U: I don’t see how the coding works. Why can’t it be a “frozen accident?”

R: Look again at N(CGN)n for small n. We say this *codes* for poly-arginine because the reaction of the *arginine* phosphate with the ribose 2’-OH between C and G is greater than for other pairings with either a different amino acid or a different two base codon. The work in Mike Yarus’ lab shows a strong interaction between arginine and CGN sequences using SELEX. That is, SELEX finds an interaction between some amino acids and their contemporary codons. That’s not a frozen accident. There is surely also a difference between simple binding of an amino acid to a codon sequence and esterification of the codon’s ribosyl 2’-OH by an amino acyl phosphate. The Yarus experiments don’t look at that. The translation from a nucleotide sequence to an amino acid sequence depends on a putative physical-chemical interaction between the amino acid and the nucleotide codons. At first there is a smaller list of amino acids involved than at present and as the mechanism evolves so does the coding.

U: Does this mean that molecular genetics started with the capturing of an N(CGN)n codon? It can be replicated in one step (palindrome) and translates into short poly-arginines. These peptides in turn catalyze the RNA replication step. And they provide ligase activity as well.

R: Yes. If the RNA replication rate is at least as fast as the microsphere replication (membrane growth and sphere division or budding) rate, then a population of spheres carrying this particular polynucleotide sequence will emerge. We see the emergence of a *genotype* within the population of spheres. The RNA is both the *gene* and the *messenger*, *mRNA*. Contemporary life separates these functions. DNA is solely for genetic memory. RNA is transcribed from the DNA and used as the messenger, mRNA. Only today the mRNA is read by tRNAs instead. DNA is well suited for the role of repository of genetic memory. It does not have ribose 2’-OH’s, by definition so to speak (*D*eoxy-ribose). Thus it is safe from the dangers of chemical interactions with amino acyl phosphates.

U: Do you mean DNA was selected for its role because deoxyribose lacks the 2’-OH group?

R: That is correct. A proto-reverse-transcriptase would be required and must have emerged very early. How the deoxy-ribose came into the picture is still unknown. In the contemporary system, a complex enzyme is involved. The mechanism is essentially the same in all organisms. This enzyme, *ribonucleotide reductase*,

does utilize iron and thiols and appears to be very ancient, perhaps a product of the iron-thioester-pyrophosphate world.

U: Why would all this complex apparatus, tRNA’s, aaRS’s, and ribosomes, evolve?

R: The simple model uses relatively few amino acids and codons, perhaps as few as 4, the two base code from C’s and G’s only (arg, pro, ala and gly). To do a better job as catalysts a better translation machinery is needed that uses more amino acids and codons and that is more faithful, i.e. less prone to errors. That’s where tRNA’s and aaRS’s come into play.

Activation of amino acids can be accelerated. Imagine the presence of catalysts for amino acid activation among the products of RNA translations (via the primitive model). Such spheres will grow faster as their membranes incorporate some of the translated polypeptide products. If the replication rate for this particular RNA sequence keeps pace with the sphere replication rate then a new genotype is created (replication will require two steps, complement generation followed by replica generation, except for palindromes).

U: A polypeptide translated from RNA that combined the binding of amino acids and the binding of pyrophosphate, P~P, could accelerate activation of amino acids. Today, the aaRS’s bind both the amino acid and the phosphate (as ATP) and they also bind tRNA’s. Maybe first there was just the P~P and aa (amino acid) binding by one RNA generated polypeptide. Just a hexapeptide/heptapeptide would suffice. Even today the aaRS’s bind aa and ATP near the binding site for the 3’-terminus of the bound tRNA. This part of the tRNA’s is quite generic or non-specific. So in essence the early binding could have been just between aa and P~P (no tRNA’s yet) and could have released activated amino acids into the microphere environment. There they would react with RNA’s, charging them with aa’s prior to translation. The increased efficiency of activation is coded for by an RNA that will be replicated fast enough to be preserved during sphere division. A population of spheres with this genotype will grow.

R: Well said ! Once we know what it means to talk about a genotype population, we can try to grasp the evolution of the contemporary translation apparatus. I think it is time to discuss the structure of contemporary aaRS’s. Is this set of catalysts an example of [IC] ? Does the *primitive RNA translator* possessing an intrinsic phyico-chemically based code have the potential to evolve into the contemporary complex structure with its ribosomes, aaRS’s, tRNA’s and other factors ?

U: What would be required in order that the contemporary structure appeared *de novo* without a primitive precursor ? It would seem that this would necessitate simultaneous emergence of numerous large polynucleotides and large polypeptides. Its random probability of natural occurrence is effectively zero. Instead, the apparatus of the primitive RNA translation, in the figures below, is much much simpler and plausible as a natural occurrence. But how can this simple system evolve 20 different aaRS's, apparently all at once ?