CODES WITHOUT COMMAS

By F. H. C. Crick, J. S. Griffith, and L. E. Orgel

MEDICAL RESEARCH COUNCIL UNIT, CAVENDISH LABORATORY, AND DEPARTMENT OF THEORETICAL CHEMISTRY, CAMBRIDGE, ENGLAND

Communicated by G. Gamow, February 11, 1957

```
(ns commas
  "CODES WITHOUT COMMAS -- with apologies to F.H.C. Crick, et al"
  (:require [clojure.set :as s]
           [clojure.math.combinatorics :as c]))
"The problem of how a sequence of four things (nucleotides) can
determine a sequence of twenty things (amino acids) is known as
the 'coding' problem."
(comment "http://www.pnas.org/content/43/5/416" is the paper.)
(comment Now is 1957. What do we know?)
(def nucleotides ["Adenine" "Cytosine" "Guanine" "Thymine"])
nucleotides ; => ["Adenine" "Cytosine" "Guanine" "Thymine"]
(def ACGT (map first nucleotides))
                                      ; => (A \ C \ T)
(def pair (zipmap ACGT (reverse ACGT)))
                                      ; \Rightarrow {\A \T \C \G \G \C \T \A}
(def strand (repeatedly (fn [] (rand-nth ACGT))))
(take 7 strand)
                                      ; => (\G \G \C \T \G \C \C)
(def dna (map (fn [b] [b (pair b)]) strand))
(take 6 dna); => ([\G \C] [\C \G] [\T \A] [\T \A] [\A \T] [\A \T])
(take 7 (map second dna))
                                     ; => (\C \G \A \T \T \C)
(def essential {:F "phenylalanine"
               :H "histidine"
               :I "isoleucine"
               :K "lysine"
               :L "leucine"
               :M "methionine"
               :T "threonine"
               :V "valine"
               :W "tryptophan"})
(def conditional {:C "cysteine"
                 :G "glycine"
                 :P "proline"
                 :Q "glutamine"
                 :R "arginine"
                 :Y "tyrosine"})
(def dispensible {:A "alanine"
                 :D "aspartic acid"
                 :E "glutamic acid"
                 :N "asparagine"
                 :S "serine"})
(def amino (merge essential conditional dispensible))
                                      ; => 20
(count amino)
(comment Now ... What can we find out?)
```

```
(c/selections ACGT 2)
                                         ; => ((\A \A)
                                              (\A \C)
                                              (A \G)
                                              (A \T)
                                              (\C\A)
                                              (\C\C)
                                              (\C \G)
                                              (\C\\T)
                                               (\G\A)
                                               (\G \C)
                                               (\G \G)
                                               (\G\T)
                                               (\T \A)
                                              (\T \C)
                                              (\T \G)
                                              (T T)
(count (c/selections ACGT 2))
                                                ; => 16
                                                ; => 64
(count (c/selections ACGT 3))
(> (count (c/selections ACGT 2)) (count amino)); => false
(> (count (c/selections ACGT 3)) (count amino)); => true
(def string (partial apply str))
(def triples (map string (c/selections ACGT 3)))
(take 7 triples)
                        ; => ("AAA" "AAC" "AAG" "AAT" "ACA" "ACC" "ACG")
(take 7 (reverse triples)); => ("TTT" "TTG" "TTC" "TTA" "TGT" "TGG" "TGC")
(count triples)
                           ; => 64
(take (count ACGT) (partition (count ACGT) 1 (cycle ACGT)))
;; => ((A \ C \ G \ T) ((C \ G \ T \ A) ((G \ T \ A \ C) ((T \ A \ C \ G)))
(def rotations
  (fn [s] (let [n (count s)]
            (map string (take n (partition n 1 (cycle s))))))
                                   ; => ("ACGT" "CGTA" "GTAC" "TACG")
(rotations ACGT)
(rotations (take 3 ACGT))
                                   ; => ("ACG" "CGA" "GAC")
(take 7 (map rotations triples))
                                        ; => (("AAA" "AAA" "AAA")
                                               ("AAC" "ACA" "CAA")
                                               ("AAG" "AGA" "GAA")
                                               ("AAT" "ATA" "TAA")
                                               ("ACA" "CAA" "AAC")
                                               ("ACC" "CCA" "CAC")
                                               ("ACG" "CGA" "GAC"))
(def codons (set (map (comp set rotations) triples)))
                                        ; => 24
(count codons)
                                         => (#{"ACC" "CCA" "CAC"}
(take 7 codons)
                                               #{"GGG"}
                                               #{"TTT"}
                                              #{"GCC" "CGC" "CCG" }
                                               #{"CAA" "ACA" "AAC"}
                                              #{"CTC" "CCT" "TCC"}
                                              #{"AGC" "CAG" "GCA"})
(count (group-by count codons))
                                        ; => 2
                                        ; => (3 1)
(map first (group-by count codons))
(def sense-codons (filter (fn [g] (= 3 (count g))) codons))
                                        ; => 20 Eureka!
(count sense-codons)
```

```
(take 7 sense-codons)
                                              #{"GAG" "GGA" "AGG"})
(def sense (map (comp first sort) sense-codons))
(count sense)
              ; => 20
(take 7 sense); => ("ACC" "CCG" "AAC" "CCT" "AGC" "ATT" "AGG")
(def nonsense (s/difference (set triples) (set sense)))
(count nonsense)
                                 ; => 44
(= (count triples)
   (+ (count sense)
      (count nonsense)))
                                 ; => true
(def code (zipmap (map vec (sort sense)) (sort (keys amino))))
(sort-by second code)
                                        ; => ([[\A \A \C] :A]
                                              [[\A \A \G] :C]
                                              [[\A \A \T] :D]
                                              [[\A \C \C] :E]
                                              [[\A \C \G] :F]
                                              [[\A \C \T] :G]
                                              [[\C \G \G] :R]
                                              [[\C \G \T] :S]
                                              [[\C \T \G] :T]
                                              [[\C \T \T] :V]
                                              [[\G \G \T] :W]
                                              [[\G \T \T] :Y])
(map string (take 7 (partition 3 1 strand)))
;; => ("TTC" "TCG" "CGG" "GGT" "GTG" "TGA" "GAT")
(def amino-keys (remove nil? (map code (partition 3 1 strand))))
(take 7 amino-keys)
                                       ; => (:R :W :M :W :G :T :D)
(def aminos (map amino amino-keys))
(take 17 aminos)
                                          => ("arginine"
                                               "tryptophan"
                                              "methionine"
                                              "tryptophan"
                                              "glycine"
                                              "threonine"
                                              "aspartic acid"
                                              "alanine"
                                              "glutamic acid"
                                              "alanine"
                                              "glycine"
                                              "valine"
                                              "asparagine"
                                              "alanine"
                                              "glutamic acid"
                                              "glutamine"
                                              "glutamine")
"Note: This is fun programming but (as of 1961) bad biology."
```