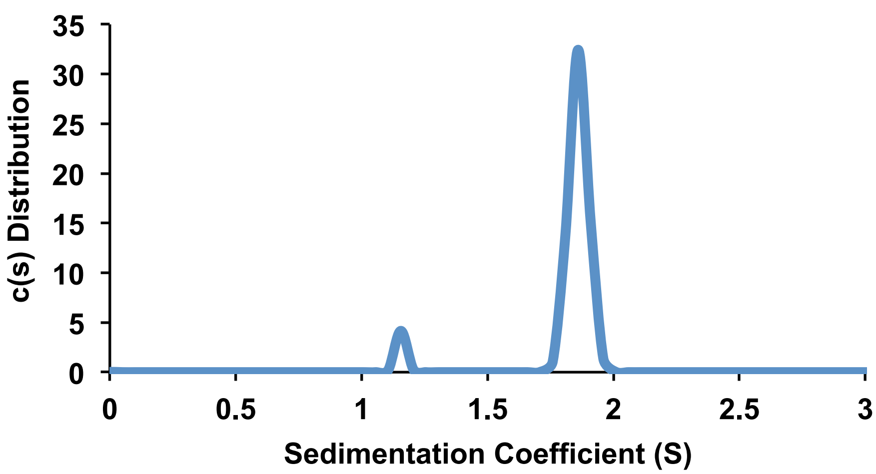
```
                        3              4      5                 6+7
HSPB1    GVSEIRHTADRWRVSLDVNHFAPDELTVKTKDGVVEITGKHEERQDEHG---YISRCFTRKYT 143
CRYAB    GLSEMRLEKDRFSVNLDVKHFSPEELKVKVLGDVIEVHGKHEERQDEHG---FISREFHRKYR 123
CRYAA    GISEVRSDRDKFVIFLDVKHFSPEDLTVKVQDDFVEIHGKHNERQDDHG---YISREFHRRYR 119
HSPB6    PVAQVPTDPGHFSVLLDVKHFSPEEIAVKVVGEHVEVHARHEERPDEHG---FVAREFHRRYR 122
HSPB7    GAGNIKTLGDAYEFAVDVRDFSPEDIIVTTSNNHIEVRA---EKLAADG---TVMNTFAHKCQ 127
HSPB8    GRTPPPFPGEPWKVCVNVHSFKPEELMVKTKDGYVEVSGKHEEKQQEGG---IVSKNFTKKIQ 144
HSPB9    AQEDNDHARDGFQMKLDAHGFAPEELVVQVDGQWLMVTGQQQLDVRDPERVSYRMSQKVHRKM 105
HSPB3    AETPPREGKSHFQILLDVVQFLPEDIIIQTFEGWLLIKAQHGTRMDEHG---FISRSFTRQYK 119
HSPB2    GASELRLSEGKFQAFLDVSHFTPDEVTVRTVDNLLEVSARHPQRLDRHG---FVSREFCRTYV 122
                    :   ::.  * *::: : .    : : .                    :

                    8         9
HSPB1    LPPGVDPTQVSSSLSPEGTLTVEAPMPKL 172
CRYAB    IPADVDPLTITSSLSSDGVLTVNGPRKQV 152
CRYAA    LPSNVDQSALSCSLSADGMLTFCGPKIQT 148
HSPB6    LPPGVDPAAVTSALSPEGVLSIQAAPASA 151
HSPB7    LPEDVDPTSVTSALREDGSLTIRARRHPH 156
HSPB8    LPAEVDPVTVFASLSPEGLLIIEAPQVPP 173
HSPB9    LPSNLSPTAMTCCLTPSGQLWVRGQCVAL 134
HSPB3    LPDGVEIKDLSAVLCHDGILVVEVKDPVG 148
HSPB2    LPADVDPWRVRAALSHDGILNLEAPRGGR 151
         :*  :.   : . *  .* * .
```

Supplemental Figure 1. Sequence alignment of ACDs from nine human sHSPs performed with Clustal Omega (Sievers et al, 2011 “Fast scalable generation of high-quality protein multiple sequence alignments using Clustal Omega”. Mol. Systems Biol. 539). Residues analogous to Cys137 in HSPB1 are highlighted in red. CRYAA and CRYAB are alternate names for HSPB4 and HSPB5, respectively.



Supplemental Figure 2. Sedimentation velocity analysis of reduced HSPB1-ACD. Protein was dialyzed against 50 mM sodium phosphate buffer, pH 7.5, 100 mM NaCl, 5 mM DTT. Sedimentation velocity was measured on a sample of 100 μM HSPB1-ACD at 20 °C at a rotor speed of 50,000 rpm. Under these conditions, the ACD sediments predominantly as a dimer ($S_{20,w}$ ~ 1.9), and < 10% of the protein sediments as a monomer ($S_{20,w}$ ~ 1.2). Sedimentation velocity experiments were conducted on a Beckman Coulter XL-A/XL-I analytical centrifuge and data were analyzed using the program SEDFIT to obtain a c(s) distribution.