

and presented by cells expressing the respective protein²¹. From this we conclude that more peptides can bind to MHC molecules than are processed by cells. Taking into account the strong adherence of naturally processed peptides to the MHC-restricted motifs, we also conclude that these motifs are not 'peptide binding motifs', but motifs representing the outcome of processing, which is likely to include MHC-dependent and MHC-independent protease activities^{8,9} and transport mechanisms²²⁻²⁴. Intracellular binding to MHC molecules of epitopes correctly processed without participation of MHC molecules cannot entirely be excluded, although it is unlikely, given our

inability to find intracellularly correctly processed epitopes independent of MHC⁸. Thus peptide binding to MHC molecules is a necessary requirement for a peptide being an MHC-restricted epitope but is not sufficient on its own.

Knowledge of the peptide motifs of individual MHC alleles should help exact T-cell epitope predictions (K.F. *et al.*, manuscript submitted; K. Deres *et al.*, unpublished) and help with synthetic or recombinant vaccine development and potentially also for intervention in autoimmune diseases or graft rejection. □

Received 6 February; accepted 4 April 1991.

1. Zinkernagel, R. M. & Doherty, P. C. *Nature* **248**, 701-702 (1974).
2. Townsend, A. R. *et al. Cell* **44**, 959-968 (1986).
3. Bjorkman, P. J. *et al. Nature* **329**, 512-518 (1987).
4. Rötzschke, O. *et al. Nature* **348**, 252-254 (1990).
5. Van Bleek, G. M. & Nathenson, S. G. *Nature* **348**, 213-216 (1990).
6. Garrett, T. P. J., Saper, M. A., Bjorkman, P. J., Strominger, J. L. & Wiley, D. C. *Nature* **343**, 692-696 (1989).
7. Rötzschke, O., Falk, K., Wallny, H.-J., Faath, S. & Rammensee, H.-G. *Science* **249**, 283-287 (1990).
8. Falk, K., Rötzschke, O. & Rammensee, H.-G. *Nature* **348**, 248-251 (1990).
9. Shimonkevitz, R., Kappler, J., Marrack, P. & Grey, H. *J. exp. Med.* **158**, 303-316 (1983).
10. Demotz, S., Grey, H. M., Appella, E. & Sette, A. *Nature* **343**, 682-684 (1989).
11. Bjorkman, P. J. *et al. Nature* **329**, 506-512 (1987).
12. DeLisi, C. & Berzofsky, J. A. *Proc. natn. Acad. Sci. U.S.A.* **82**, 7048-7052 (1985).
13. Rothbard, J. B. & Taylor, W. R. *EMBO J.* **7**, 93-100 (1988).
14. Cornette, J. L., Margalit, H., DeLisi, C. & Berzofsky, J. A. *Meth. Enzym.* **178**, 611-633 (1989).
15. Sette, A. *et al. Proc. natn. Acad. Sci. U.S.A.* **86**, 3296-3300 (1989).
16. Maryanski, J. L., Verdini, A. S., Weber, P. C., Salemme, F. R. & Corradin, G. *Cell* **60**, 63-72 (1990).
17. Bastin, J., Rothbard, J., Davey, J., Jones, I. & Townsend, A. *J. exp. Med.* **165**, 1508-1523 (1987).
18. Bjorkman, P. J. & Davis, M. M. *Cold Spring Harb. Symp. quant. Biol.* **54**, 365-374 (1989).
19. Bouillot, M. *et al. Nature* **339**, 473-475 (1989).
20. Frelinger, J. A., Gotch, F. M., Zweerink, H., Wain, E. & McMichael, A. J. *J. exp. Med.* **172**, 827-834 (1990).
21. Schild, H., Rötzschke, O., Kalbacher, H. & Rammensee, H.-G. *Science* **247**, 1587-1589 (1990).
22. Townsend, A. *et al. Nature* **340**, 443-448 (1989).
23. Elliott, T., Townsend, A. & Cerundolo, V. *Nature* **348**, 195-197 (1990).
24. Cerundolo, V. *et al. Nature* **345**, 449-452 (1990).
25. Rüschoff, E., Kuon, W. & Hämmerling, G. J. *Trans. Proc.* **15**, 2093-2096 (1983).

26. Lemke, H., Hämmerling, G. J. & Hämmerling, U. *Immunol. Rev.* **47**, 175-206 (1979).
27. Ozato, K. & Sachs, D. H. *J. Immunol.* **126**, 317-321 (1981).
28. Parham, P. & Brodsky, F. M. *Hum. Immunol.* **3**, 277-299 (1981).
29. Taylor, P. M., Davey, J., Howland, K., Rothbard, J. B. & Askonas, B. A. *Immunogenetics* **26**, 267-272 (1987).
30. Braciale, T. J. *et al. J. exp. Med.* **166**, 678-692 (1987).
31. Braciale, T. J., Sweetser, M. T., Morrison, L. A., Kittlesen, D. J. & Braciale, V. L. *Proc. natn. Acad. Sci. U.S.A.* **86**, 277-281 (1989).
32. Kuwano, K., Braciale, T. J. & Ennis, F. A. *FASEB J.* **2**, 2221 (1988).
33. Maryanski, J. L., Pala, P., Cerottini, J. C. & Corradin, G. *J. exp. Med.* **167**, 1391-1405 (1988).
34. Maryanski, J. L., Pala, P., Corradin, G., Jordan, B. R. & Cerottini, J. C. *Nature* **324**, 578-579 (1986).
35. Sibille, C. *et al. J. exp. Med.* **172**, 35-45 (1990).
36. Romero, P. *et al. Nature* **341**, 323-326 (1989).
37. Weiss, W. R. *et al. J. exp. Med.* **171**, 763-773 (1990).
38. Kast, W. M. *et al. Cell* **59**, 603-614 (1989).
39. Oldstone, M. B. A., Whitton, J. L., Lewicki, H. & Tishon, A. *J. exp. Med.* **168**, 559-570 (1988).
40. Tevethia, S. S. *et al. J. Virol.* **64**, 1192-1200 (1990).
41. Carbone, F. R. & Bevan, M. J. *J. exp. Med.* **169**, 603-612 (1989).
42. Schumacher, T. N. M. *et al. Cell* **62**, 563-567 (1990).
43. Walker, B. D. *et al. Proc. natn. Acad. Sci. U.S.A.* **86**, 9514-9518 (1989).
44. Gotch, F., McMichael, A. & Rothbard, J. *J. exp. Med.* **168**, 2045-2057 (1988).
45. Santos-Aguado, J., Crimmins, M. A. V., Mentzer, S. J., Burakoff, S. J. & Strominger, J. L. *Proc. natn. Acad. Sci. U.S.A.* **86**, 8936-8940 (1989).
46. Claverie, J. M. *et al. Eur. J. Immunol.* **18**, 1547-1553 (1988).
47. Falk, K. *et al. J. exp. Med.* (in the press).

ACKNOWLEDGEMENTS. We thank J. Klein for support, A. Townsend for cell lines, S. Faath for technical assistance, and L. Yakes for typing the manuscript. This work was supported by Sonderforschungsbereich 120 and 323.

LETTERS TO NATURE

Statistical evidence for a galactic origin of gamma-ray bursts

J. L. Atteia*, C. Barat*, E. Jourdain*, M. Niel*, G. Vedrenne*, N. Blinov*, A. Chernenko†, V. Dolidze†, A. Kozlenkov†, A. Kuznetsov†, I. G. Mitrofanov†, A. Pozanenko†, R. Sunyaev† & O. Terekhov†

* Centre d'Etude Spatiale des Rayonnements, 9 Avenue du Colonel Roche, BP 4346, 31029 Toulouse Cedex, France

† Space Research Institute, Profsoyuznaya 84/32, 117810 Moscow, USSR

ASTRONOMICAL bursts of gamma-rays (GRBs) were first discovered 20 years ago, and ~100 are recorded every year by satellite-borne instruments. Bursts last for at most a few seconds, recur only on a timescale of years, if at all, and come from objects which have remained undetected at all other wavelengths. It has been impossible to establish a distance scale for GRBs, and no association with known astronomical objects has been demonstrated. Here we analyse the spatial distribution of GRBs^{1,2} with a view to understanding their true radial distribution. Our data consist of three samples, totalling 244 GRBs, obtained by three French-Soviet experiments flown on the Venera 13 and 14 and the Phobos missions. We conclude that the underlying GRB distribution is not uniformly distributed in space, but falls off with distance. Our analysis of the weak sources in particular suggests that GRBs are associated with the galactic plane.

There has recently been interest in using the V/V_{\max} distribution to study the radial distribution of the sources^{3,4}, where for a given burst V is the volume of the smallest sphere containing the source, and V_{\max} is the maximum volume accessible to the

instrument. This ratio is defined as follows: if D is the (unknown) distance of the GRB source and D_{\max} the maximum distance at which it can be detected, then $V/V_{\max} = (D/D_{\max})^3$, and as the number of detected counts, C , scales as D^{-2} , we can write $V/V_{\max} = (C_{\max}/C_{\min})^{-3/2}$ where C_{\max} is the maximum number of counts and C_{\min} the minimum number required to detect a burst. The V/V_{\max} distribution is free of instrumental selection effects as long as C_{\max} and C_{\min} are calculated in the same time intervals and energy range as those used to trigger the experiment³ (detailed analysis shows that some bias can still affect the V/V_{\max} distribution; Hartmann *et al.*, manuscript in preparation). If the number of sources per unit volume is constant, corresponding to an infinite uniform density population, the V/V_{\max} values are uniformly distributed between 0 and 1. Here we present the V/V_{\max} distribution for bursts detected by the Signe experiments on the Soviet Venera 13 and 14 probes, and by the Lilas and Apex experiments on the Phobos probe. We use both the mean value $\langle V/V_{\max} \rangle$ and a Kolmogorov-Smirnov (KS) test to compare the observed V/V_{\max} distribution with a uniform one. Two of the three data sets exhibit a significant deviation from a uniform distribution, which may be interpreted as a deficit of sources at large distances. We show that the faintest sources (in the V/V_{\max} sense) seem to be concentrated in the galactic plane, evidence which supports a galactic-disk distribution of GRB sources. The V/V_{\max} analysis has been used previously to study the radial distribution of burst samples⁴⁻⁷, but here we associate a low $\langle V/V_{\max} \rangle$ value with the observation of angular anisotropy.

Table 1 gives the main characteristics of the three experiments used here (details available for Signe⁸ and in preparation for Lilas and Apex (C. Barat *et al.*, manuscript in preparation)). The Signe experiment had four identical detectors, the Lilas

TABLE 1 Principal characteristics of the three samples of bursts

Experiment	Venera-Signe	Apex	Lilas
Detector	Nal (cyl.)	CsI (cyl.)	Nal (cyl.)
Size: diameter \times height (cm)	9 \times 3.7	10 \times 10	5.3 \times 3
Energy range	50–350 keV	120–700 keV	20–300 keV
Lifetime	11/81–04/83	08/88–03/89	08/88–03/89
Number of triggers	1,930	509	616
Number of bursts	169	58	47
Burst detection frequency (yr ⁻¹)	~125	~115	~90

experiment two. When V/V_{\max} analysis is performed on a burst sample containing events recorded by several detectors, it must be done as follows: the lowest V/V_{\max} value is taken if, as here, the sample contains all events seen by one or more detectors; if the sample is restricted to events detected by all the detectors, then the highest V/V_{\max} value is taken. The trigger algorithm was the same for the three experiments: a trigger occurs when the number of counts in Δt seconds in an energy range ΔE exceeds the background level (measured over 1 or 2 minutes) by more than N (usually 7 or 8) standard deviations. Usually several values of Δt are used simultaneously, but for consistency we have restricted the present analysis to bursts capable of triggering the instruments in a 1-s window common to all three instruments. Table 1 indicates that most triggers are not due to cosmic bursts. As it is important to retain all the true GRBs and nothing else, we have paid particular attention to selection of events. For the Signe experiment, 'false triggers' are caused either by heavy particles or solar events. The former can be identified by their characteristic exponential decay and soft spectrum; solar bursts are readily eliminated by comparison with data on solar activity. After this primary event selection, comparison with GRB data from other instruments showed that 73% of Signe GRBs were detected by two spacecraft at least. Because of its high energy threshold (see Table 1), Apex detected only 10 solar events, all associated with strong solar flares and easily recognizable; most of the event triggers were identified as being due to heavy particles traversing the detector and were easily eliminated (as for Signe). The Lilas experiment was found to trigger only on solar events and cosmic bursts. As the two Lilas detectors had the same orientation with respect to the sun, the solar-flare-induced events were characterized by a similar flux on both detectors and by their soft spectrum. We used a procedure based on these observational attributes to eliminate solar events. The efficiency of this selection was checked by

comparison with data on solar activity from the World Data Center (the region of the Sun visible from Phobos was identical to that visible from the Earth during 75% of the mission). Only four events of the 616 recorded by Lilas had their classification changed by this procedure. We are therefore confident that more than 90% of our lists of bursts from the three experiments are true GRBs.

Figure 1 shows V/V_{\max} cumulative distribution for the entire set of 244 bursts together with the theoretical distribution for a uniform population of sources. If the spatial distribution of the sources is uniform, the V/V_{\max} distribution is also uniform. If the spatial distribution is not uniform, the situation is much more complex, and the V/V_{\max} distribution depends on factors such as the spatial distribution of the sources or their luminosity function. Here we use the data simply to check the uniformity of the spatial distribution of GRB sources; more information can be extracted from the shape of the observed curve if detailed simulations of the GRB population, beyond the scope of this paper, are carried out. Figure 1 shows that the data are not compatible with a uniform distribution of GRBs. The hypothesis of spatial uniformity is rejected with a confidence level $\geq 4\sigma$ as indicated by a KS test (probability = 5×10^{-6}) and by the value $\langle V/V_{\max} \rangle = 0.4 \pm 0.018$; the uncertainty is $(12N)^{-1/2}$, where N is the number of bursts in the sample³. The curve indicates a deficit of sources at large distances, as only one-third of the sources have $V/V_{\max} > 0.5$. Figure 2, which presents the cumulative C_{\max}/C_{\min} distribution for bursts recorded with Signe⁷, shows the same effect: the region with $C_{\max}/C_{\min} > 2$, with ~80 events, is characterized by a slope of -1.5, corresponding to uniform population of sources, whereas for $C_{\max}/C_{\min} < 2$, the slope decreases, thus indicating the deficit (significance 3.2σ).

These observations could be explained by sources at cosmological distances⁹, by a galactic halo with a decreasing density of sources or by a galactic disk population. One way to distinguish between these possibilities is to use the determination of source positions on the sky, but previous angular distribution analysis^{10,11} did not reveal any galactic structure. Of the 169 GRBs detected by Venera 13 and 14, 51 events have been localized¹². We have divided these events into two classes of almost equal significance (Fig. 2): 24 'bright bursts' with $C_{\max}/C_{\min} \geq 2.5$ and 27 'faint bursts' with $C_{\max}/C_{\min} < 2.5$ (the boundary between the classes is close to the point where the curve C_{\max}/C_{\min} flattens). The main idea of this subdivision is to remove brighter and *a priori* closer sources which may blur possible structures (a similar approach is used in ref. 13). We have then used the method of Hartmann and Epstein¹¹ to study the angular distribution of sources within each class. The spatial distribution is described by its first two moments and more

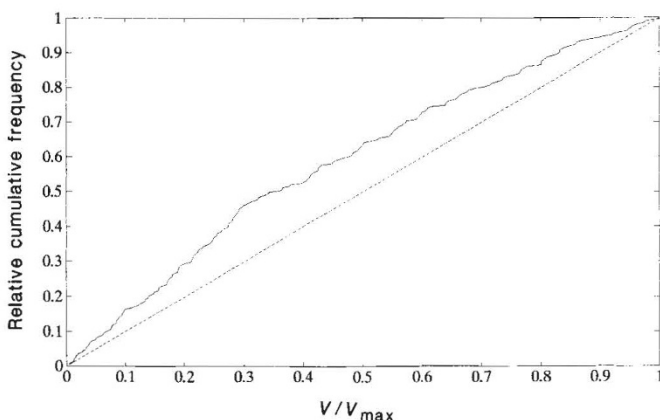


FIG. 1 V/V_{\max} distribution of 244 gamma-ray bursts from all three detectors. Note the deficit of sources at large distances with respect to a uniform population (only one-third of the sources have $V/V_{\max} > 0.5$). The mean value, $\langle V/V_{\max} \rangle$, is 0.419 ± 0.018 .

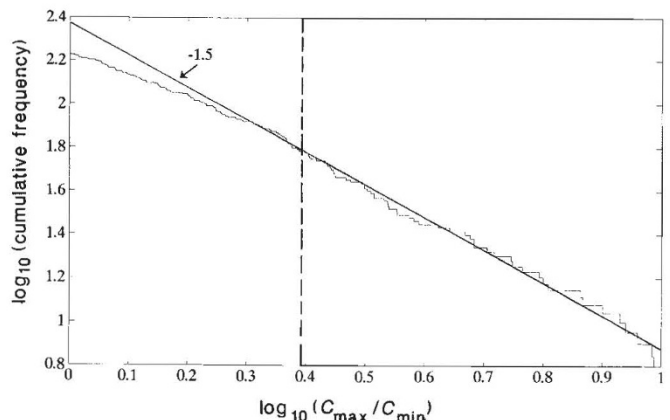


FIG. 2 Distribution of C_{\max}/C_{\min} , for 169 gamma-ray bursts detected by the Signe instruments on Venera 13 and 14. A deficit of weak bursts is apparent by comparison with the $-3/2$ slope expected for a uniform population. The dashed line separates 'bright' from 'faint' bursts (see text).

precisely by three parameters: P , the magnitude of the dipole vector; η , the absolute value of the difference between the two most similar eigenvalues of the quadrupole tensor; and ζ , the remaining eigenvalue of the quadrupole tensor (see ref. 11 for details). No strong anisotropy is present for the class of 'bright bursts' ($P = 0.07$, $\eta = 0.258$, $\zeta = 0.328$). The distribution of 'faint bursts' ($\zeta = -0.636$, $P = 0.146$, $\eta = 0.096$) is much more interesting. The high absolute value of ζ and the low absolute value of η indicate respectively that faint sources are concentrated in a plane and have good axial symmetry. A Monte Carlo simulation shows that when 27 bursts are randomly distributed on the celestial sphere, such a concentration in a plane is found in only eight cases out of 10^4 . Furthermore, the normal to this plane is $9 \pm 10^\circ$ from the galactic pole. The events studied here were detected by both Signe and Konus instruments on Venera and, as the Signe detectors lie in the ecliptic plane and have a 1.5-yr lifetime, we do not believe the experiment to be biased in favour of the galactic plane. We therefore interpret this result as showing that GRBs have a galactic origin and that the departure of the V/V_{\max} curves from uniformity is due to the decreasing density of sources for increasing distances from the galactic plane. The sampling depth of current instruments is a few times the scale height of the distribution deduced from these results. Moreover, the absence of centre-anticentre anisotropy for faint sources (indicated by low η) indicates that the sources are no further than a few kiloparsecs from the Sun. Finally, the difference in spatial distribution between 'bright' and 'faint' sources proves that the mean V/V_{\max} value of a sample of bursts provides a fair estimate of its relative distance (obviously this is not true for individual bursts).

Models that explain GRBs as due to the interaction of old neutron stars with the interstellar medium^{14,15} predict a scale height of the sources of ~ 200 pc. This height is consistent with the distribution of the interstellar gas and of the low-velocity neutron stars which are capable of accreting at sufficiently high rates¹. As the sampling depth of current observations is a few times the scale height, the GRB sources are visible within several hundred parsecs of the Sun, and two observational results should be carefully considered. First, the absence of angular clustering of localized sources¹⁰ does not seem compatible with the known inhomogeneity of the local interstellar medium. Second, the absence of persistent X-ray counterparts¹⁶, if confirmed by ROSAT, may be a problem for these models.

These last considerations show the importance of measuring the spatial distribution of GRBs if we are to understand these objects. We expect the BATSE experiment¹⁷, which has high sensitivity and localization capability, on the Gamma Ray Observatory to provide further information, and the concentration of sources towards the galactic plane reported here should become apparent after several months of operation. \square

Received 30 October 1990; accepted 2 April 1991.

- Paczynski, B. *Astrophys. J.* **348**, 485–494 (1990).
- Hartmann, D., Epstein, R. I. & Woosley, S. E. *Astrophys. J.* **348**, 625–633 (1990).
- Schmidt, M., Higdon, J. C. & Hueter, G. *Astrophys. J.* **329**, L85–L87 (1988).
- Higdon, J. C. & Schmidt, M. *Astrophys. J.* **355**, L13–L17 (1990).
- Higdon, J., Metz, S. M., Share, G. H., Messina, D. & Iadiccio, A. *Proc. TAOS Workshop on Gamma-Ray Bursts* (eds Cheng, H., Epstein, R. I. & Feniman, E. E.) (Cambridge University Press, UK, 1990).
- Mitrofanov, I. et al. *Proc. TAOS Workshop on Gamma-Ray Bursts*, (eds Cheng, H., Epstein, R. I. & Feniman, E. E.) (Cambridge University Press, UK, 1990).
- Mitrofanov, I. et al. *Soviet Astron. J.* **68**, (1991).
- Barat, C. et al. *Astrophys. Space Sci.* **75**, 83–91 (1981).
- Paczynski, B. *Astrophys. J.* **306**, L43–L46 (1986).
- Hartmann, D. & Blumenthal, G. *Astrophys. J.* **342**, 521–526 (1989).
- Hartmann, D. & Epstein, R. I. *Astrophys. J.* **346**, 960–966 (1989).
- Golenetskii, S. V. et al. preprint no. 1026, A. F. Ioffe Phys.-Tech. Inst., Leningrad (1986).
- Pozanenko, A. & Mitrofanov, I. *Astrophys. Space Sci.* **164**, 277–283 (1990).
- Hameury, J. M., Bonazzola, S., Heyvaerts, J. & Ventura, J. *Astr. Astrophys.* **111**, 242–251 (1982).
- Blaes, O., Blandford, R., Madau, P. & Koornin, S. *Astrophys. J.* **363**, 612–627 (1990).
- Pizzichini, G. et al. *Astrophys. J.* **301**, 641–649 (1986).
- Fishman, G. J. et al. *Proc. Gamma Ray Observatory Science Workshop* (Goddard Space Flight Center, Greenbelt, Maryland, 1989).

ACKNOWLEDGEMENTS. We thank J.-M. Hameury, S. Bonazzola, K. Hurlay and D. Hartmann for helpful discussions, and A. J. Dean for reading the manuscript.

Formation of hierarchical multiple protostellar cores

Alan P. Boss

Department of Terrestrial Magnetism, Carnegie Institution of Washington, 5241 Broad Branch Road, NW, Washington, DC 20015, USA

BINARY pre-main-sequence stars^{1,2} seem to occur as frequently as binary main-sequence stars^{3,4}; triple pre-main-sequence star systems have also been detected⁵, and hierarchical main-sequence multiple stars continue to be identified⁶. (Hierarchical systems contain both closely spaced stars and stars orbiting at much greater distances.) These observations suggest that essentially all binary stars were formed before the main-sequence phase of evolution. The detection of a number of binary young stellar objects^{7,8} seems to indicate that binary formation must occur no later than the protostellar phase (further observations are needed to establish if this is the case for multiple star systems). Here I describe numerical hydrodynamical calculations showing that stable hierarchical systems of multiple protostellar cores can form through gravitationally driven fragmentation during the collapse of an isolated gas cloud, suggesting that the hierarchical systems observed may be the result of the hydrodynamical collapse of rapidly rotating clouds.

Fragmentation during the isothermal collapse phase of protostellar evolution is one of the leading mechanisms for explaining the formation of binary and multiple stars^{9–13}. Although it is well known that fragmentation can form binary protostellar cores or trapezium-like (unstable) multiple protostellar cores^{13,14}, until now fragmentation calculations have not demonstrated the formation of a stable, hierarchical protostellar core system.

The calculations were carried out with a new explicit, Eulerian, three-dimensional hydrodynamics code which is accurate to second order in spatial finite differences (A.P.B., in preparation). To obtain the hydrodynamical fluxes, I use consistent advection and an extension in spherical coordinates of van Leer monotonic interpolation¹⁵. The code is accurate to first order in time; this should be adequate given the large number ($\sim 6 \times 10^4$) of time steps used in the models. The gravitational potential is obtained by a spherical harmonic expansion with terms up to and including $l, m = 16$. The spatial resolution is 51 grid points in radius, effectively 45 in colatitude (assuming symmetry through the equatorial plane) and 64 in azimuth (with no symmetry about the rotation axis).

The hydrodynamical equations are solved in conservation-law form, ensuring global conservation of mass and angular momentum. The code is designed to conserve angular momentum locally, as measured by the preservation of the initial angular momentum spectrum during axisymmetric collapse¹⁶. The radial momentum fluxes are corrected for the effects of volume centring in spherical geometry¹⁷. The Q^{rr} and $Q^{\theta\theta}$ components of the artificial viscosity tensor are used to stabilize the scheme against shocks¹⁸; the artificial viscosity vanishes during homologous collapse. Convergence testing (L. S. Finn and J. F. Hawley, personal communication, 1989) on spherical and three-dimensional test cases has demonstrated the second-order accuracy of the code. The code can maintain a stable polytropic equilibrium with non-axisymmetric 'noise' of $\approx 1\%$.

The initial conditions for protostellar collapse are taken from observations of molecular cloud complexes. Dense cloud cores¹⁹ seem typical of one mode of low-mass star formation. Line widths are consistent with near-virial equilibrium²⁰, and the cores have sizes ~ 0.1 pc, mean densities $< 2 \times 10^5 \text{ cm}^{-3}$, temperatures ~ 10 K and masses $> 0.5 M_\odot$ ²¹. The cloud cores are centrally condensed and in some cases have considerable rotation²². Dense cloud cores of solar mass seem to be less affected by magnetic fields than more massive and diffuse clouds^{23,24}.