	699	261
St. Louis, MO	582	949	800	1188	740	296	348	545	408	843	858	514	858	637	780	242	255	1668	1942	1231	370	553	310	1028	890	989	1007	887	1540	802	2257	678		1359	949	1909	2157	2112	2238	992	1060	916
Salt Lake City, UT	1959	2255	2120	2431	2149	1411	1682	1796	1746	1240	497	1725	2206	1206	1592	1528	1185	418	706	2621	1434	1309	1700	2351	1735	2275	2397	2193	646	1933	768	2225	1359		1364	812	730	775	924	2315	2424	2130
San Antonio, TX	1022	1857	1702	2108	1307	1245	1247	1488	1405	271	975	1458	1470	265	193	1192	788	1263	1388	1435	1397	1188	977	1965	574	1889	1211	1795	1089	1528	2224	1490	949	1364		1688	1793	1748	2301	1929	1238	1548
San Diego, CA	2230	2841	2736	3285	2480	2277	2257	2625	2317	1337	1043	2544	2578	1303	1578	2151	1633	330	126	2881	2275	2083	2043	2927	1934	2851	2657	2779	384	2505	1937	2598	1909	812	1688		525	480	1314	2891	2611	2705
San Francisco, CA	2554	3022	2899	3198	2801	2233	2449	2563	2526	1791	1267	2492	2959	1757	1984	2353	1903	578	377	3238	2186	2077	2409	3158	2300	3062	3014	2960	806	2710	638	2979	2157	730	1793	525		45	786	3122	2977	2897
San Jose, CA	2509	3067	2944	3243	2756	2278	2294	2608	2571	1746	1312	2537	2914	1712	1939	2398	1858	531	332	3193	2231	2122	2364	2303	2255	3127	2969	3005	761	2665	683	2934	2112	775	1748	480	45		831	3167	2932	2942
Seattle, WA	2954	3005	2792	3163	2873	2184	2485	2533	2500	2222	1426	2457	2989	2188	2445	2375	1984	1204	1193	3469	2043	1691	2548	3101	2731	3025	3245	2943	1597	2649	173	3089	2238	924	2301	1314	786	831		3065	3276	2880
Stamford, CT	908	205	251	176	660	874	673	529	576	1704	1997	570	539	1738	1862	708	1263	2631	2951	1365	984	1301	989	36	1448	40	697	148	2567	407	3328	551	992	2315	1929	2891	3122	3167	3065		1250	290
Tampa, FL	458	1043	1169	1427	590	1215	972	1209	966	1286	1933	1224	710	1320	1045	949	1292	2312	2554	270	1206	1615	664	1293	639	1208	78	1114	2147	1123	3245	899	1060	2424	1238	2611	2977	2932	3276	1250		967
Washington, DC	641	202	39	443	384	696	519	358	389	1414	1707	525	249	1448	1301	572	1066	2434	2754	1096	786	1116	708	326	1165	236	872	140	2370	231	2943	261	916	2130	1648	2705	2897	2942	2880	290	967	


pg. 4 & 5
Alaska
pg. 6 & 7
Puerto Rico,
U.S. Virgin Islands
and Hawaii
Seattle
Tacoma
Spokane
Sweetgrass
Great Falls
Portland
Billings
Eugene
Minneapolis/
Saint Paul
Duluth
Sault
Ste. Marie
Moulton
Portland
Boston
Albany
Buffalo
Bridgeport/
New Haven
Stamford
New York
Philadelphia
Atlantic City
Baltimore
Washington, D.C.
Richmond
Durham/
Raleigh
Sioux
Falls
Madison
Milwaukee
Detroit
Cleveland
Chicago
Indianapolis
Columbus
Pittsburgh
Salt Lake
City
Omaha
Des
Moines
Lincoln
Cheyenne
Reno
Sacramento
San
Francisco
Bay Area
Denver
Colorado Springs
Pueblo
Topeka
Kansas
City
St.
Louis
Louisville
Cincinnati
Las Vegas
Wichita
Knoxville
Nashville
Chattanooga
Charlotte
Los Angeles
Santa Fe
Albuquerque
Oklahoma
City
Amarillo
Fort
Smith
Little
Rock
Memphis
Columbia
Orange County
Phoenix
San Diego
Tucson
El Paso
Fort
Worth
Dallas
Shreveport
Jackson
Birmingham
Atlanta
Macon
Savannah
Montgomery
Jacksonville
Tallahassee
Mobile
Baton
Rouge
New
Orleans
Orlando
Tampa/
St. Petersburg
Miami
Austin
San
Antonio
Houston
Big Bend
Nat. Park
Yellowstone
Nat. Park
Grand Teton
Nat. Park
Glacier
Nat. Park
Yosemite
Nat. Park
Kings Canyon
& Sequoia Nat. Parks
Death Valley
Nat. Mon.
Lake Mead
Nat. Rec.
Area
Grand
Canyon
Nat. Park
Glen Canyon
Nat. Rec.
Area
Hells Canyon
Nat. Rec.
Area
Adirondack
Park
Great Smoky
Mountains
Nat. Park
Walt Disney World
Everglades
Nat. Park
miles 160 240 320 400 800 1200 1600
kilom. 100 150 200 250 500 750 1000
1250 1500 1750 2000 2250 2500 2750 3000 3250 3500 3750 4000 4250 4500 4750 5000 5250 5500 5750 6000 6250 6500

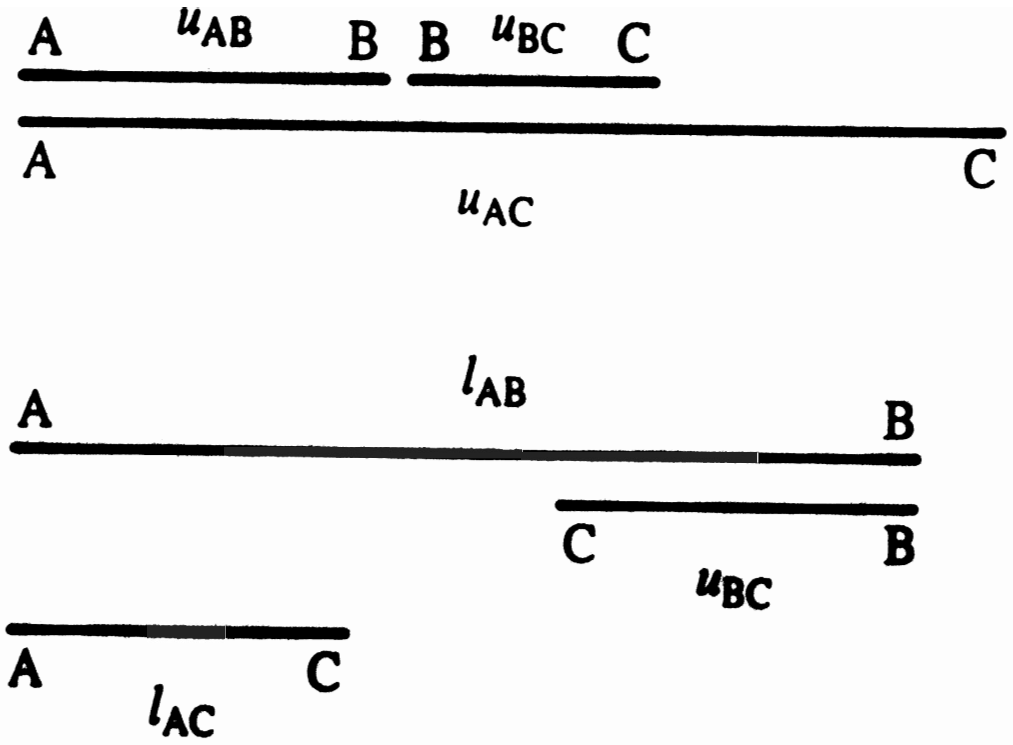


Fig. 8.14 The two triangle inequalities used in distance geometry.

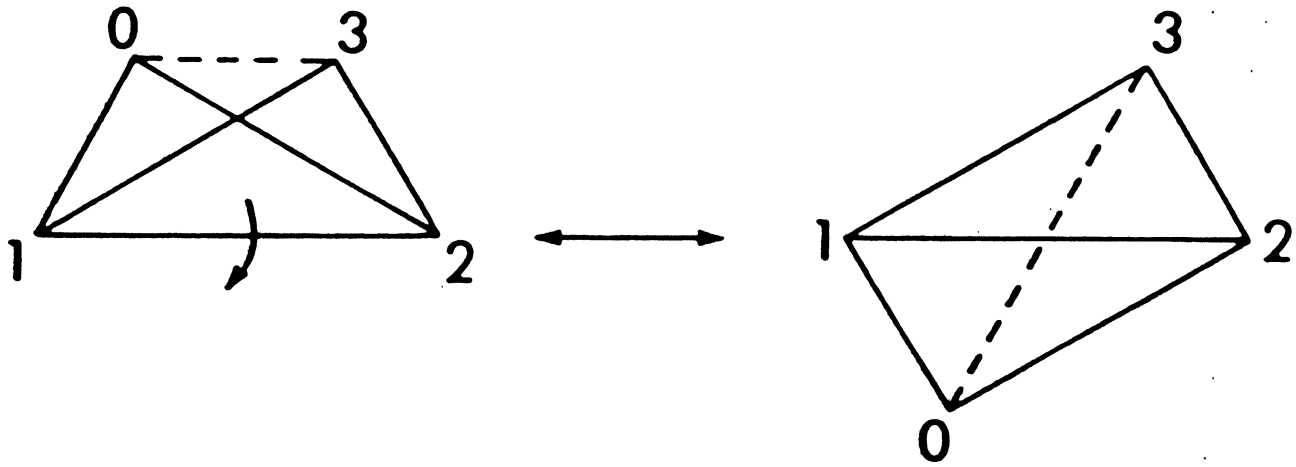
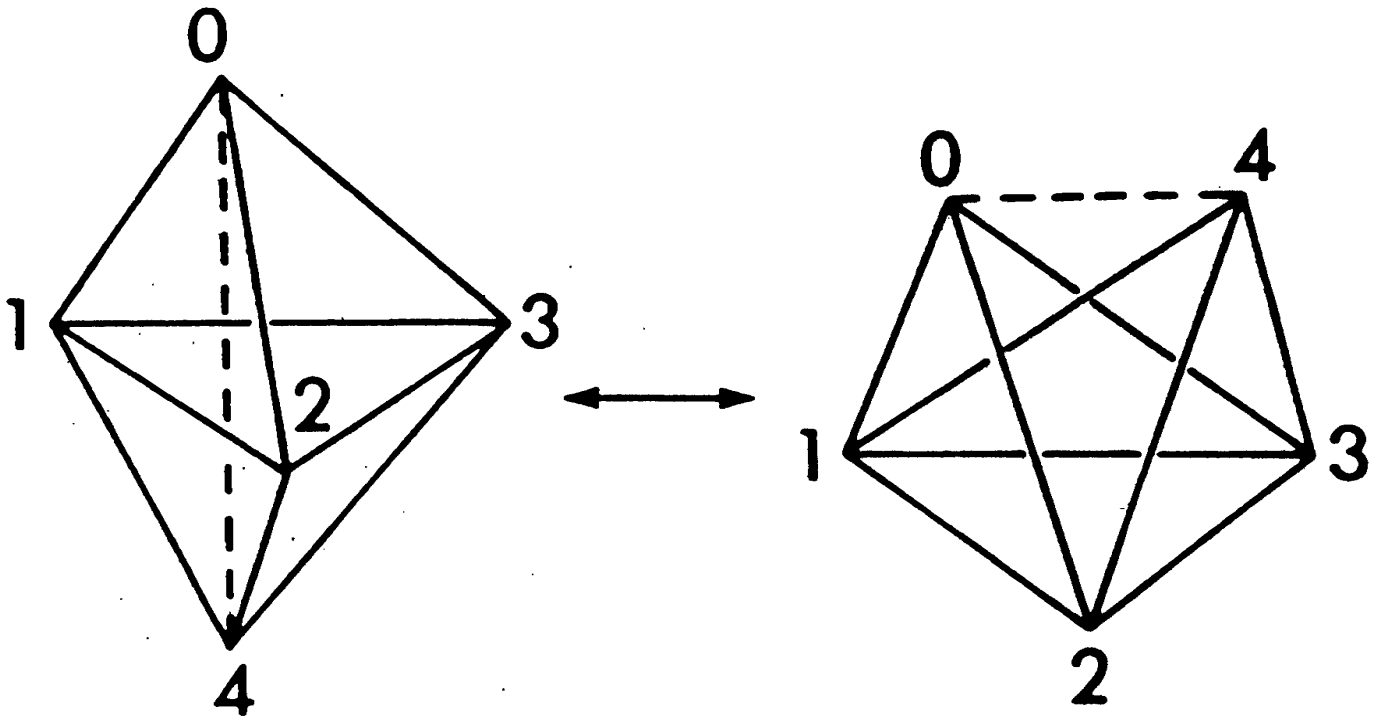


Figure 1. The two possible solutions of the tetrangle equality for a configuration of four points.



The two possible solutions of the pentangle equality for a configuration of five points.

DISTANCE GEOMETRY PROTOCOL

INPUT
Distance, Chirality and Torsion Constraints

BOUNDS SMOOTHING
Upper Triangle, Lower Triangle, Quadrangle

TRIAL DISTANCE SELECTION
Choose Distances between the Bounds

EMBEDDING
Compute Centroid, Metric Matrix, Principal Components, then Atomic Coordinates

REFINEMENT
Nonlinear Optimization to satisfy Constraints

KEY EQUATIONS

Metric Matrix = $g_{ij} = x_i * x_j$

$$d^2_{i0} = 1/N \sum d^2_{ij} - 1/N^2 \sum d^2_{jk}$$

$$g_{ij} = (d^2_{i0} + d^2_{j0} - d^2_{ij}) / 2$$

$$g_{ij} = \sum x_{ik} x_{jk} = \sum w_{ik} w_{jk} \lambda_k$$

$$x_{ik} = \lambda_k^{1/2} * w_{ik}$$

METRIZATION METHODS

Random Fractional
Triangle Correlated
Ordered Atom Based
Four-Point Atom-Based
Random Pair-Based (*)

(*) Uses a Modified Murchland Shortest Path Update Algorithm

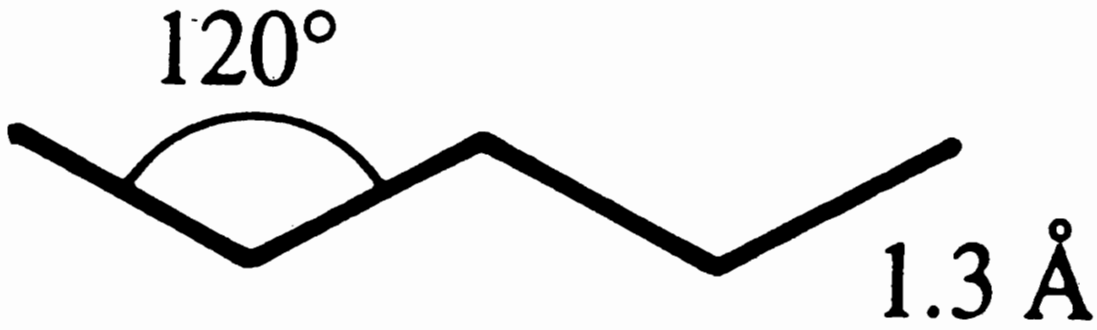


Fig. 8.15 Five-carbon fragment to illustrate distance geometry

initial bounds matrix

$$\begin{pmatrix} 0.0 & 1.3 & 2.2517 & 3.4395 & 99.0 \\ 1.3 & 0.0 & 1.3 & 2.2517 & 3.4395 \\ 2.2517 & 1.3 & 0.0 & 1.3 & 2.2517 \\ 2.6 & 2.2517 & 1.3 & 0.0 & 1.3 \\ 2.8 & 2.6 & 2.2517 & 1.3 & 0.0 \end{pmatrix}$$

smoothed bounds matrix

$$\begin{pmatrix} 0.0 & 1.3 & 2.2517 & 3.4395 & 4.5033 \\ 1.3 & 0.0 & 1.3 & 2.2517 & 3.4395 \\ 2.2517 & 1.3 & 0.0 & 1.3 & 2.2517 \\ 2.6 & 2.2517 & 1.3 & 0.0 & 1.3 \\ 2.8 & 2.6 & 2.2517 & 1.3 & 0.0 \end{pmatrix}$$

randomly assigned distance matrix

$$\begin{pmatrix} 0.0 & 1.3 & 2.25 & 3.11 & 3.42 \\ & 0.0 & 1.3 & 2.25 & 2.85 \\ & & 0.0 & 1.3 & 2.25 \\ & & & 0.0 & 1.3 \\ & & & & 0.0 \end{pmatrix}$$

We calculate the *metric matrix*, **G**, each of whose elements (i, j) is equal to the scalar product of the vectors from the origin to atoms i and j:

$$G_{ij} = \mathbf{i}.\mathbf{j} \tag{8.4}$$

The elements G_{ij} can be calculated from the distance matrix using the cosine rule:

$$G_{ij} = (d_{io}^2 + d_{jo}^2 - d_{ij}^2)/2 \tag{8.5}$$

d_{io} is the distance from the origin to atom i and d_{ij} is the distance between atoms i and j.

It is usual to take the centre of the molecule as the origin of the coordinate system. The distance of each atom from the centre can be calculated directly from the interatomic distances using the following expression:

$$d_{io}^2 = \frac{1}{N}\sum_{j=1}^{N} d_{ij}^2 - \frac{1}{N^2}\sum_{j=2}^{N}\sum_{k=1}^{j-1} d_{jk}^2 \tag{8.6}$$

The metric matrix **G** is a square symmetric matrix. A general property of such matrices is that they can be decomposed as follows:

$$\mathbf{G} = \mathbf{V}\mathbf{L}^2\mathbf{V}^T \tag{8.7}$$

The diagonal elements of $\mathbf{L}^2$ are the eigenvalues of **G** and the columns of **V** are its eigenvectors. The atomic coordinates can be derived from the metric matrix by rewriting equation (8.4) as

$$\mathbf{G} = \mathbf{X}\mathbf{X}^T \tag{8.8}$$

X is a matrix containing the atomic coordinates. Equating equations (8.7) and (8.8) gives $\mathbf{X} = \mathbf{V}\mathbf{L}$

$$\mathbf{X} = \mathbf{V}\mathbf{L} \tag{8.9}$$

As **L** has only diagonal entries, the matrix **L** is identical to its transpose: $\mathbf{L} = \mathbf{L}^T$. The atomic coordinates are thus obtained by multiplying the square roots of the eigenvalues by the eigenvectors.

metric matrix

$$\begin{pmatrix} 3.571 & 1.569 & -0.427 & -2.276 & -2.436 \\ 1.569 & 1.256 & 0.105 & -1.122 & -1.808 \\ -0.427 & 0.105 & 0.644 & 0.261 & -0.583 \\ -2.276 & -1.122 & 0.261 & 1.569 & 1.569 \\ -2.436 & -1.808 & -0.583 & 1.569 & 3.259 \end{pmatrix}$$

eigenvalues

8.18, 1.74, 0.26, 0.10 and 0.0

matrix of eigenvectors

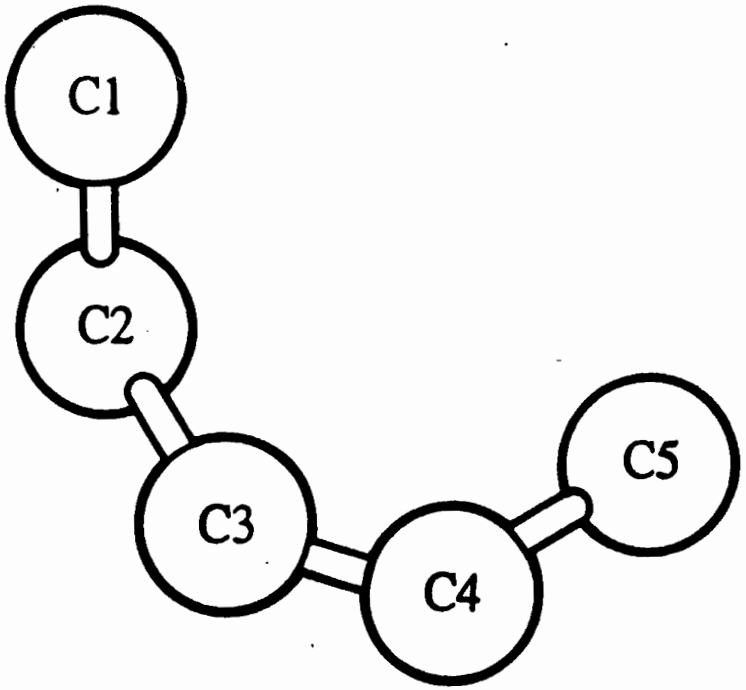
$$\mathbf{W} = \begin{pmatrix} 0.621 & 0.455 & -0.425 & 0.164 \\ 0.355 & -0.184 & 0.800 & 0.020 \\ 0.0 & -0.573 & -0.368 & -0.580 \\ -0.408 & -0.287 & -0.153 & 0.727 \\ -0.567 & 0.590 & 0.145 & -0.330 \end{pmatrix}$$

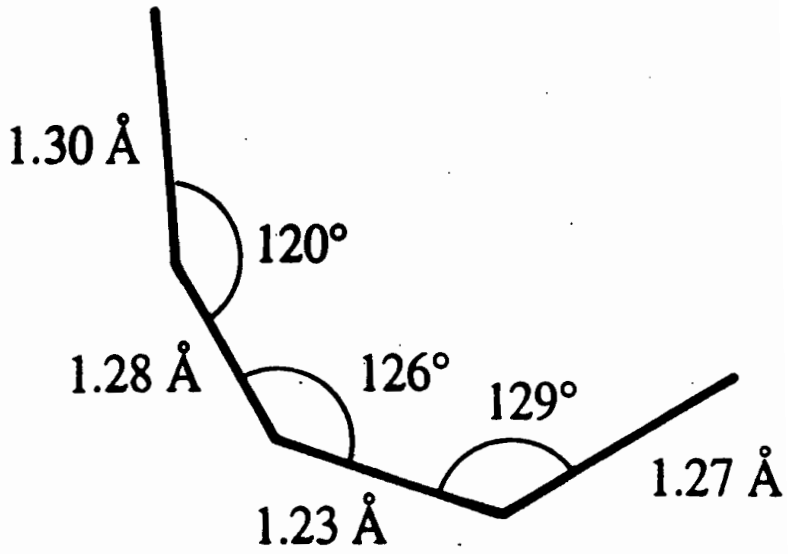
$$x_i = \sqrt{\lambda_1} W_{i1}$$

$$y_i = \sqrt{\lambda_2} W_{i2}$$

$$z_i = \sqrt{\lambda_3} W_{i3}$$

Atom	*x coordinate*	*y coordinate*	*z coordinate*
1	1.777	0.601	− 0.218
2	1.014	− 0.244	0.410
3	− 0.001	− 0.757	− 0.188
4	− 1.166	− 0.379	− 0.079
5	− 1.623	0.799	0.075





$$\begin{pmatrix} 0.0 & 1.299 & 2.24 & 3.10 & 3.42 \\ & 0.0 & 1.29 & 2.24 & 2.85 \\ & & 0.0 & 1.23 & 2.25 \\ & & & 0.0 & 1.25 \\ & & & & 0.0 \end{pmatrix}$$

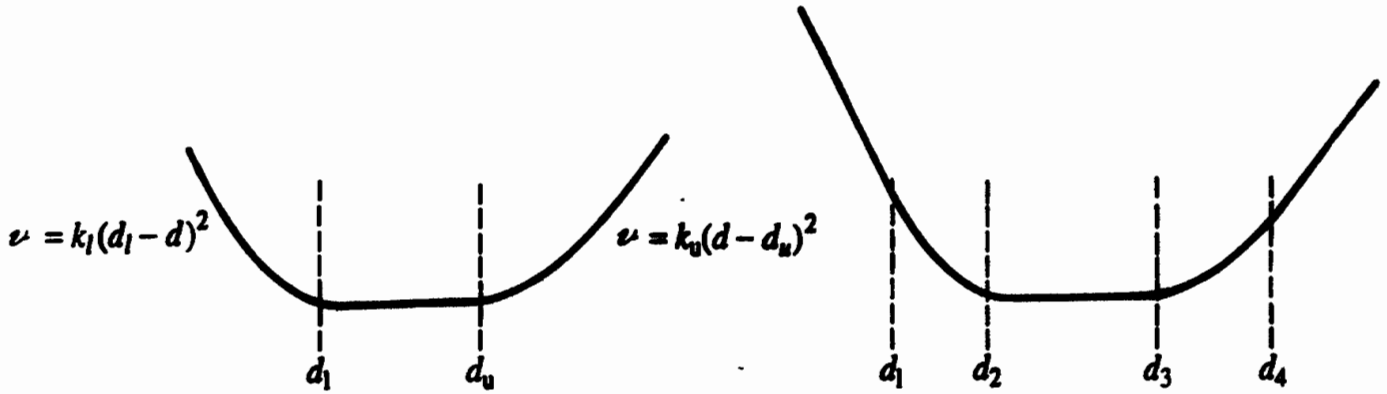


Fig. 8.23 A restraining potential that does not penalise structures in which the distance lies between the lower and upper distances d_l and d_u and uses harmonic functions outside this range (left). The harmonic potentials may also be replaced by linear restraints further from this region (right).

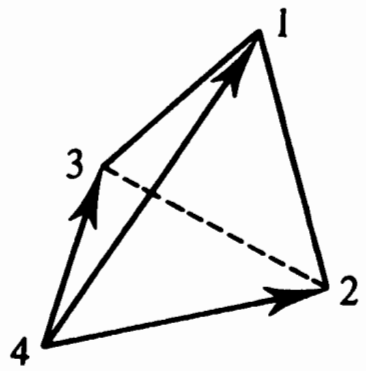


Fig. 8.17 The stereochemistry about tetrahedral atoms can be maintained with an appropriate chiral constraint.

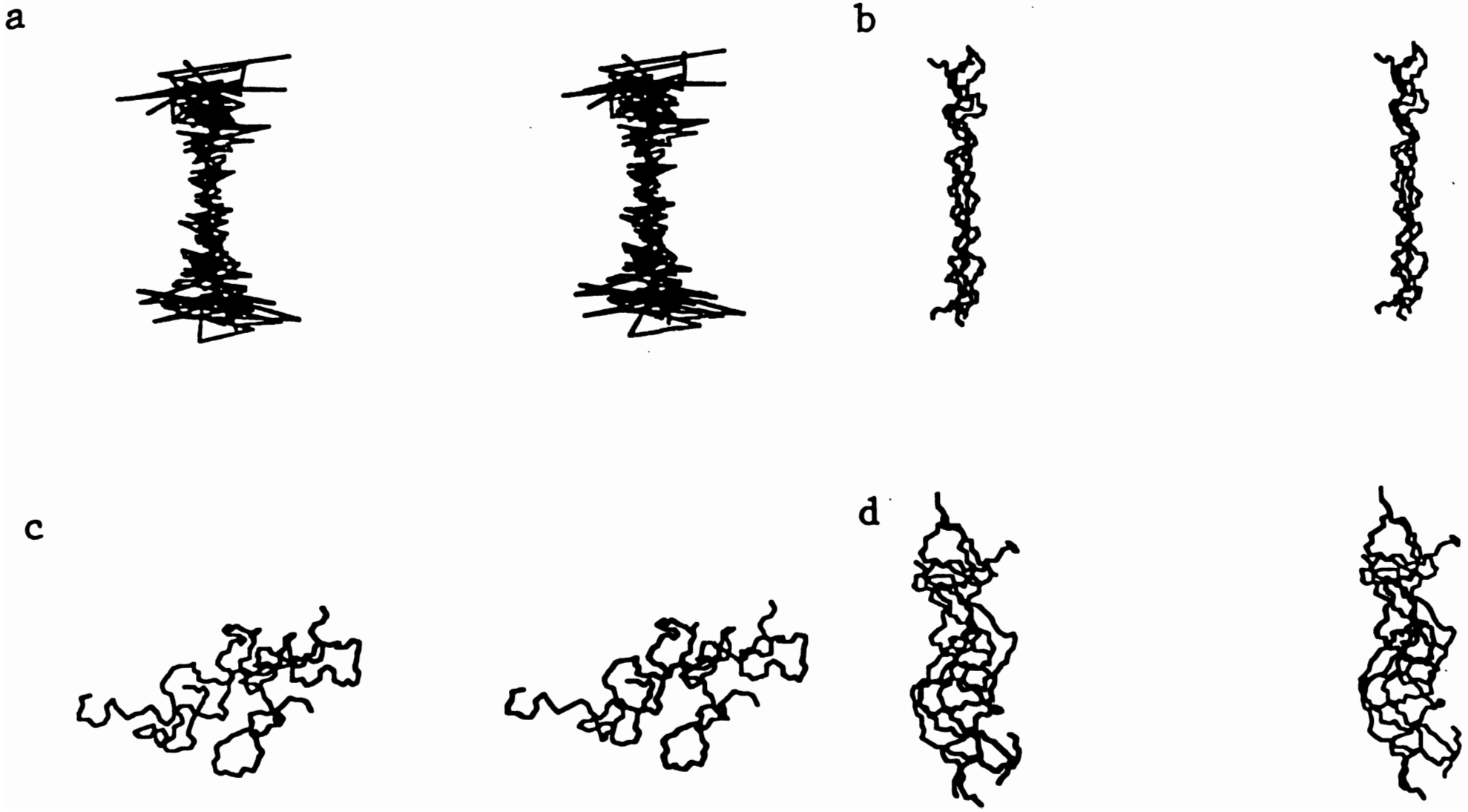
During the optimisation of the structure against the distance constraints it is usual to incorporate *chiral constraints*. These are used to ensure that the final conformation is the desired stereoisomer. Chiral constraints are necessary because the interatomic distances in two enantiomeric conformations are idential and as a consequence the 'wrong' isomer may quite legitimately be generated. Chiral constraints are usually incorporated into the error function as a chiral volume, calculated as a scalar triple product. For example, to maintain the correct stereochemistry about the tetrahedral atom number 4 in Figure 8.17, the following scalar triple product must be positive:

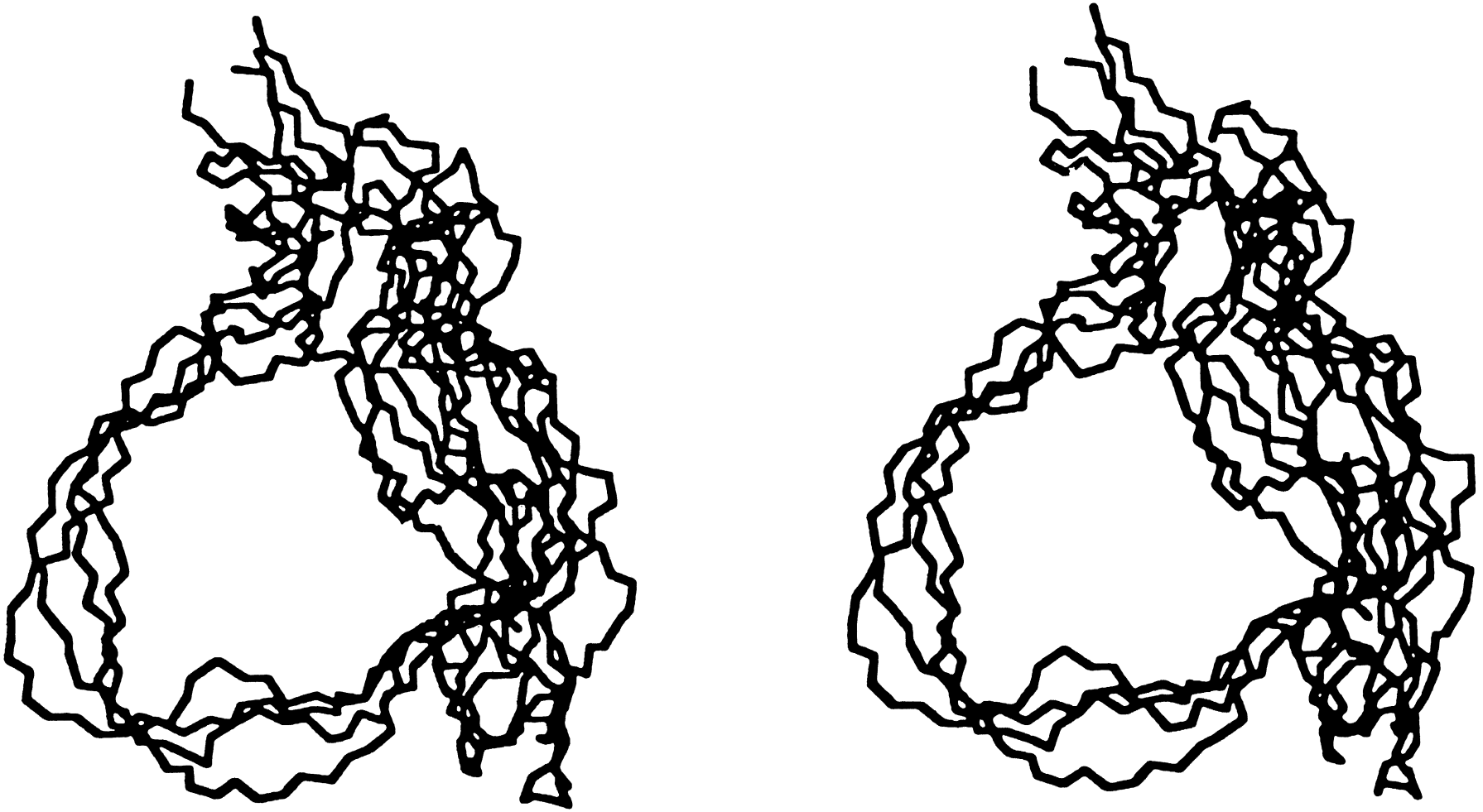
$$(\mathbf{v}_1 - \mathbf{v}_4).[(\mathbf{v}_2 - \mathbf{v}_4) \times (\mathbf{v}_3 - \mathbf{v}_4)] \tag{8.21}$$

The other stereoisomer corresponds to a negative chiral volume. Chiral constraints are included in the penalty function by adding terms of the following form:

$$(V_{ch} - V_{ch}^{*})^2 \tag{8.22}$$

V_{ch}^{*} is the desired value of the chiral constraint. Chiral constraints can also be used to force groups of atoms to lie in the same plane by requiring the chiral volume to have a value of zero.


a
b
c
d



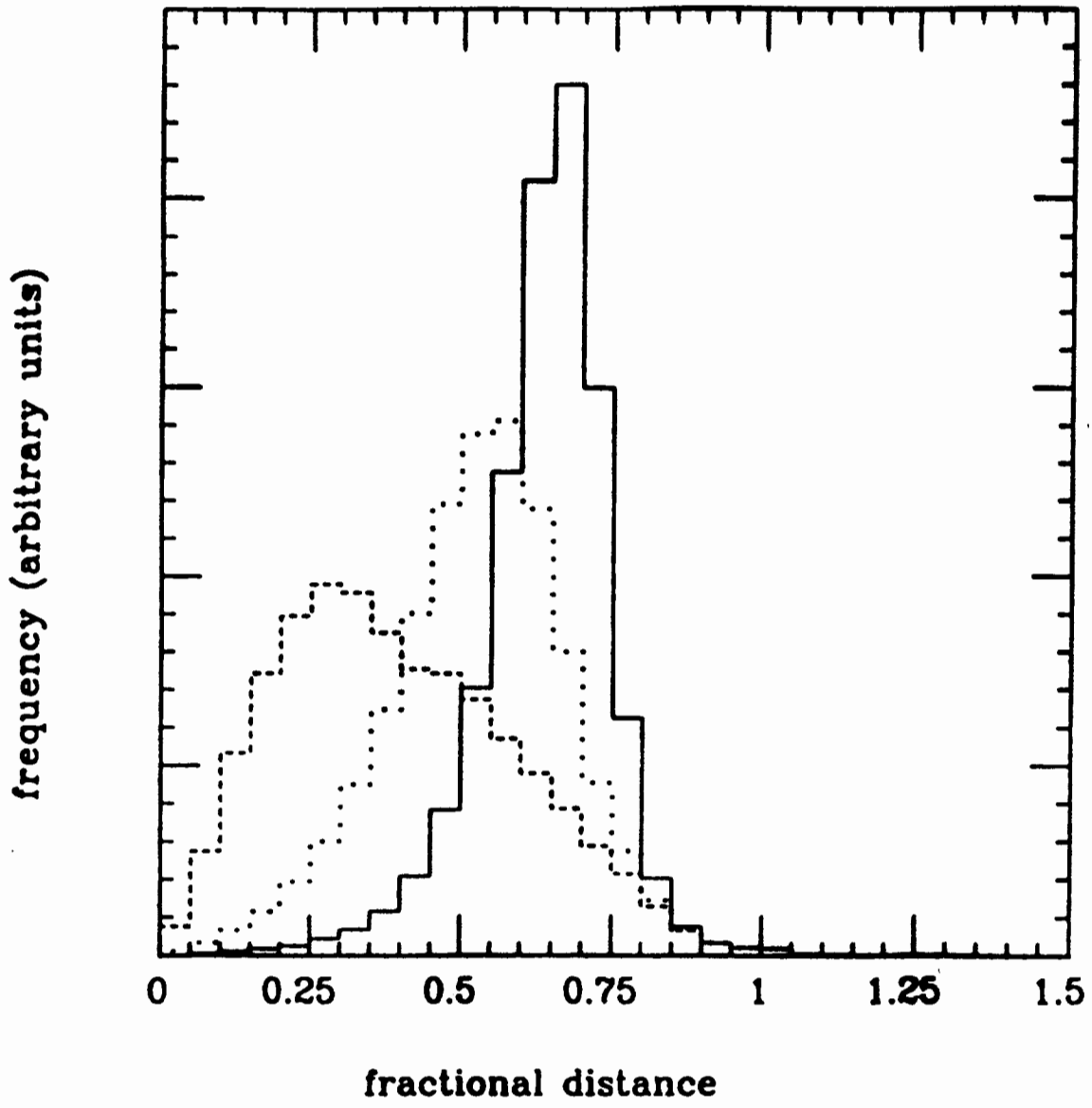


Figure 1. Histogram for the fractional distance, (distance(crystal) − lower bound)/(upper bound − lower-bound). Bounds taken from the all-(H-H) data set (solid line), 10% data set (dotted line) or disulfide-only data set (dashed line).

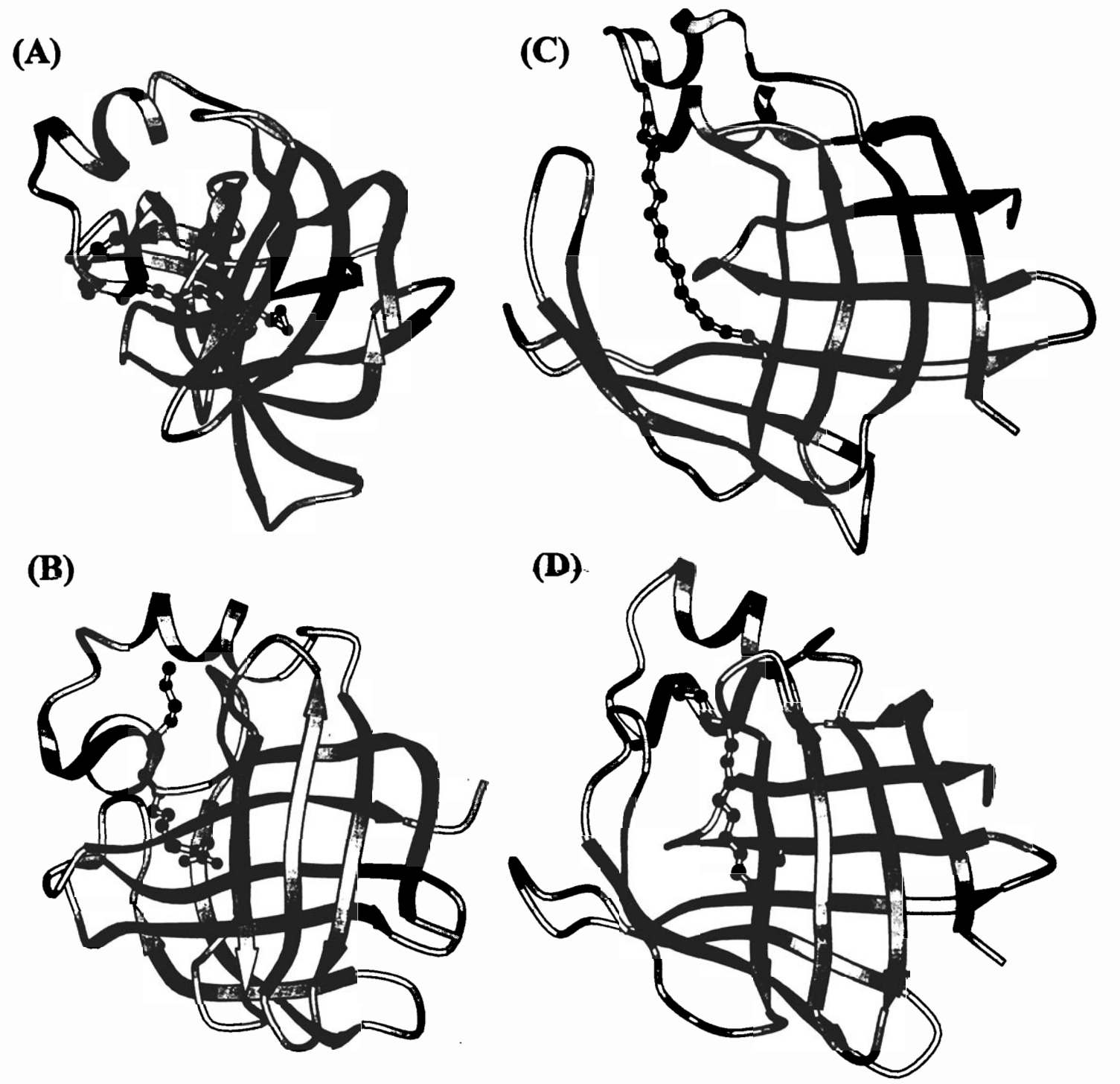


Figure 10. Ribbon diagrams illustrating the influence of the distance geometry metrization algorithm on the calculated structures both prior to ((A) and (C)) and after ((B) and (D)) simulated annealing refinement. All of the calculations were performed using DISTGEOM, which has the option of altering the trial distribution and the type of metrization employed. The structures in (A) and (B) were calculated using four-atom metrization with a uniform trial distribution; this is the type of algorithm implemented in X-PLOR version 3.1. The structures in (C) and (D) were c ·ılated using pairwise-5% metrization with an optimized Gaussian trial distribution. This latter algorithm was used ı .e current study. For reference, the correct positions of secondary structure elements, as defined by $^{1}H/^{13}C$ chemical shifts, are indicated in each ribbon diagram; this is not meant to imply that regions of the calculated structures shown here actually adopt ϕ/ψ angles consistent with regular α-helix and β-sheet, especially in the distorted structures shown on the left. All of the calculations used the final set of distance restraints listed in Table 3. The structures shown are examples from an ensemble of structures obtained for each set of calculations; other members of the ensemble showed the same general characteristics as shown here.

Protein Engineering: Map Distance Geometry Problem

Initial Table of Intercity Mileages :

	A	B	C	D	F	H	M	P
A	0	1084	715	1519	860	875	814	776
B	1084	0	976	2008	1902	1961	1069	308
C	715	976	0	1017	970	1073	95	767
D	1519	2008	1017	0	763	1038	1036	1770
F	860	1902	970	763	0	236	1064	1595
H	875	1961	1073	1038	236	0	1150	1648
M	814	1069	95	1036	1064	1150	0	849
P	776	308	767	1770	1595	1648	849	0

Applying Triangle Inequality to the Distances :

```
A to M Distance Changed from   814 to   810 via A --> C --> M
B to H Distance Changed from  1961 to  1959 via B --> A --> H
B to H Distance Changed from  1959 to  1956 via B --> P --> H
B to D Distance Changed from  2008 to  1993 via B --> C --> D
D to H Distance Changed from  1038 to   999 via D --> F --> H
```

Distance Geometry Metric Matrix :

	A	B	C	D	F	H	M	P
A	245203	159156	-108504	-512045	53837	117256	-126632	171728
B	159156	1248166	172302	-842907	-883683	-911418	131519	926866
C	-108504	172302	49014	26397	-144907	-173690	98811	80578
D	-512045	-842907	26397	1038068	528985	397501	61202	-697201
F	53837	-883683	-144907	528985	602071	650655	-186196	-620762
H	117256	-911418	-173690	397501	650655	754934	-204967	-630270
M	-126632	131519	98811	61202	-186196	-204967	157632	68631
P	171728	926866	80578	-697201	-620762	-630270	68631	700430

Distance from each City to the Map Centroid :

City	Distance to Centroid
A	495
B	1117
C	221
D	1019
F	776
H	869
M	397
P	837

Eigenvalues and Eigenvectors of Metric Matrix :

-164207.0202	-31467.5657	0.0000	4993.2342
0.7015	-0.1262	0.3536	-0.2326
-0.2545	-0.4255	0.3536	-0.2421
0.0964	0.7715	0.3536	-0.2294
0.3626	-0.2271	0.3536	0.1407
-0.4811	0.0921	0.3536	-0.4662
-0.2226	-0.1110	0.3536	0.4979
-0.1213	-0.2468	0.3536	-0.0569
-0.0811	0.2730	0.3536	0.5885
14258.5892	96761.3462	1028672.7147	3846507.8266
0.1134	0.0399	-0.5400	0.0821
-0.4188	-0.2519	0.0845	0.5697
-0.3758	0.1587	0.2177	0.0641
-0.0008	-0.3632	0.6044	-0.4182
0.3685	-0.2895	-0.2173	-0.3885
-0.4703	0.1887	-0.3910	-0.3944
0.3353	0.7708	0.2929	0.0617
0.4485	-0.2535	-0.0513	0.4236

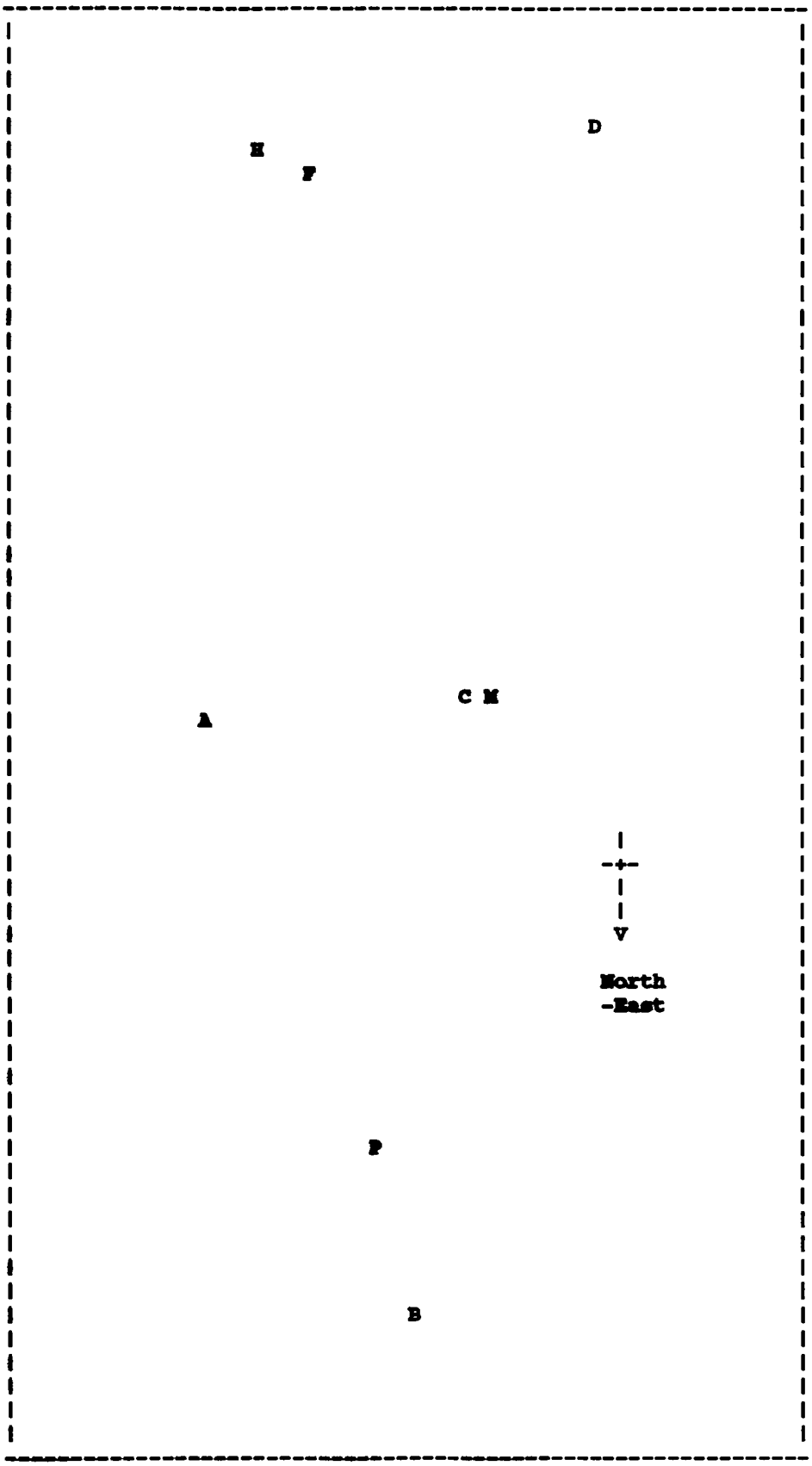
Distance Geometry Generated Map Coordinates :

City	X-Coordinate	Y-Coordinate
A	161	-548
B	1117	86
C	126	221
D	-820	613
F	-762	-220
H	-774	-397
M	121	297
P	831	-52

Final Table of Intercity Mileages :

	A	B	C	D	F	H	M	P
A	0	1147	769	1520	979	947	846	833
B	1147	0	1001	2008	1904	1951	1018	318
C	769	1001	0	1024	991	1091	76	756
D	1520	2008	1024	0	835	1011	993	1780
F	979	1904	991	835	0	177	1023	1602
H	947	1951	1091	1011	177	0	1132	1641
M	846	1018	76	993	1023	1132	0	791
P	833	318	756	1780	1602	1641	791	0

Map Showing the Locations of the Cities :


D
E
F
C M
A
North
-East
P
B