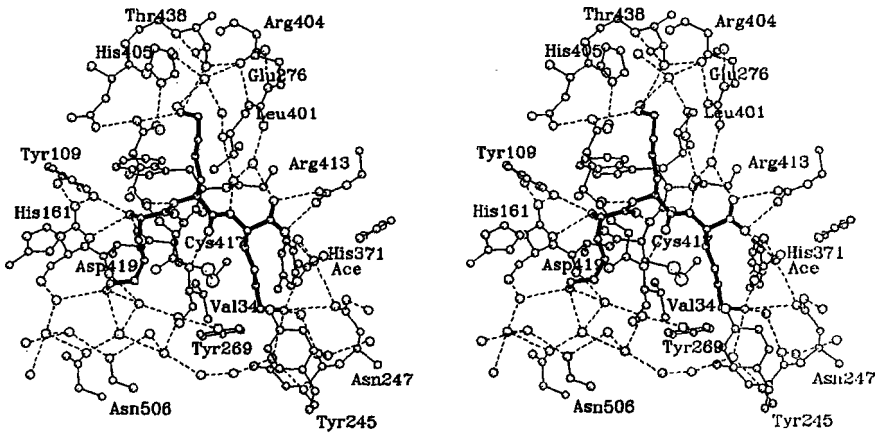

Fig. 4. Stereo diagram showing potential hydrogen bonding and electrostatic interactions (dashed lines) between the trilysine ligand (thicker bonds) and OppA.

gand binding appears, therefore, to be based chiefly on the avoidance of potentially unfavorable interactions with the repertoire of ligand side chains.

The burial of peptide ligands within OppA according to the Venus flytrap mechanism in some sense represents the final stage of a folding process to form a protein with a variable peptide core and a unique surface structure that is efficiently recognized bv the membrane comoonents of the transport system. The manner in which OppA accommodates the diverse peptide side chain functional groups is quite distinct from the way this is achieved in major histocompatibility complex molecules and chaperone proteins. In the crystal structures of the latter, the peptide ligands are located on the surfaces of the molecules and many of the side chains are directed into the solvent (7).

The covalent coupling of synthetic antibacterial compounds to peptides has proved a successful route to overcoming the problem of membrane impermeability assdciated with some of these drugs (4). This "Trojan horse" approach (8) relies on the unusually broad specificity of the oligopeptide permease. Knowledge of the structure of the initial receptor for this transport system, OppA, will be valuable in guiding the design of effective peptide-based antibiotics.

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16. This work was supported by the Medical Research Council, the Science and Engineering Research Council, and the Imperial Cancer Research Fund. C.F.H. is a Howard Hughes International Research Scholar. We would like to thank I. Glover, R. Denny, and P. Moody for assistance in collecting x-ray data and D. Edwards, U. Gileadi, S. Hyde, and S. Mowbray for helpful discussions.

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Habitat Fragmentation, Species Loss, and Biological Control

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Fragmentation of habitats in the agricultural landscape is a major threat to biological diversity, which is greatly determined by insects. Isolation of habitat fragments resulted in decreased numbers of species as well as reduced effects of natural enemies. Manually established islands of red clover were colonized by most available herbivore species but few parasitoid species. Thus, herbivores were greatly released from parasitism, experiencing only 19 to 60 percent of the parasitism of nonisolated populations. Species failing to successfully colonize isolated islands were characterized by small and highly variable populations. Accordingly, lack of habitat connectivity released insects from predator control.

Research in conservation biology analyzes both species richness and the functioning or stability of ecosystems. Modern agricultural methods fragment natural ecosystems; and the subsequent increase in isolation typically results in changes in community structure and function, including loss of species in isolated islands and disruption of the food web (1). Communities of herbivorous insects and their natural enemies (such as parasitoids) centered on a single plant species provide a small ecosystem in which the interactions between the organisms can be experimentally analyzed. Insects amount to more than half of all living organisms and

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have a greater impact on terrestrial ecosystems than any other type of animal (2, 3).

For this report we tested the hypothesis that extinctions in small and isolated habitat patches should not affect all insect species equally. Natural enemies of phytophagous insects are expected to become extinct first, thereby increasing the risk of pest outbreaks (3, 4). We analyzed communities of stem borers and seed feeders of red clover (Trifolium pratense). Eighteen clover habitats, each covering 1.2 m^2, were experimentally established in an agricultural landscape dominated by crop fields and small, fragmented meadows (northeast of Karlsruhe, Germany). The clover islands were separated from the nearest meadow with .naturally occurring clover plants, by 100 to 500 m, so that effects of habitat connectivity could be tested.

The endophage insect community was identified by dissection and rearing (Tables 1 and 2). Of the eight herbivore species, five fed on seeds in the flowerheads (Apion apricans, A. *assimile*, A. trifolii, Bruchidius *varius*, and *Bruchophagus* gibbus), two were stem-boring weevils (A. seniculus and A. uirens), and one was a stem-boring gall midge (Table 1). Of the parasitiod species, 12 attacked the Apion species, and one attacked the gall midge (Table 2). All but one of the total 21 species (the polyphagous eupelmid wasp Macroneura *vesicularis*) feed only on clover or clover herbivores. The pteromalid wasp Spintherus dubius was the most numerous parasitoid, providing 79% of all parasitoid specimens and was the only parasitoid species found in all 18 clover patches. Each other parasitoid species provided fewer than 7% of the specimens.

Herbivore abundance in the clover islands was negatively correlated with the distance to the next meadow (Fig. 1). Certain characteristics of the host plant (stem diameter, stem length, and dry weight of the flowerheads) were not related to herbivore abundance. For the stem-boring herbivores, we found a 75% reduction in population density and for the seed-feeding Apion spp., a smaller but significant decrease in population density in clover islands relative to fields (Fig. 1A). Immigration rate decreased with increasing distance from the nearest reservoir population. The largest distance tested, 500 m, was crossed by all but two of the herbivores. (The weevils A. *assimile* and A. trifolii, which were also scarce in the near natural, old meadows, were absent in three and nine, respectively, of the 18 clover patches.) Isolation reduced the populations of stem-boring Apion spp. more than those of seed-feeding Apion spp. This probably reflects the high proportion of short-winged females among the stem-boring weevils (5). In contrast, the most abundant species of seed-feeding weevils (A. apricans and A. assimile) always have large wings and are thereby more able to follow changing resources (6). Such increased flight capability may carry a cost of reduced fecundity but enables high dispersal rates and success in the unpredictable, fragmented environment of the agricultural landscape (7).

Numbers of parasitoid species attacking the clover herbivores were negativelv correlated with distance between clover islands and meadows. Eight to twelve parasitoid species were found in the meadows, but only two to four species in the patches 500 m from the nearest meadow (Fig. 2A). Numbers of species were closely correlated with both numbers of parasitoid individuals (regression analysis, $F = 23.7$, $r^2 = 0.597$, $n = 18$, $P < 0.001$) and percent parasitism ($F = 21.2$, $r^2 = 0.570$, $n = 18$, $P < 0.001$). Therefore, isolation of the clover islands reduced both parasitoid diversity and the percent parasitism (Fig. 2, B to D), supporting conclusions from experimental predator removal (8). For the stem-boring Apion spp., parasitism in isolated clover patches was only 30% of that found in larger ecosystems (Fig. 2B). Host mortality in the five most isolated patches was only 19% of that observed in control patches. For the seed-feeding Apion spp., average parasitism in clover islands was 75% of that found in the controls (Fig. 2C), because the responsible parasitoid, S. dubius, was very abundant in all 18 clover patches. The seed feeders in the five most isolated islands had 60% of the control parasitism. *Spintherus* dubius is the most abundant and widespread chalcid wasp in set-aside fields and fallows of the study area (9). If S. dubius was excluded from the analysis (Fig. 2D), parasitization decreased to 10% on the most isolated patches.

Therefore, habitat isolation affects species diversity, having the greatest impact on parasitoids, thereby releasing pest insects from parasitism and potentially allowing

Table 1. *The herbivores of the endophage insect community of red clover (T. pratense). Mean abundance was calculated on the basis of n = 5 controls.*

Family and species	Location	Mean abundance (n/m^2)
Coleoptera Curculionidae		
Apion apricans Hbst.	*Flowerheads*	1135
Apion assimile K.	*Flowerheads*	484
Apion seniculus K.	*Stems*	277
Apion trifolii L.	*Flowerheads*	49
Apion virens Hbst.	*Stems*	45
Col. *Bruchidae*		
Bruchidius varius Ol.	*Flowerheads*	98
Hymenoptera Eurytomidae		
Bruchophagus gibbus Bohe.	*Flowerheads*	176
Diptera Cecidomyiidae		
Lasioptera sp. *nov.*	*Stems*	39

Table 2. *The parasitoids of the endophage insect community of red clover (T. pratense). The Apion* spp. *are hosts for all parasitoids listed except Aprostocetus vassolensis Grah., whose host is Lasioptera sp. Parasitism was calculated on the basis of n = 5 controls.*

Family and species	Location	Parasitism (%)
Hymenoptera Braconidae		
Triaspis floricola Wesm.	*Stems*	1.5
Triaspis obscuripennis Ns.	*Stems*	1.6
Colastes sp.	*Stems*	0.9
Hymenoptera Eulophidae		
Aprostocetus cf. *tompanus (Erdos)*	*Stems*	0.3
Aprostocetus vassolensis Grah.	*Stems*	4.6
Aprostocetus sp.	*Flowerheads*	4.3
Entedon cf. procioni (Erdos)	*Stems*	2.5
Hymenoptera Eupelmidae		
Macroneura vesicularis (Retz.)	*Stems*	2.7
Hymenoptera Pteromalidae		
Spintherus dubius Ashm.	*Flowerheads*	28.9
Trichomalus campestris (Walk.)	*Flowerheads and stems*	2.4
Trichomalus fulvipes (Walk.)	*Stems*	6.8
Trichomalus helvipes (Walk.)	*Flowerheads*	1.7
Hymenoptera Torymidae		
Pseudotorymus apionis Mayr	*Flowerheads*	4.8

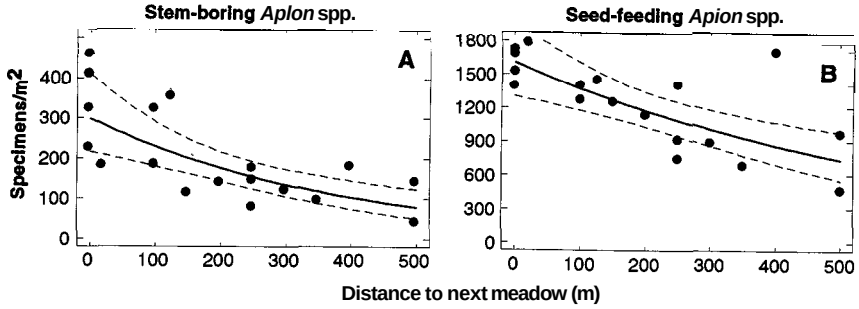


Fig. 1. Abundance of Apion species in relation to isolation of the clover patches. (A) Population density of stem-boring weevils (A. seniculus and A. virens): $\ln Y = 5.70 - (2.63 \times 10^{-3})X$, $F = 19.48$, $r^2 = 0.549$, $n = 18$, $P < 0.001$. (B) Population density of seed-feeding weevils (A. apricans, A. assimile, and A. trifolii): $\ln Y = 7.38 - (1.55 \times 10^{-3})X$, $F = 16.5$, $r^2 = 0.508$, $n = 18$, $P < 0.001$. Data are based on dissections of 2160 stems and 1080 flowerheads. Samples consisted of two subsamples (29.06.92 and 29.07.92) on each of the 18 clover patches. Each sample per patch consisted of dissections, rearings, and species identifications of the univoltine inhabitants of 120 stems and 60 flowerheads. Five clover patches (the controls) were placed in five meadows (size: $\bar{x} = 178.500$ m², SD = 78970 m²) characterized by naturally developed clover populations (cover of red clover: $\bar{x} = 14\%$, SD = 5.5%), and 13 clover patches were placed on edges of crop fields 100 to 500 m away from the next meadow. Each patch was created in March 1992, covered 1.2 m², and consisted of 12 pots dug into the ground, and each pot was planted with 2-year-old clover plants and had a 5-liter water reservoir. The red clover (variety Odenwälder Rotklee) had been sown in an experimental field in April 1990.

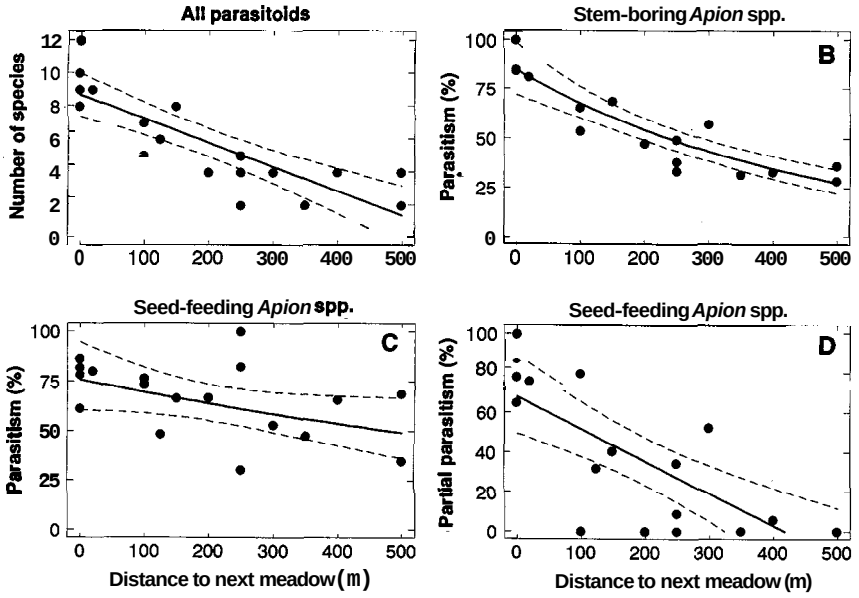


Fig. 2. Effects of habitat isolation on number of parasitoid species and parasitization. Isolation is measured as the distance to the next meadow. Characteristics of hosts or host insects were not related to percent parasitism. Parasitism (%) is the arcsine-transformed percentage of the maximal parasitization. (A) Number of parasitoid species: $Y = 8.67 - 0.015X$, $F = 35.5$, $r^2 = 0.689$, $n = 18$, $P < 0.001$. (B) Parasitism of stem-boring weevils (A. *seniculus* and A. virens): $\ln Y = -4.43 - (2.23 \times 10^{-3})X$, $F = 56.9$, $r^2 = 0.78$, $n = 18$, $P < 0.001$. (C) Parasitism of seed-feeding weevils (A. apricans, A. assimile, and A. *trifolii*): $\ln Y = -4.33 - (8.64 \times 10^{-4})X$, $F = 4.33$, $r^2 = 0.213$, $n = 18$, $P = 0.05$. (D) Parasitism of seed-feeding weevils without the dominant parasitoid S. dubius: $Y = 67.9 - 0.163X$, $F = 22.3$, $r^2 = 0.583$, $n = 18$, $P < 0.001$.

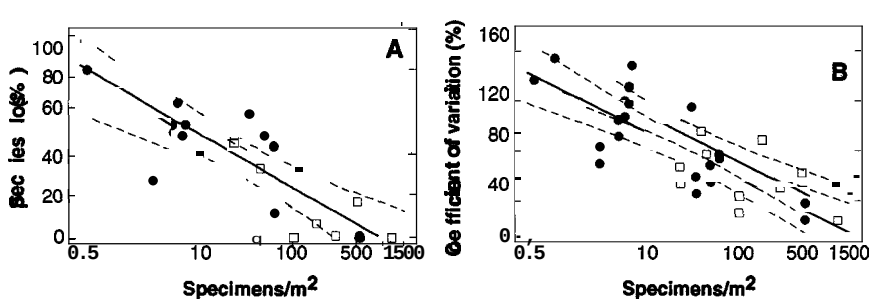
pest outbreaks. Limitations of pest populations are often due to the direct effects of top-down control exerted by parasitoids (3, 10, 11). The percentage of parasitism provides an estimate of the outcome of classical biological control because biocontrol is more likely to be successful in pests with high percent parasitism (10, 12).

Our results also show the importance of an abundant and widely distributed species like S. dubius for biocontrol. Biocontrol that is based only on a rare species is likely to be ineffective. Ecosystem functions may often depend more on widespread and abundant species than on rare species. However, the parasitic Hymenoptera, which are naturally rare (9, *13*), may still be judged as important satellite species, for their regulatory effects may greatly increase when environment or food web structure changes (11, 14).

General conclusions from our experimental clover islands were supported by comparisons between near natural, 30-year-old meadows. Percent parasitism of a seed-feeding weevil (A. ochropus) in pods of *Vicia sepium* growing in these old meadows was positively correlated with habitat size (15). The rate of parasitism ranged from 40% on the small habitats to 83% on the large ones. In addition, fragments of old meadows had only a few species of parasitoids (15). These old habitats and the experimentally established islands shared the same patterns of both species loss and reduced biocontrol.

Certain features characterize species that were absent from the most isolated islands. Species fail to colonize a habitat when their populations are small and fluctuate widely (*16*). Indeed, the percentage of uncolonized clover islands was negatively correlated with the abundance of individuals of a given species (Fig. 3A) and positively correlated with the coefficient of variation describing population variability ($F = 24.3$, $r^2 = 0.562$, $n = 21$, $P < 0.001$; in parasitoids only, $r^2 = 0.553$, $n = 13$). Species that failed to colonize the isolated habitat fragments existed as populations that were both small and variable (Fig. 3B). In most known cases, population variability increases with abundance (16, 17). In our system, both small size and increased variability were good predictors of species losses,

Fig. 3. Relations between species loss and coefficient of variation with abundance of all 21 species (herbivores □, parasitoids ●): (A) Species loss and abundance: $Y = 77.1 - 9.66 \ln X$, $F = 28.4$, $r^2 = 0.589$, $n = 21$, $P < 0.001$. (B) Coefficient of variation and abundance: $Y = 1.32 - 0.1601 \ln X$, $F = 38.7$, $r^2 = 0.671$, $n = 21$, $P < 0.001$. Species loss was calculated as percentage of the $n = 18$ clover patches without a record. Coefficients of variation ($SD/\bar{x}$) [without transformations, using $(x + 1)$ gave very similar results] were based on the $n = 5$ clover patches on the meadows.



explaining 60 or 56% of the variance. Natural enemies in fragmented habitats are more likely to be lost than their phytophagous prey because population growth starts only after the successful establishment of prey populations, and populations will be smaller in small habitat islands. The result is that food chains should be shorter in small islands than in larger habitats (18).

Small populations isolated by disturbed environments are characteristic features of the agricultural landscape. The time between population crashes (determined by cutting of vegetation or ploughing) may often be shorter than the recovery time of natural enemies, especially when they prey on only one or two species (19). In such situations of local loss and recolonization, predator-prey systems and multitrophic cascade effects begin to depend on metapopulation processes (20), such that only mobile and abundant natural enemies can regulate actual or potential pests.

In addition, release of dominant competitors from natural control may cause competitive exclusion of herbivores. Competition is a structuring factor in endophagous but not ectophagous insect communities (21), and as expected, we found competition to be important for the insects spatially restricted to the clover flowerheads. Extinction of weak competitors resulting from the release of dominant ones may be a further indirect consequence of reduced biocontrol.

We conclude that habitat fragmentation affects natural enemies more than their phytophagous hosts. Fragmentation reduced not only biodiversity but also the rate of predation or parasitism. The rate of parasitism is linked to the success of biocontrol; habitat isolation can be expected to release herbivores from the control of predators or parasitoids. Accordingly, designs of the agricultural landscape that maintain habitat connectivity may contribute to the biocontrol of potential or actual pests.

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Structure of the Equine Infectious Anemia Virus Tat Protein

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Trans-activator (Tat) proteins regulate the transcription of lentiviral DNA in the host cell genome. These RNA binding proteins participate in the life cycle of all known lentiviruses, such as the human immunodeficiency viruses (HIV) or the equine infectious anemia virus (EIAV). The consensus RNA binding motifs [the trans-activation responsive element (TAR)] of HIV-1 as well as EIAV Tat proteins are well characterized. The structure of the 75–amino acid EIAV Tat protein in solution was determined by two- and three-dimensional nuclear magnetic resonance methods and molecular dynamics calculations. The protein structure exhibits a well-defined hydrophobic core of 15 amino acids that serves as a scaffold for two flexible domains corresponding to the NH_2- and COOH-terminal regions. The core region is a strictly conserved sequence region among the known Tat proteins. The structural data can be used to explain several of the observed features of Tat proteins.

Equine infectious anemia virus Tat protein is a monomeric protein of 75 amino acids (1). From sequence comparisons of lentiviral Tat proteins, it was concluded that immunodeficiency virus Tat protein sequences are in general subdivided into several regions: an NH_2-terminal region, a Cys-rich region, a core region, a basic region, a Glu-rich region, and a COOH-terminal region (2). The Cys-rich region is thought to bind two Zn^{2+} ions (3), and the basic region is involved in binding of the TAR RNA recognition sequence (4). The Cys-rich region and a sequence homologous to the HIV-1 Tat COOH-terminus are not present in the EIAV Tat protein. The highly conserved core region encompasses amino acids Tyr^{35} through Tyr^{49} in EIAV Tat protein. In this study we used both chemically synthesized (5) and bacterially expressed protein (6).

The nuclear Overhauser enhancement spectroscopy (NOESY) cross-peak pattern (Fig. 1) shows that the protein has a tendency to form weak helices from amino acid Ala^{10} to Asn^{13} as well as through the core and basic regions (that is, amino acids His^{36}

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