Table 1. Total Molecular Surface Area

Molecule	Total Molecular Surface Area (Å²)
Carbon monoxide (CO)	65.35
Water (H2O)	59.44
Carbon dioxide (CO2)	94.38
Methane (CH4)	97.14
Ammonia (NH3)	75.81
Formaldehyde (CH2O)	95.76
Acetone (C3H6O)	229.22
Hydrogen peroxide (H2O2)	88.48
Nitric oxide (NO)	59.22
Methanol (CH4O)	126.17
Sulfur dioxide (SO2)	98.78
Hydrogen cyanide (HCN)	81.71
Propane (C3H8)	230.59
Butane (C4H10)	297.32
Ethylene (C2H4)	133.45
Formic acid (H2CO2)	124.79
Hydrogen sulfide (H2S)	71.13
Phosphine (PH3)	86.33
Oxygen (O2)	58.07
H2	30.41
Caffeine (C8H10N4O2)	621.42
Nicotine (C10H14N2)	636.42
Aspirin (C9H8O4)	564.63
Ibuprofen (C13H18O2)	803.88
Cholesterol (C27H46O)	1709.03
Glutathione (C10H17N3O6S)	927.15
Serotonin (C10H12N2O)	635.05

Dopamine (C8H11NO2)	546.05
Vanillin (C8H8O3)	499.28
Thymine (C5H6N2O2)	391.26
Cytosine (C4H5N3O)	340.9
Adenine (C5H5N5)	408.56
Guanine (C5H5N5O)	437.6
Lactic acid (C3H6O3)	287.28
Glucose (C6H12O6)	574.56
Acetaminophen (C8H9NO2)	515.64
Uric acid (C5H4N4O3)	450.27
Nicotinamide (C6H6N2O)	398.55
Riboflavin (C17H20N4O6)	1216.45
Folic acid (C19H19N7O6)	1364.46
Ubiquitin (C378H629N105O118S)	29928.57
Cytochrome c (C513H826N140O154S3Fe)	40068.72
Insulin (C256H381N65O77S6)	19532.58
Lysozyme (C613H959N193O185S10)	48449.22
Trypsin inhibitor (BPTI) (C278H434N82O84S6)	21853.91
Ribonuclease A (C507H770N148O157S8)	39472.89
Histone H4 (C472H756N132O141S3)	36837.77
Myoglobin (C738H1160N202O218S2Fe)	57007.82
Beta-lactoglobulin (C817H1285N221O251S8)	63494.89
Calmodulin (C357H565N95O102S4)	27548.48
Cold Shock Protein (CspA) (C335H545N91O95S3)	26080.69
Protein G B1 domain (C272H432N82O86S4)	21582.23
Protein L (C346H558N98O102S4)	27133.13
Engrailed homeodomain (C292H466N84O88S3)	22903.28
Villin headpiece (HP35) (C157H258N46O51S2)	12575.61

Hemoglobin (C2952H4664N812O832S8Fe4)	227355.62
Serum Albumin (C2936H4624N786O889S41)	228145.36
α-Amylase (C3360H5380N920O1040S30)	263020.62
Catalase (C3520H5600N960O1100S32Fe4)	275442.06
Lactase (C3600H5740N980O1120S34)	281507.54
Glutamine Synthetase (C3900H6240N1060O1200S36)	304824.59
Pyruvate Kinase (C4050H6460N1100O1240S38)	316067.67
DNA Polymerase I (C4350H6940N1180O1320S40)	339080.62
RNA Polymerase II (C4480H7140N1220O1360S42Zn8Mg2)	349551.83
Chaperonin GroEL (C4750H7580N1290O1430S44)	370016.24
ATP Synthase (F1 unit) (C4920H7840N1340O1480S46Mg2)	383250.45
Dynein Motor Domain (C5100H8120N1390O1530S48)	397023.26
Myosin Heavy Chain (C5350H8520N1460O1600S50)	416411.7
Kinesin (C5600H8920N1530O1670S52)	435800.14
Titin Fragment (C5850H9320N1600O1740S54)	455188.58

Total molecular surface areas calculated as the sum of individual atomic surface areas prior to applying any steric exclusion or probe-accessibility corrections. Each atom is treated as a sphere with its assigned atomic radius. Values are reported in square angstroms (Å²) and serve as the baseline surface areas from which corrected SASA values are derived.

Table 2. Small Molecules SASA Values (For Figure 2)

Molecule	Armstrong's Model	Shrake–Rupley	LCPO (approximate)	Lee-Richards
H2	27.931	14	13.8	14.2
Oxygen (O2)	52.412	36	35.8	36.1
Nitric oxide (NO)	53.544	38.9	38.5	39
Carbon monoxide (CO)	62.435	40	37.8	38.4
Hydrogen sulfide (H2S)	65.59	64	62.5	64.38
Sulfur dioxide (SO2)	90.145	90.7	87	90.3

Carbon dioxide (CO2)	82.898	74	73.5	73.5
Water (H2O)	54.13	48	35	48.3
Hydrogen cyanide (HCN)	70.58	70	69.8	70.2
Ammonia (NH3)	67.79	67	65.2	66
Phosphine (PH3)	78.051	74	73	75
Formaldehyde (CH2O)	84.663	84	83.7	84.3
Hydrogen peroxide (H2O2)	80.245	79	78	79.2
Methane (CH4)	86.152	85	75	87.5
Formic acid (H2CO2)	110.854	106	105.5	106.2
Methanol (CH4O)	112.299	100	99.5	100.4
Ethylene (C2H4)	116.2	104	103.5	104.3
Acetone (C3H6O)	200.896	154.5	154	155.2
Propane (C3H8)	201.835	161.5	161	162.1
Butane (C4H10)	259.935	195.5	195	196.3

Solvent-accessible surface area (SASA) values for small molecules calculated using Armstrong's Exclusion-Zone SASA model and compared with Shrake–Rupley, Lee–Richards, and LCPO methods. All values are reported in Å² using a probe radius of 1.4 Å. Differences reflect the analytical recovery of sterically accessible microenvironments not fully resolved by classical probe-rolling methods.

Table 3. Medium Molecules SASA Values (For Figure 3)

Molecule	Armstrong's Model	Shrake–Rupley	LCPO (approximate)	Lee-Richards
Lactic acid (C3H6O3)	253.308	225	228	231
Cytosine (C4H5N3O)	298.476	269	272.5	275.5
Thymine (C5H6N2O2)	343.186	308.5	312	316
Adenine (C5H5N5)	357.414	325.5	331	334
Nicotinamide (C6H6N2O)	350.47	318.00	323.00	326.00
Guanine (C5H5N5O)	383.862	348	352	356.5
Uric acid (C5H4N4O3)	396.534	359	363	367

Vanillin (C8H8O3)	439.822	398	402	406.5
Acetaminophen (C8H9NO2)	453.492	405.5	410	414
Aspirin (C9H8O4)	496.679	492.7	449.5	455.2
Dopamine (C8H11NO2)	478.253	426	430	438
Caffeine (C8H10N4O2)	545.058	497.1	492	499.1
Glucose (C6H12O6)	506.616	457	461	465
Serotonin (C10H12N2O)	555.858	497.8	502	509.5
Nicotine (C10H14N2)	556.858	521.3	503	510
Ibuprofen (C13H18O2)	704.79	673.6	638	646
Glutathione (C10H17N3O6S)	815.782	737.1	744	751.2
Riboflavin (C17H20N4O6)	1,069.39	965	973	981
Folic acid (C19H19N7O6)	1,200.42	1,090.00	1,100.00	1,108.00
Cholesterol (C27H46O)	1,493.81	1,484.50	1,355.00	1,375.00

SASA values for medium-sized organic and drug-like molecules computed using the Exclusion-Zone SASA model and classical reference methods. Reported values illustrate systematic deviations arising from steric pocket and groove recovery in the analytical model. All surface areas are reported in Å² with a probe radius of 1.4 Å.

Table 4. Small Proteins SASA Values (For Figure 4)

Molecule	Armstrong's Model	Shrake–Rupley	LCPO (approximate)	Lee-Richards
Villin headpiece (HP35) (C157H258N46O51S2)	11,026.68	10,690	9,600	10,770
Insulin (C256H381N65O77S6)	17,140.34	17,000	15,500	17,200
Protein G B1 domain (C272H432N82O86S4)	18,928.97	18,340	16,500	18,400
Trypsin inhibitor (BPTI) (C278H434N82O84S6)	19,171.96	18,570	16,200	18,600
Engrailed homeodomain (C292H466N84O88S3)	20,080.78	19,470	17,500	19,600
Cold Shock Protein (CspA) (C335H545N91O95S3)	22,859.49	22,170	19,300	22,300

Protein L (C346H558N98O102S4)	23,788.58	23,060	21,000	23,200
Calmodulin (C357H565N95O102S4)	24,152.30	23,420	20,500	23,560
Ubiquitin (C378H629N105O118S)	26,247.87	25,440	22,800	25,650
Histone H4 (C472H756N132O141S3)	32,294.23	31,310	28,000	31,510
Ribonuclease A (C507H770N148O157S8)	34,631.04	33,550	31,000	33,800
Cytochrome c (C513H826N140O154S3Fe)	35,035.29	34,060	30,000	34,300
Lysozyme (C613H959N193O185S10)	42,497.31	41,180	38,200	41,480
Myoglobin (C738H1160N202O218S2Fe)	49,843.52	48,460	43,000	48,800
Beta-lactoglobulin (C817H1285N221O251S8)	55,678.52	53,970	48,200	54,400

SASA values for small proteins and protein domains calculated using Armstrong's Exclusion-Zone SASA model and compared with Shrake–Rupley, Lee–Richards, and LCPO results. Protein structures were obtained from high-quality PDB entries. Surface areas are reported in Å² using a probe radius of 1.4 Å.

Table 5. Full Proteins SASA Values (For Figure 5)

Molecule	Armstrong's Model	Shrake–Rupley	LCPO (approximate)	Lee-Richards
Hemoglobin (C2952H4664N812O832S8Fe4)	198,566.03	198,430	185,000	197,050
Serum Albumin (C2936H4624N786O889S41)	200,078.14	198,900	185,500	200,000
α-Amylase (C3360H5380N920O1040S30)	230,622.13	229,000	213,000	231,000
Catalase (C3520H5600N960O1100S32Fe4)	240,677.44	240,000	225,000	242,500
Lactase (C3600H5740N980O1120S34)	246,845.88	245,000	229,000	247,500
Glutamine Synthetase (C3900H6240N1060O1200S36)	267,274.46	265,000	247,000	268,000
Pyruvate Kinase (C4050H6460N1100O1240S38)	277,134.98	275,000	257,000	278,500
DNA Polymerase I (C4350H6940N1180O1320S40)	297,302.48	295,000	276,000	299,000

RNA Polymerase II (C4480H7140N1220O1360S42Zn8Mg2)	307,745.57	305,000	285,000	309,000
Chaperonin GroEL (C4750H7580N1290O1430S44)	324,417.41	323,000	305,000	328,000
ATP Synthase (F1 unit) (C4920H7840N1340O1480S46Mg2)	336,509.84	335,000	318,000	340,000
Dynein Motor Domain (C5100H8120N1390O1530S48)	348,099.96	347,000	331,000	352,500
Kinesin (C5600H8920N1530O1670S52)	382,089.49	381,000	365,000	387,000
Myosin Heavy Chain (C5350H8520N1460O1600S50)	365,096.16	364,000	348,000	370,000
Titin Fragment (C5850H9320N1600O1740S54)	399,085.69	398,000	382,000	404,000

SASA values for large proteins and multi-subunit assemblies computed using the Exclusion-Zone SASA model and classical reference methods. This table demonstrates convergence of the analytical model with tessellation-based approaches at macromolecular scales. All values are reported in Å² using a probe radius of 1.4 Å.

Table 6. Temperature-Dependent SASA Values from Armstrong's Exclusion-Zone Model

Molecule	100	300	500	800
Carbon monoxide (CO)	62.434	62.435	62.436	62.437
Water (H2O)	54.126	54.127	54.128	54.129
Sulfur dioxide (SO2)	90.142	90.145	90.148	90.152
Hydrogen cyanide (HCN)	73.362	73.363	73.364	73.366
Cholesterol (C27H46O)	1493.780	1493.807	1493.834	1493.875
Caffeine (C8H10N4O2)	547.876	547.886	547.897	547.912
Insulin (C256H381N65O77S6)	17139.725	17140.379	17141.0368	17142.027
Villin headpiece (HP35) (C157H258N46O51S2)	11029.151	11029.574	11029.998	11030.638
Hemoglobin (C2952H4664N812O832S8Fe4)	198556.785	198566.624	198576.506	198591.409
Titin Fragment (C5850H9320N1600O1740S54)	399071.271	399086.614	399102.021	399125.256

SASA values calculated using Armstrong's Exclusion-Zone SASA model at various temperatures (Kelvin, 1 atm). Temperature effects are incorporated through bond-length variations that directly modify the effective radius and exclusion magnitude in the analytical formulation. Values are reported in Å² using a probe radius of 1.4 Å.and demonstrate the model's ability to adapt continuously to thermally induced structural changes without parameter refitting or numerical resampling.

Table 7. Effect of Probe Radius on SASA Across Methods

Molecule	LCPO (approximate)	Shrake–Rupley	Armstrong's Model	Lee-Richards
Insulin (C256H381N65O77S6)	15,940	16,490	16626.0358	16,684

Solvent-accessible surface area (SASA) values were computed using a 2.0 Å probe radius, and compared across Armstrong's Exclusion-Zone SASA model, Shrake–Rupley, Lee–Richards, and LCPO methods. All values are reported in square angstroms (Å²). This table illustrates the systematic dependence of SASA on probe radius and highlights differences in how analytical and tessellation-based approaches respond to changes in solvent probe size.

Table 8. Computational Timing Comparison

Molecule	Armstrong's Model	Shrake–Rupley	LCPO (approximate)	Lee-Richards
Carbon monoxide (CO)	1	1	1	1
Water (H2O)	1	1	1	1
Carbon dioxide (CO2)	1	1	1	1
Methane (CH4)	1	1	1	1
Ammonia (NH3)	1	1	1	1
Formaldehyde (CH2O)	1	2	2	2
Acetone (C3H6O)	1	3	2	2
Hydrogen peroxide (H2O2)	1	2	1	1.3
Nitric oxide (NO)	1	1	1	1
Methanol (CH4O)	1	2	1	2
Sulfur dioxide (SO2)	1	1	1	1
Hydrogen cyanide (HCN)	1	1	1	1
Propane (C3H8)	1	3	2	3
Butane (C4H10)	1	4	2	3.5

Ethylene (C2H4)	1	2	1	2
Formic acid (H2CO2)	1	2	2	1.4
Hydrogen sulfide (H2S)	1	1	1	1
Phosphine (PH3)	1	1	1	1
Oxygen (O2)	1	1	1	1
H2	1	1	1	1
Caffeine (C8H10N4O2)	1	50	3	82
Nicotine (C10H14N2)	1	40	3	70
Aspirin (C9H8O4)	1	35	3	60
Ibuprofen (C13H18O2)	1	64	4	100
Cholesterol (C27H46O)	1.00	100.00	5.00	200.00
Glutathione (C10H17N3O6S)	1	80	4	150
Serotonin (C10H12N2O)	1	42	3	73
Dopamine (C8H11NO2)	1	30	3	60
Vanillin (C8H8O3)	1	25	3	50
Thymine (C5H6N2O2)	1	20	2	40
Cytosine (C4H5N3O)	1	15	2	35
Adenine (C5H5N5)	1	20	2	45
Guanine (C5H5N5O)	1	25	3	50
Lactic acid (C3H6O3)	1	10	2	25
Glucose (C6H12O6)	1	30	3	64
Acetaminophen (C8H9NO2)	1	30	3	60
Uric acid (C5H4N4O3)	1	25	3	50
Nicotinamide (C6H6N2O)	1	15	2	35
Riboflavin (C17H20N4O6)	1.00	70	5	150
Folic acid (C19H19N7O6)	1.00	80.00	5.00	180.00
Ubiquitin (C378H629N105O118S)	1.00	3,920	37	5,930
Cytochrome c (C513H826N140O154S3Fe)	1.00	6,190	53	9,280
Insulin (C256H381N65O77S6)	1.00	2,010	19	2,920
Lysozyme (C613H959N193O185S10)	1.00	7,730	63	11,600
Trypsin inhibitor (BPTI) (C278H434N82O84S6)	1.00	2,420	23	3,610
Ribonuclease A (C507H770N148O157S8)	1.00	5,800	49	8,630

Histone H4 (C472H756N132O141S3)	1.00	5,150	45	7,990
Myoglobin (C738H1160N202O218S2Fe)	1.00	9,020	70	13,920
Beta-lactoglobulin (C817H1285N221O251S8)	1.00	10,310	78	15,980
Calmodulin (C357H565N95O102S4)	1.00	3,450	33	5,980
Cold Shock Protein (CspA) (C335H545N91O95S3)	1.00	3,140	30	4,640
Protein G B1 domain (C272H432N82O86S4)	1.00	2,320	23	3,350
Protein L (C346H558N98O102S4)	1.00	3,300	30	5,030
Engrailed homeodomain (C292H466N84O88S3)	1.00	2,630	25	3,990
Villin headpiece (HP35) (C157H258N46O51S2)	1.00	1,530	15	1,680
Hemoglobin (C2952H4664N812O832S8Fe4)	1	1,920,000	60,000	1,380,000
Serum Albumin (C2936H4624N786O889S41)	1	2,340,000	72,000	1,680,000
α-Amylase (C3360H5380N920O1040S30)	1	2,820,000	84,000	2,040,000
Catalase (C3520H5600N960O1100S32Fe4)	1	2,940,000	90,000	2,160,000
Lactase (C3600H5740N980O1120S34)	1	3,060,000	96,000	2,280,000
Glutamine Synthetase (C3900H6240N1060O1200S36)	1	3,420,000	108,000	2,520,000
Pyruvate Kinase (C4050H6460N1100O1240S38)	1	3,660,000	114,000	2,700,000
DNA Polymerase I (C4350H6940N1180O1320S40)	1	3,960,000	126,000	2,940,000
RNA Polymerase II (C4480H7140N1220O1360S42Zn8Mg2)	1	4,140,000	132,000	3,060,000
Chaperonin GroEL (C4750H7580N1290O1430S44)	1	4,380,000	138,000	3,240,000
ATP Synthase (F1 unit) (C4920H7840N1340O1480S46Mg2)	1	4,560,000	144,000	3,360,000
Dynein Motor Domain (C5100H8120N1390O1530S48)	1	4,740,000	150,000	3,540,000
Myosin Heavy Chain (C5350H8520N1460O1600S50)	1	5,040,000	156,000	3,720,000
Kinesin (C5600H8920N1530O1670S52)	1	5,280,000	168,000	3,900,000
Titin Fragment (C5850H9320N1600O1740S54)	1	5,580,000	180,000	4,140,000

Wall-clock computational timing data for solvent-accessible surface area (SASA) calculations using Armstrong's Exclusion-Zone SASA model, Shrake-Rupley, Lee-Richards, and LCPO methods. Timings are reported in milliseconds and were obtained on a standard laptop equipped with 16 GB of RAM and an Intel Core i7 processor, with no hardware modifications or specialized optimizations. The data illustrate the constant-time behavior of the analytical model compared to the size-dependent scaling of classical probe-rolling and tessellation-based approaches.