junction light emitter. Therefore, a single carrier charging or injection event never affects subsequent events.

A continuous charging of unit charge e to the pn junction does not necessarily result in a single carrier injection, and so a subsequent single photon emission has no correlation with a single carrier charging by the receiver output photocurrent. Therefore, there can be no direct correspondence between a single photon detected by the receiver and single photon emission by the emitter. One may argue that if a pn junction is supplied with a unit charge e by the photocurrent, then a single photon should be emitted from the junction because of the energy conservation law. A single photon is certainly emitted as a result of the unit charging if one waits for a very long time, but then an emitted single photon is completely masked by many thermal photons emitted during the same time interval.

However, the collective effect of many carriers can still self-regulate the number of injected carriers in a macroscopic limit. A detailed calculation (*7*) indicates that the injected carrier number is regulated to below the Poisson limit only when the measurement time T_o is long enough or the current I is large enough so that the average number of carriers $n_e = (I/e)T_o$ exceeds k_BTC/e^2. The condition can be understood as the collective junction voltage increase or drop by n_e carriers, $(e/C)\ n_e$, being equal to the thermal voltage k_BT/e. For a typical pn junction light emitter with C = 1 nF and T = 300 K, this critical carrier number is on the order of 10^8. The observed intensity quantum correlation between an incoming and outgoing wave (*1*, *2*) is indeed in this macroscopic limit. Hence, the proposed device cannot regenerate a signal energy with the accuracy Δn_e better than $(k_BTC/e^2)^{1/2} \approx 10^4$.

To reach the single photon limit, such as in an ideal QND measurement, the junction voltage increase or drop (e/C) by single carrier charging or injection must be much larger than the thermal voltage k_BT/e. In such a case, the continuous charging of a unit charge e and discrete injection of a single carrier have one-to-one correspondence (Fig. 1B) (*8*). The above requirement, $e/C \gg k_BT/e$, is known as the requirement for Coulomb blockade in a tunnel junction (*9*). Just as this condition must be met for regulated single electron tunneling (high-precision current standard) (*9*), single photon manipulation with a semiconductor pn junction also must satisfy this condition (*8*).

Given developments in nanostructure fabrication technologies, we can expect great effort in this area. A quantum optical repeater consisting of semiconductor receiver and emitter must meet the goal of a single photon manipulation before a QND measurement can be possible. Recent results, such as those in (*1*, *2*), are steps along the way, but the goal still remains elusive.

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Will Transgenic Crops Generate New Viruses and New Diseases?

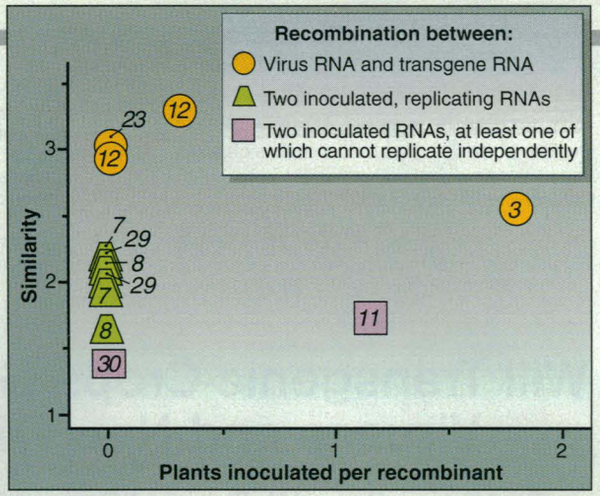
Bryce W. Falk and George Bruening

Plant viruses cause significant losses of important food and fiber crops. To stop these harmful viruses, agriculturists have tried several strategies, including use of insecticides or other agents to reduce the number of virus vectors or removal of the plants that are the source of the virus. Other defenses include the use of virus-free plant propagation material and the introduction of resistance genes into crop species by traditional plant breeding. Each of these methods has its practical drawbacks, and their effectiveness varies from crop to crop, location to location, and even year to year. A recent and potentially powerful new approach is to express certain segments of plant virus genomes in transgenic plants, a procedure that confers resistance against the corresponding virus (*1*, *2*). Is there risk in this method? A report by Greene and Allison in this issue of *Science* (*3*) clearly and elegantly shows that genomic recombination can occur when transgenic *Nicotiana benthamiana* plants expressing a segment of a cowpea chlorotic mottle virus (CCMV) genomic RNA are inoculated with a mutant CCMV that contains a deletion. The transgenic RNA of the plant and the genomic RNA of the virus are apparently available in sufficient quantities and in the proper form and place to allow recombination. Could such recombination produce dangerous new viruses? Greene and Allison cautiously conclude that "RNA recombination should be considered when analyzing the risks posed by virus-resistant transgenic plants."

Most known plant viruses have small genomes composed of single-stranded RNA, usually of 10,000 nucleotide residues or less. RNA-RNA recombination is a rare event in plant virus replication but presumably contributes to evolution of the viral genome (*4*–*6*). Indeed, under strong selective pressure for the recombinant RNA, intermolecular RNA-RNA recombination has been demonstrated for four groups of RNA plant viruses—alfalfa mosaic virus, bromoviruses, carmoviruses, and tombusviruses (*7*–*11*), and for the plant pararetrovirus cauliflower mosaic virus (*12*). RNA-RNA recombination occurs between closely related RNA molecules, but also between dissimilar RNAs—possibly at sites of similar RNA structure (*4*, *13*).

Under usual agricultural conditions plant viruses have many opportunities to interact genetically. Viral genes are already distributed over vast acreages by insect and other natural virus vectors and by infected propagation materials (for example, seeds, seed potatoes, tree and vine cuttings). These infected plants can then be infected again by other viruses. These multiple, as well as single, infections occur commonly in both crop and weed hosts. For example, cucurbits {including melons, cucumbers, and squash [a genetically engineered, virus-resistant version of which may be released soon (*14*)]} are often doubly infected by viruses. Indeed, five independent viruses have been recovered from a single plant (*15*). Mixed infection probably occurs even more often than reported, because subliminal infections (*16*, *17*) (in which inoculated cells become infected but the infection does not spread) go undetected. In fact, most plant viruses can infect most plant protoplasts, suggesting that individual plant cells can easily be infected by viruses that do not infect the whole plant. Mixed subliminal and conventional infections have likely already brought together combinations of virus genes that some have assumed could be in proximity only when a virus infects a plant that is transgenically expressing the genes of other viruses (*18*). Thus, recombination in the field, between a virus that cannot systemically infect a particular plant and viruses that do, does not have a zero probability.

The authors are in the Department of Plant Pathology and Center for Engineering Plants for Resistance Against Pathogens (CEPRAP), University of California, Davis, CA 95616, USA.



Instances of RNA-RNA recombination. Similarity: the logarithm of the number of matching nucleotide residues in the recombining region; plants inoculated per recombinant: a logarithmically presented measure of the frequency of detected recombination. Data points are identified by reference number.

Whatever interactions do occur in mixed infections rarely result in new pathogenic viruses. Even though ordinary infections in agricultural and natural settings continuously provide viruses with multiple opportunities to interact, new viral diseases are usually due to minor variants of already known viruses and not to new viruses of recombinant origin. In fact, existing viruses are surprisingly stable, having evolved into fit competitors that evolve only slowly.

But what about the not so natural situation in which transgenic plants express viral genes? To protect against pathogenic viruses, plants are being engineered to express that virus's coat protein gene (*19*), a fragment of the RNA replicase gene (*20*), or a defective virus movement protein gene (*21*). The use of antisense and ribozyme strategies for plant protection would also require the expression of a segment of the virus genome. Will the widespread deployment of genetically engineered plants promote or enhance plant-virus RNA recombination? And, more importantly, if such recombination events occur, will they result in the evolution of more virulent and difficult-to-control viruses, perhaps of wider host range, than otherwise would be created, for example, by mutation and by recombination between viral genomes? Although we cannot now definitively answer these questions, we understand enough about the factors that influence RNA-RNA recombination and about the use of virus-derived resistance genes to make some good guesses.

Selective pressure seems to be necessary to detect recombination. Recombination occurs between viral RNAs and cellular RNA (*22*) and, as exemplified by the Greene and Allison report, between viral and trangenic RNAs (*3*, *12*, *23*, *24*) when the virus is under high selective pressure. Under weakly selective or nonselective conditions, no recombination was detected in one system between pairs of replicating virus genomic RNAs (*25*) or between infecting virus and virus-derived transgene sequences, even during multiple passage series (*26*). Presumably even greater selective pressure must be applied to see the rarer recombinations between less similar sequences.

A survey of reported cases of recombination shows that recombination between two RNAs was detected under selective pressure within regions of moderate similarity (about 100 identical residues) (see figure, squares and trapezoids). However, recombinations between transgene and virus RNAs were within longer identical regions (about 1000 residues) (see figure, circles), suggesting such recombination does not occur more readily than virus-virus recombination.

Whether recombination between viral sequences results in viruses with significant economic or ecological impact depends on several factors. The recombination must occur at a frequency comparable to or greater than the frequency for production of the same virus genomic RNA by mutation and recombination between virus genomic RNAs. The recombinant must be competitive and induce significant disease. The frequency with which recombination can be expected to occur in a crop plant, between transgene and virus genomic RNA sequences, depends on the degree of sequence and structural similarity (*4*); the subcellular concentration (*12*) and location of RNA molecules; whether one, two, or more recombinational events are required; and whether the recombinant genomic RNA is competitive.

For most transgenic plant constructions, the expressed sequences will be similar to the sequences of the target virus genomic RNA. Of course, transgene sequences and nontarget virus genomic RNAs are likely to be dissimilar, in theory providing the possibility of novel recombinants. Recombination between similar sequences is likely to be more frequent than recombination between dissimilar sequences regardless of whether the recombinational event is between transgene RNA and genomic RNA or between two genomic RNA molecules. We cannot predict whether recombination of similar sequences or dissimilar sequences is more likely to generate virus with adverse consequences. Recombinants that combine genes from viruses of different groups have in a few instances resulted in viable virus, but these viruses have been significantly less competitive than either of the parental viruses (*27*), suggesting that corresponding natural recombinants also will be uncompetitive and will be lost.

We believe that it is unlikely that recombinants between transgene RNA and viral genomic RNA will occur at frequencies greater than they already are occurring by recombinations between virus genomic RNAs in natural conventional and subliminal infections. It also is unlikely that any given new virus will be more viable than competing viruses throughout the full infection cycle: transmission to the new host, uncoating and gene expression, replication, assembly of new virions, and possibly infection of alternative hosts.

The virus-resistant cultivars developed by traditional plant breeding have fostered the emergence of virulent virus strains (*28*), but the cost to agriculture of such virus strains is much less than the cost of abandoning plant breeding. Similarly, the potential benefits of engineered resistance genes far outweigh the vanishingly small risk of creating new and harmful viruses in significant excess over those being created by natural processes.

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