will correlate with the age of the language. Al-Sayyid Bedouin Sign Language has been around about twice as long as Nicaraguan Sign Language, and has passed through more family generations. On the other hand, Nicaraguan Sign Language is passed to a new cohort of 15–20 learners each year, a number that approximates a 20-year Al-Sayyid Bedouin Sign Language generation. By comparing the rates of development in the two languages, we can determine which aspects of language appear with iterations of child learners, and which appear merely with years of use.

The situations also differ in the social context in which the system is passed down, and the age at which it is first encountered. Early exposure typically enables better language-learning [18]. This suggests that younger children may have more language-creating abilities than older children, or at least more years to apply such abilities. Al-Sayyid Bedouins are exposed to signing from birth, within the family environment. Nicaraguan Sign Language is transmitted from peer to peer, starting at the age of four or six when a child enters school. Historically, mature sign languages, such as American Sign Language and Australian Sign Language, underwent both kinds of transmission. They have been passed down in families with deaf parents, particularly those with deaf children. But because most deaf children have hearing parents, sign languages are even more commonly transmitted from child to child within a school environment [6]. It seems the particulars of the social community can vary; what is crucial for language birth is a context that provides intergenerational contact, an opportunity for a partially developed system to be passed on to new children. This is lacking in the case of homesign, and may be a determining factor.

There are other dimensions on which these communities vary: the proportion of deaf to hearing users, and the resulting degree of bilingualism; the gestural practices of hearing people (that is, the richness of raw materials available); the availability of written materials; the presence of all-deaf families; and many others. We cannot know the relative importance of these factors with certainty. But we can make some educated guesses about what situations best promote language creation. Early exposure is key (the younger the better); some critical mass of individuals must be brought together (the more the better); and a social mechanism must be available for passing the language down to new generations. The new case of Al-Sayyid Bedouin Sign Language will help constrain the ranges of these candidate properties, enabling researchers to hone in on the critical mass, critical age, and critical transmission frequency needed for a language to be born.

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Virus Evolution: Fitting Lifestyles to a T

The structure of a double-stranded RNA virus outer shell has revealed unexpected similarities with virions of positive-strand RNA viruses. These similarities intersect with emerging parallels in RNA replication to create intriguing evolutionary possibilities.

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Viruses are exceptionally diverse in morphology, replication strategies, genetic organization and many other characteristics.

Such differences raise significant questions about the diversity of virus origins and the possible extent of functional and evolutionary relationships among existing viruses. These issues are
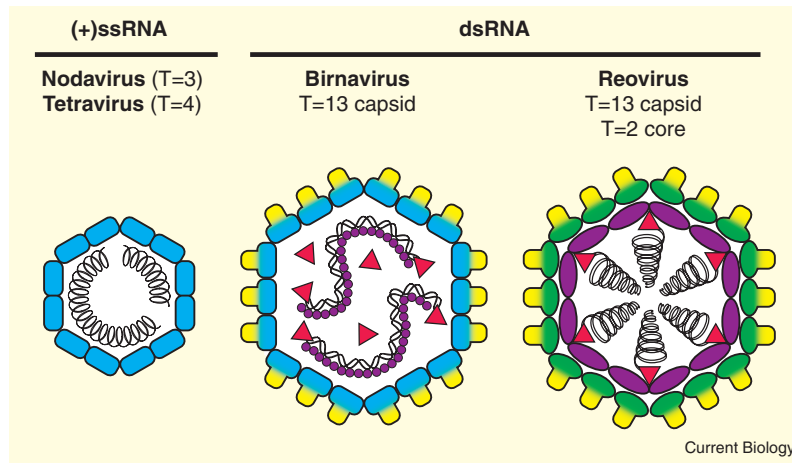
Figure 1. Cross-sectional diagrams comparing selected features of *Nodaviridae/Tetraviridae, Birnaviridae*, and *Reoviridae* virions.

Outer capsid proteins of nodaviruses and birnaviruses have similar, tangential β-barrel domains (blue), while birnaviruses and reoviruses or rotaviruses have radial β-barrel domains (yellow). Nodavirus, birnavirus and reovirus capsids enclose, respectively, naked ssRNA, filamentous complexes of dsRNA with protein VP3 (circles) and polymerase (triangles), and T=2 cores with ordered dsRNA and transcription complexes.

important for increasing our basic biological understanding and for practical applications, since underlying similarities linking virus classes could provide a basis for antiviral approaches that have a broader spectrum. Recent findings, including a new structural study of birnaviruses [1], reveal structural, functional and likely evolutionary links between positive-strand RNA and double-stranded (ds) RNA viruses at multiple levels, and in some cases extend these to reverse transcribing viruses [2–5].

Most viruses store and replicate their genomes solely via RNA intermediates. The infectious virion particles of such viruses may contain the genome either as positive-strand (i.e. mRNA-sense) single-stranded (ss) RNA, or as negative-strand (i.e. mRNA-antisense) ssRNA, or as dsRNA. These different genome forms are associated with significant differences in viral replication and transcription strategies: for example, virions of dsRNA viruses contain all the necessary machinery to transcribe the enclosed genomic dsRNA into mRNAs, while positive-strand ssRNA viruses encapsidate only RNA and form separate RNA synthesis complexes (Figure 1).

The protein capsids of many positive-strand RNA viruses and all known dsRNA viruses embody extensions of icosahedral symmetry (Figure 1). These quasi-icosahedral capsids contain 60 copies of a capsid protein multimer, with the number of subunits per multimer matching the allowable values of a triangulation number T [6]. For integers h and k, the increasing values of $T = h^2 + hk + k^2$ define ways to assemble capsids that are progressively larger than a perfect isosahedron (T = 1), using subunit–subunit interactions that are nearly equivalent (quasi-equivalent) rather than perfectly equivalent throughout the capsid. dsRNA viruses in the *Reoviridae* and *Cystoviridae* families consist of one or more T=13 outer capsid shells surrounding an inner, transcriptionally active T=2 core [7–9]. The dsRNA *Totiviridae*, which may be primitive or degenerate relatives of the *Reoviridae* and *Cystoviridae*, also have a T=2 transcriptionally active core but lack an outer capsid shell and the ability to transmit infection extracellularly [10].

The dsRNA birnaviruses, like *Reoviridae* and *Cystoviridae*, possess a T=13 outer capsid shell, composed of 60T=780 copies of viral capsid protein VP2 [1,11]. These birnavirus virions are also transcriptionally competent, but lack an

icosahedrally ordered inner core. Instead, the outer capsid encloses the viral dsRNA, the polymerase VP1, and many copies of the birnaviral protein VP3 in a complex whose order has not been well determined but is recoverable from virions as a ribonucleoprotein filament [12].

In a recent study in *Cell*, Coulibaly *et al.* [1] have shown that a number of features position birnavirus VP2 as an intermediate between the outer shell proteins of the dsRNA T=13 *Reoviridae* and those of the positive-strand ssRNA T=3 nodaviruses and T=4 tetraviruses [13,14]. Facing the capsid interior, these capsid proteins all have base domains composed of amino-terminal and carboxy-terminal α helices. In nodaviruses, tetraviruses and birnaviruses, a carboxy-terminal α-helix forms a hydrophilic channel at the 5-fold axes, which has been suggested to allow release of nodavirus genomic RNA to initiate infection and birnavirus transcripts to initiate viral gene expression [1,14].

Above the base, birnavirus VP2 contains intermediate shell (S) and exterior projection (P) domains, which contain an anti-parallel β-barrel motif conserved in capsid proteins of many RNA and DNA viruses [6]. However, these S domains and P domains correspond to distinctly oriented β-barrel domains in the nodavirus/tetravirus capsid proteins and the *Reoviridae* capsid proteins, respectively (Figure 1). The VP2 S domain β-barrel strands are tangential to the capsid surface, as in nodavirus/tetravirus capsids and most capsid shell proteins with this motif, and share other structural features with nodaviruses/tetraviruses. The VP2 P domain, however, parallels *Reoviridae* outer capsid proteins in having the β-barrel strands oriented radially. As one possible evolutionary explanation of these relationships, Coulibaly *et al*. [1] propose that a birnavirus precursor derived its outer capsid protein from a nodavirus-like or tetravirus-like virus, and then donated the resulting capsid

to a pre-existing totivirus to create a precursor of the *Reoviridae* and *Cystoviridae*.

As the authors note, variations on this evolutionary model are also possible. While positive-strand RNA viruses assemble their RNA replication and transcription complexes as distinct, non-virion structures within the infected cell, recent results show that the RNA replication complexes of at least some positive-strand RNA viruses are similar to the replicative cores of dsRNA virus and retrovirus virions [5]. Like *Reoviridae* cores, these positive-strand RNA virus replication complexes are compartments induced by many copies of a self-interacting viral NTPase, containing positive-strand and negative-strand viral RNA templates, the viral RNA-dependent RNA polymerase, and viral RNA capping proteins. A further similarity exists specifically between birnavirus and tetravirus RNA polymerases. While conserving the palm–fingers–thumb design of nearly all polymerases, the birnavirus and tetravirus polymerases both have an unusual circular permutation of conserved palm sequence motifs A, B and C from their usual amino- to carboxy-terminal order of A–B–C to the order C–A–B, suggesting that both were derived from a common ancestor [3].

Such parallels between the RNA synthesis complexes of dsRNA and positive-strand RNA viruses suggest that a positive-strand RNA virus might have donated both the transcriptionally active core and the outer capsid protein to generate a reovirus precursor. The major steps needed for such an evolutionary transition from positive-strand to dsRNA virus are the same as those needed for birnavirus acquisition of a nodavirus/tetravirus capsid protein. First, the capsid protein would need to switch from packaging viral RNA alone to packaging the full transcription complex. In some positive-strand RNA viruses, viral RNA encapsidation is linked to RNA replication [15], suggesting possible interactions between capsid protein and RNA synthesis

factors that could facilitate such a transition.

Additionally, to accommodate the larger volume of the replication complex compared with RNA alone, capsid protein self-interactions would need to modulate from a multiplicity of T=3 or T=4 to T=13. Conservation of related β-barrel domains across capsids of varying T number suggests that such transitions have occurred multiple times in virus evolution, aided by the similarity of quasi-equivalent subunit interactions in different T states and the ability of some capsid proteins to assemble capsids of alternative T numbers [6,16].

Further questions about birnavirus virions include the distribution and functions of protein VP3, which is present at levels approaching VP2, but is not icosahedrally ordered [1,11]. VP3 interacts with the viral dsRNA and polymerase to make filamentous ribonucleoproteins (Figure 1) [12,17]. It will be interesting to see if such filaments are the active form of the genomic RNA for transcription and if VP3 parallels some functions of *Reoviridae* T=2 core proteins. Additional issues relate to the covalent linkage of birnavirus RNA 5' ends to the viral polymerase, and how birnavirus genome replication relates to that of other viruses that use protein-primed synthesis from an RNA template, such as the positive-strand RNA picornaviruses and reverse-transcribing hepatitis B viruses [2,4]. The recent discoveries suggest that ongoing progress in such areas will further advance efforts to trace functional and evolutionary connections among viruses.

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