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Making Music with Enzymes

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MAKING MUSIC WITH ENZYMES

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My residency took place in the context of the research developed by partners based at the Technical University of Denmark. I interacted with Pablo Iván Nikel and his team of scientists, including Manuel José N. Domíngues and Nicolas Krink, at the Novo Nordisk Foundation Center for Biosustainability. These scientists helped me to understand the SinFonia project's challenges and how the consortium has tried to tackle them. The interactions with these scientists prompted me to become introspective about my creative process. To my mind, as a musician with a scientific background, the distinction between composing a symphony and conducting a scientific experiment is somewhat blurred; I also realize that this is not necessarily the case for all artists and scientists.

In this chapter, I will discuss my process when it comes to composing music and will articulate the role played by science in my creative process. I will unpack why working at the intersection of art and science is so interesting to me. I will then present the pieces of electronic music that I composed during my residency, as well as their background story and the system that I designed to make music with DNA codes.

I often find myself confronting the following dichotomy when I introspect my compositional practice: on the one hand, I think of music as the intuitive expression of ineffable thoughts, highly personal impressions of the world around me, and as the irrational manifestation of emotions. On the other hand, I am keen to maintain that music should be logical, systematic, and should follow guiding rules. In general, I think that rationality plays an important role in music composition, especially in classical music. It is definitely prominent when I develop art-science interdisciplinary projects.

Any attempt to distinguish the rational from the irrational in musical composition ought to take the scientific developments, and above all the music technology, of the time into account. The most influential music technology of our time is undoubtedly the computer: it is a general-purpose device that can be programmed to carry out musical tasks such as, for example, generating music following sets of arithmetic and logical operations. One of computers' most important benefits is that they facilitate musical composition, informed by processes and data abstracted from phenomena other than music; for example, these can include meteorologic, hydrologic, and genetic data, respectively.

The use of computers to generate original musical compositions dates back to the mid-1950s. In 1956, Lejaren Hiller composed *The Illiac Suite for String Quartet*, which was allegedly the first composition to contain computer -generated materials. Hiller teamed up with Leonard Isaacson to program the mainframe computer ILLIAC at the University of Illinois in the USA to generate music by following rules. The computer produced music using both the rules of counterpoint and a technique known as Markov chains to generate sequences of patterns. The computer's output was transcribed manually into standard musical notation on a score to be played by a string quartet.

I use the computer to generate materials for my compositions regularly. These materials include riffs, sequences, rhythms, melodies, entire sections lasting for several minutes, and indeed synthesized sounds. More often than not, musical form emerges as I work with the compositional materials at hand. To begin with, I tend to not have an overarching plan for the form my pieces end up taking. The compositions emerge from the handling of the materials that I am working with to compose a particular piece.

For the most part, my computer-generated materials are discarded, and I usually amend certain selected ones in order to fit particular compositional contexts, aims, and so on. Ultimately, it is my ear that has the final say. However, this compositional process's dynamics beg further understanding. I often find myself asking why I find working with computer-generated materials exciting. If I discard most of the materials generated by the computer, and often edit those that I select for a particular piece, then why do I not write these materials myself instead?

One of the reasons that I find working with computers exciting is because they can generate musical materials that I would not have been able to produce on my own manually. This mindset is akin to John Cage's thinking when he preferred to set up the conditions for music to happen, rather than composing music set in stone. Cage liked being surprised by the outcomes of such happenings (Cage, 1994). By the same token, I enjoy being surprised by the outcomes of a computer.

Technically, there are two approaches to designing computer systems to generate music, which I refer to as 'Artificial Intelligence' (or AI) and 'algorithmic' approaches, respectively.

The AI approach is concerned with embedding the system with musical knowledge to guide the generative process. For instance, computers have been programmed with rules of common practice for counterpoint in order to generate polyphonic music (Jacobs & Regia, 2011). Machine-learning technology has enabled computers to learn musical rules automatically from given scores, which are subsequently used in order to generate music. Conversely, the algorithmic approach is concerned with translating data that is generated from (seemingly unmusical) models onto music. Examples of this approach abound; for instance, computers have been programmed to generate music from chaotic functions (Dabby, 1996), fractals (Dodge, 1998), and, indeed, even DNA (Miranda, 2020). My work on generating music with DNA is discussed in greater detail below.

Aesthetically, the algorithmic approach tends to generate highly novel and unusual music, whereas the AI approach tends to generate imitations of certain types of music that exist already. Both approaches have their own merits and pitfalls. Even though I strive to combine both, I often adopt the algorithmic one; I adopted the algorithmic approach to compose the pieces for my SinFonia residency. However, before I describe the residency work, it is important to first spell out how I use computer-generated materials in my work.

There are two approaches to composing with computer-generated materials which I refer to as the 'purist' and 'utilitarian' approaches, respectively. The purist approach to computer-generated music tends to be more concerned with the correct application of the rules that are programmed in the system, than with the musical results per se. In this case, the computer's output tends to be considered as the final composition. That is, in this case, the composer would not normally modify the materials produced by the computer. It is thought that this would meddle with either the model or system's integrity.

The utilitarian approach can be found at the other end of the spectrum. This is the approach adopted by those who consider the output from the computer as raw materials for further work. In this case, composers normally tweak the results to fit their aesthetic preferences, to the extent that the system's output might not even be easily identifiable in the final composition. Obviously, there is a blurred line dividing these two approaches, but practices combining aspects of both abound.

The computer's role in my compositions has oscillated between two extremes: on the one hand, I have simply assumed the authorship of compositions that were entirely generated by a computer, but which were programmed to follow my exact instructions. On the other hand, I have composed with pencil on stave paper, using the computer only to typeset the final score. I shall argue that both approaches to composition are not incompatible; rather, they are manifestations of creative processes that are becoming progressively more polarized due to technology's increasing sophistication. Let us unpack this further.

First, I should mention that I have become increasingly less interested in the purist approach as my career has progressed. Indeed, the exciting computer music challenge of the 20th century is over. People questioned whether computers would be able to compose music with the development of AI towards the end of the last century and there were various attempts at formulating criteria to address a so-called "musical Turing test" (Begum et al., 1998). It is now abundantly apparent that computers can be programmed to compose music of a reasonably convincing technical quality automatically. I have been developing systems to do this over the past twenty years and other colleagues have done likewise. Paradoxically, the news media continues to periodically report that, yet again, someone has built a system that can compose music; this is no longer a novelty.

The caveat with computer-composed music is that technical quality *per se* does not necessarily make a piece of music compelling. Music needs to be embedded in cultural and emotionally meaningful contexts which composers express in subtle, often ineffable ways. A computer would not be capable of composing a piece such as Tchaikovsky's *1812 Overture*. Its backstory, myriad of references, drama, and so on are aspects of musicianship that computers, as we know them today, cannot grasp.

One thread that I am currently contemplating, to unravel the role played by the computer in my own compositional practice, explores an idea suggested by philosopher Friedrich Nietzsche ([1872]1993). In a nutshell, Nietzsche suggested that great artistic creations could only result from the articulation of a mythological dichotomy referred to as the Apollonian and Dionysian.

Apollo is the god of the sun and is associated with rational and logical thinking, self-control, and order in ancient Greek mythology. Conversely, Dionysus is the god of wine and is associated with irrationalism, intuition, passion, and anarchy. These two gods represent two conflicting creative drives, constantly stimulating and provoking one another. As I understand it, Nietzsche proposed that this (metaphorical) mythological process would lead to increasingly high levels of artistic and scientific achievement. This approach to creativity resonates with the way in which my creative mind seems to work: One side of me is methodical and objective, keen to use automatically generated music, computer systems, formalisms, and models. For instance, I have developed systems to generate music using Cellular Automata, Genetic Algorithms, grammars, and simulations of biological cells. Conversely, another side of me is anarchic, intuitive, and metaphorical, and I often feel that one side tends to counter the other while I am composing: the more I swing to my Apollonian side, the stronger the Dionysian force that pulls me to the opposite side becomes, and vice-versa. These push-and-pull dynamics transpire most prominently in my mind when I develop interdisciplinary projects with scientists. The SinFonia residency work was no exception in this respect.

McGilchrist (2009) discussed the 19th century Apollonian versus Dionysian dichotomy in the context of 21st century Neuroscience. He aligns this dichotomy with the notion of 'brain asymmetry' (Davidson, 1996; Springer & Deutsch, 1998; Hugdahl & Westerhausen, 2010). In broad strokes, one could consider that specific brain functions tend to be more Apollonian or Dionysian than others. Indeed, several attempts have been made to associate areas of the brain with such functions, but these associations remain largely elusive. Nevertheless, they are useful as working tools for discussion. For instance, the Apollonian brain might involve the frontal lobe of the cortex and the left hemisphere. Generally, these areas are known to be in charge of focusing attention to detail, seeing wholes in terms of their constituents, and making abstractions; they are systematic and logical.

The Dionysian brain might include sub-cortical areas, which are much older in the evolutionary timeline, and the right hemisphere. These areas are connected to our emotions. The right hemisphere tends to perceive the world holistically, leading towards unfocused general views. The Dionysian brain tends to forge connections between allegedly unrelated concepts, while the Apollonian brain is concerned with unilateral meanings. The notion that the Apollonian and the Dionysian brains tend to counter each other is reminiscent of the way in which the brain functions at all levels. Inhibitory processes pervade our brain's functioning, from the microscopic level of neurons communicating with one another to the macroscopic level of interaction between larger networks of millions of neurons.

Hence, formalisms, rules, schemes, methods, number crunching, computing, and so on, are of the utmost importance for my *métier*: They enable me to stretch my Apollonian musical side far beyond my ability to do so by hand, thereby prompting my Dionysian side to counteract accordingly. I would say that this cognitive push-and-pull is a vital driving force behind my musical creativity. Interdisciplinary projects, involving residencies in scientific research laboratories and collaborations with scientists, thus harness my Apollonian-Dionysian push-and-pull. I should say that this is not as clear as I am trying to convey here, however. I tend to get excited about the science that I encounter in these labs and often invest a lot of my time learning the details. It is not uncommon for me to want to contribute to the scientific endeavor as well. One example of this is my work with Brain-Computer Interfaces (BCI). What started as a wish to compose music with brainwaves 20 years ago, ended up being a long research endeavor to understand how the brain processes music (Daly et al., 2020)and to develop BCI technology to enable severely motor-impaired people to make music (Miranda & Castet, 2014).

The remit of my SinFonia residency was to create a composition informed and inspired by a metabolic process referred to as bio-fluorination, which produces fluorochemicals. Fluorine is an important chemical element for our modern world, and so are fluorochemicals – i.e., chemicals that contain fluorine. They are used in manufacturing industries as diverse as electronics, fashion, and medicine. Currently, fluorochemicals are made using chemical processes. However, these are deemed to be of limited capacity to discover new compounds. Moreover, those chemical processes pollute the environment significantly when produced on an industrial scale. SinFonia's ambition is to change this by way of synthetic biology. The project is interested in developing ways to harness the genetic make-up of bacteria[1] in order to make them synthesize fluorochemicals for us.

As a starting point, I wanted to learn as much as possible about fluorochemicals and how they can be synthesized. I could not possibly start composing before satiating my Apollonian side with as much scientific knowledge as I could absorb about Nikel's lab work. The lab was genetically enhancing bacteria to synthesize these compounds and I found this to be inspiring. The techniques that are being developed for synthesizing compounds reminded me of the techniques that electronic musicians use to synthesize sounds. In the same way that chemical components react and combine to form new ones, sinewaves are carefully added together to form new sounds and filters are applied to transform sounds.

[1] SinFonia is engineering the bacterium *Pseudomonas putida* to execute bio-fluorinations.

Broadly, I learned how the team was developing methods to alter the genetic information of the bacterium *Pseudomonas putida* to synthesize new types of fluorochemicals. One approach to doing this was to steer the organism to produce the enzymes needed to carry out a sequence of metabolic reactions,[2] which would ultimately result in a useful fluorochemical called fluoroacetate. This reaction sequence is shown in Figure 2.2. Five metabolites are produced from fluoride's initial reaction with the enzyme S-Adenosyl methionine (or SAM), before ending up with fluoroacetate; these are named as follows:

FDA (5'-fluoro-5'-deoxyadenosine)
FDR (5'-fluoro-5'-deoxy-D-ribose)
FDRP (5'-fluoro-5'-deoxy-D-ribose-1-phosphate)
5-FDRibulP (5'-fluoro-5'-deoxy-D-ribulose-1-phosphate)
Fluoroacetaldehyde

The enzymes required to carry out the metabolic reactions, depicted in Figure 2.2, are Fluorinase, Nucleosidase, Kinase, Isomerase, Aldolase, and Aldehyde dehydrogenase. My Dionysian side began to connect concepts when Manuel handed me those enzymes' DNA codes. Having composed with DNA sequences before, I was keen to customize and improve the generative music method that I had developed for the previous project. I ended up developing a new system: the "Genetic Musinator System".

[2] That is, life-sustaining chemical reactions that take place inside an organism to generate energy.

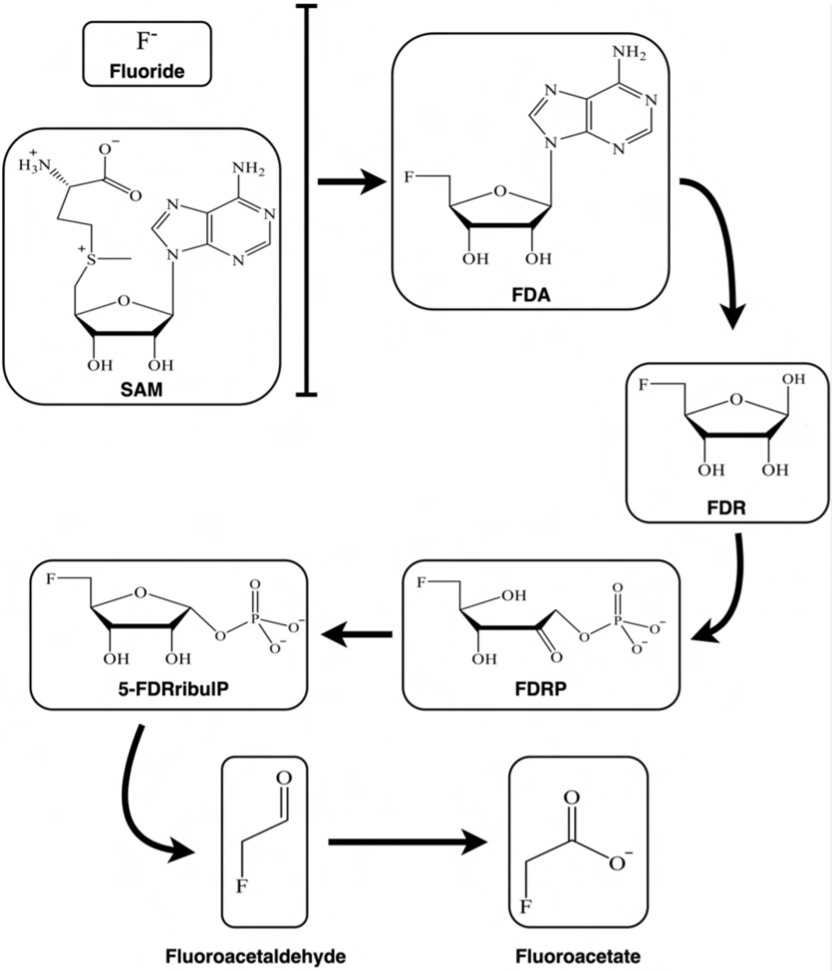

fig. 2.2 Fluoride's initial reaction with the enzyme SAM provides a substrate for metabolic reactions, producing the fluorochemical Fluoroacetate.

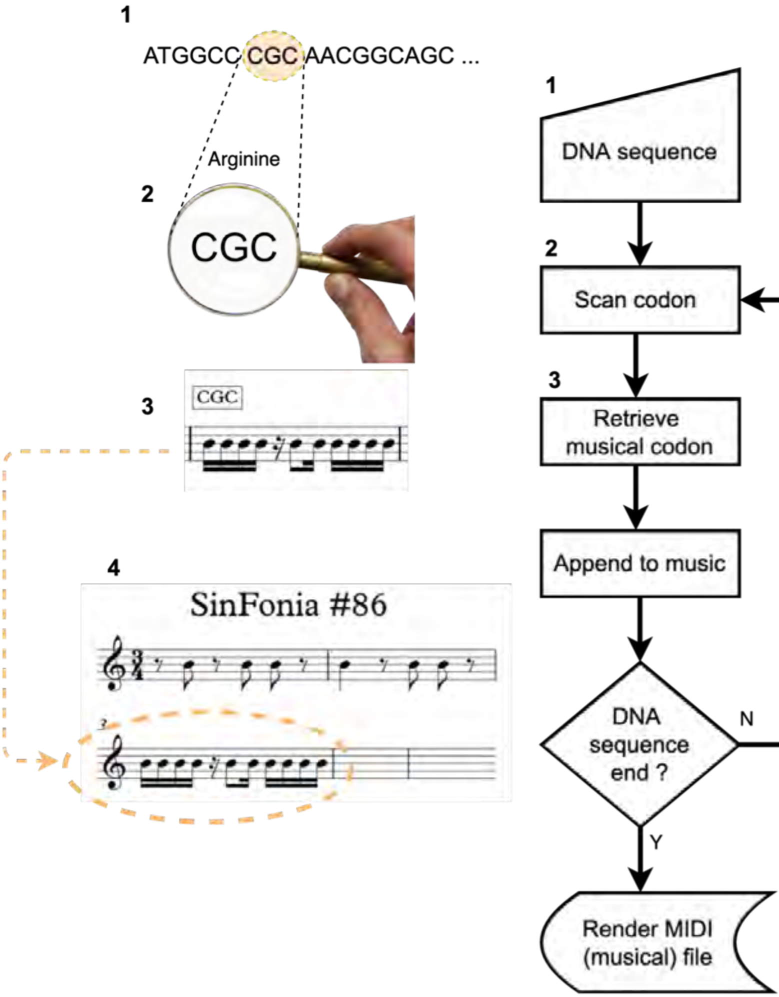

fig. 2.3 The Genetic Musinator System flowchart.

In a nutshell, the system scans a given DNA strand and (a) generates variations of the strands and (b) translates the codons[3] of the original strand, and variations thereof, into musical sequences. The system uses lexicons of musical codons in order to translate the codons into music. I designed twelve different lexicons for this. For instance, in Figure 2.3, as the system scans a given DNA strand, it identifies the codon CGC, which corresponds to the amino acid Arginine. However, the amino acid's name does not matter here. Instead, the system uses this code to retrieve a 'musical codon' from a lexicon (Figure 2.3, step 3). The system then appends this to the musical sequence that is currently being generated for the respective DNA strand.

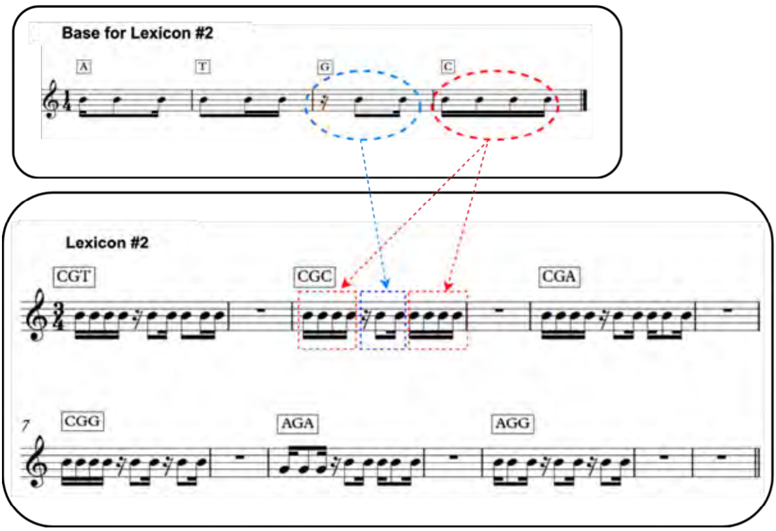

fig 2.4 An example of a lexicon's nucleo-rhythms (top) and an excerpt of the lexicon.

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[3] A codon is a triplet of nucleotides representing the DNA or RNA of an amino acid. For instance, the amino acid Methionine is presented by the codon ATG.

The base for each lexicon comprises four 'nucleo-rhythms', each of which represents a DNA (or RNA) nucleotide, A (Adenine), G (Guanine), C (Cytosine), or T (Thymine) (or U, for Uracil in RNA). For instance, Figure 2.4 depicts the nucleo-rhythms for Lexicon #2 (top) and an excerpt of the lexicon (bottom). Each lexicon contains 64 musical codons.

The sequence of reactions shown in Figure 2.2 served as, and generated, inspiration for the composition. To me, the chain of reactions from fluoride and SAM, which ended up with fluoroacetate, resembles a storyline the protagonists of which are chemical elements and compounds. This reminded me of how composers forge musical discourses through the articulation of musical elements (notes, motifs, etc.) and musical compounds (tunes, melodies, etc.). I then envisaged a composition whereby musical representations of the enzymes involved in the chemical reactions, shown in Figure 2.2, are articulated to tell a metaphorical story: the story of fluoroacetate.

Firstly, I generated six individual short compositions, one for each enzyme: Fluorinase, Nucleosidase, Kinase, Isomerase, Aldolase, and Aldehyde dehydrogenase, respectively. I did this by inputting the DNA codes for each of the enzymes into the "Genetic Musinator System". The system generated sets of MIDI files, its automatically generated variations corresponding to the respective original DNA strand. Each of these was considered to be an individual musical track. The tracks were uploaded into a "Digital Audio Workstation" (DAW)[4] and mixed to generate the respective compositions. At this stage, my Apollonian side refrained from editing the tracks produced by the system, but my Dionysian side chose the timbres and selected the tracks to be included in the mix; not all variations were used.

I unleashed my Dionysian side once the 'enzyme' pieces were completed. I uploaded all of the tracks into a musical processor and freely composed them into a larger musical structure. Think of a DAW as the musical equivalent of a word processor. In the same way that one uses a word processor to write words, form sentences, copy and paste phrases and paragraphs, a musical processor enables me to work with 'musical words', 'musical sentences', and 'musical paragraphs'.

The final composition tells a metaphorical story, whereby the six enzyme pieces were deconstructed and their elements (i.e., tracks) were combined

[4] A "Digital Audio Workstation" (DAW) is a piece of software used for recording, editing, and producing music.

and re-combined to represent the process of bio-fluorination. The order of appearance and combinations were dictated by aesthetic preferences purely; that is, by purely Dionysian impulses. The piece begins with tracks from Nucleosidase, and then Aldehyde dehydrogenase enters the scene. A new ingredient appears in the mix as these two 'react': Aldolase. These three musical enzymes somehow make room for the appearance of Isomerase. Subsequently, Kinase emerges. Finally, the Fluorinase enters the scene in order to consolidate the composition and is accompanied by a soothing piano melody.

The team at Novo Nordisk Foundation Center for Biosustainability were just fantastic at patiently explaining what they were doing. It certainly helped the interaction that all of them love music and are amateur musicians themselves. Affinity, respect, and open-mindedness are *sine qua non* for creative art-science projects' success, in my experience. All parties need to understand the respective methodologies, objectives, and materials of the respective fields; that is, music, biology, and chemistry. I feel that we all strived in order to achieve this.

The SinFonia residency left me with an appetite to immerse myself in the world of synthetic biology. I believe that creative musical processes might also inspire and inform the synthesis of new biological forms in much the same way that the processes to engineer bacteria to synthesize fluorochemicals inspired and informed the composition of *SinFonia*. My work shows how to make a piece of music as though one were processing DNA sequences. Despite the fact that the composition's final stages involved a great deal of Dionysian anarchy, I believe that it could be possible to formalize what I did at this stage too with rules. Thus, the question that emerges in the back of my mind is: Would there be a way of synthesizing meaningful DNA sequences as if one was composing music? I am itching to initiate the experiments!

Recordings of the composition were released on SoundClick.

The individual enzymes are as follows:

Aldolase: https://soundclick.com/r/s8h8qm
Fluorinase: https://soundclick.com/r/s8h8ql
Aldehyde Dehydrogenase: https://soundclick.com/r/s8h8qk
Isomerase: https://soundclick.com/r/s8h8qj
Kinase: https://soundclick.com/r/s8h8qi
Nucleosidase: https://soundclick.com/r/s8h8qh

The final *SinFonia* piece is available at the following link:
https://www.soundclick.com/music/songInfo.cfm?songID=14247892

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