Responsable Dr. Esteban Valverde	IFIBIO “Houssay” UBA-CONICET Bracelet stimulator for Tourette's patients	Ticket # 20210910
Start date: 10/09/2021		End date: 17/03/2023

The idea of a stimulator for Tourette’s patient came from Bárbara Maiquez et. al. [1], who observed the decrease in tics by stimulating the median nerve non-invasively, at the level of the wrist, by means of pulse trains at 12Hz.

In the original work of Maiquez et. al., they used a Digimiter constant current stimulation device, model DS7AH. This device is used in the laboratory and the authors propose the construction of a wristband-type device for the patient to wear all the time and activate it, for example, when they feel that tics are coming.

I was asked for a patient to collaborate in the development of the electronic circuit and the possibility of this device being brought to reality.

A very first design was developed on an Arduino, a step-up source at home, and tested different types of electrodes (stainless steel and disposable ECG electrodes). The diagram is the one in Figure 1.

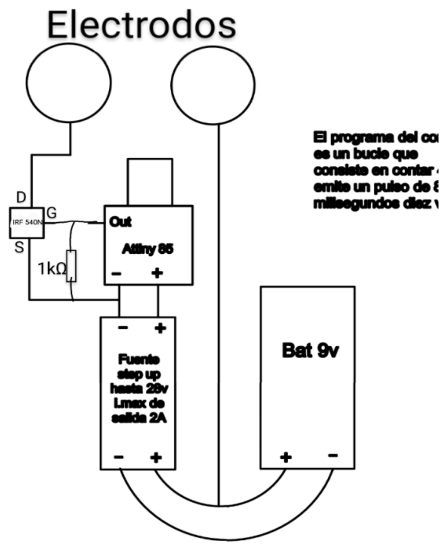

Fig. 1 original diagram

The diagram in Figure 1 shows that the Arduino ATtiny85 sends pulses through a variable amplitude port and operates an N-Channel MOSFET, IRF520N. This is powered at 28V, in order to allow a high patient resistance (around 1KΩ for maximum stimulation current of 20mA).

The configuration of the circuit appears to be a source of current, but a resistor between Source and ground is missing to fix the excitation current. Consequently, I understand that the system operates at constant voltage. The 1KΩ resistor seems to serve the function of turning off the Mosfet when the output of the pulse trains is at 0V.

I proposed the following modification of the circuit (see Figure 2), in order to control at constant current in the range of 0 – 20mA, with a maximum resistance between electrodes of 1KΩ.

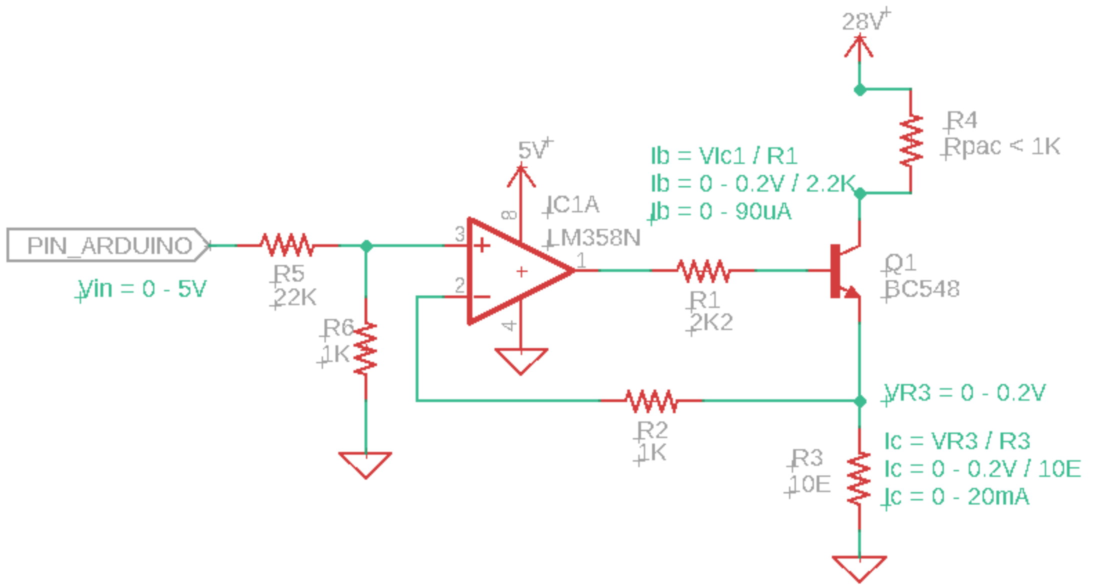

Fig. 2. Modification to obtain a constant current circuit

Basically, the output current of the transistor is controlled by the voltage of the op-2 pin and the emitter resistor. As the operational is in follower mode, the output of the same (pin 1) will have the necessary voltage to ensure the voltage set in the transistor emitter. This current is enough to turn on the transistor and bring it to the static working area.

The voltage in the emitter is fixed with the resistive divider at the input of the operational (pin 3), which, from a variation of 0 - 5V, brings the emitter resistance to a variation of 0 - 200mV. This ensures a maximum current of 20mA through the 10E emitter resistor.

In this case, the voltage drop between electrodes, for 1KΩ of this resistor, is 20V, setting the voltage VCE = 28 – 20 – 0.2 = 7.8V. This value leaves the BC548 transistor within the working zone. The static curve of the BC548 is shown in Figure 3. The line drawn on this curve corresponds to values measured at DC in the transistor and coincides with the theoretical values. In this figure, it can be seen in a dotted line that for 20mA of collector current, the limit of VCE = 2V can be reached by keeping the base current IB constant. This means that the maximum allowable electrode resistance would be RELE = VELE / ICmax = (28 – 2 – 0.2)/0.02A = 25.8V/0.02A = 1290Ω. So, for a stimulation current of 2mA, you could have a maximum patient resistance of 12.9KΩ.

If you change this transistor for another one, or for a MOSFET, you don't need to put R1. Marcos tried the IRF520N and it worked properly.

If the patient's resistance increases, then the transistor is taken to the cut-off. Consequently, the current by the patient decreases because the supply voltage limit of 28V is exceeded.

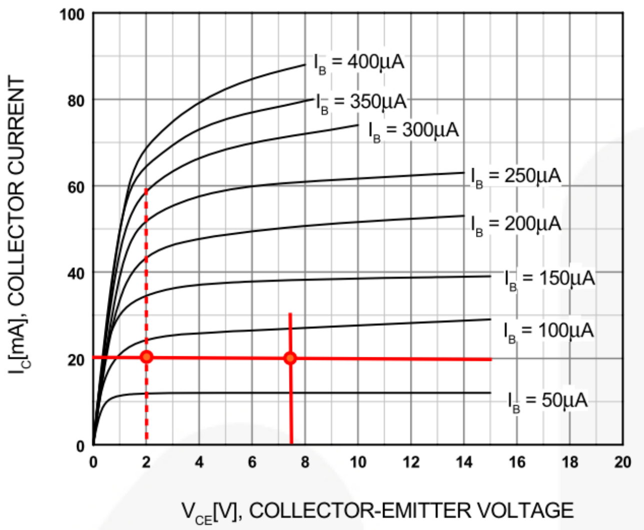

Fig. 3. BC548 Response Curve

Up to this point, a patient put the circuit together and commented that he didn't feel like he was stimulating properly. In the simulations I did in the lab with instrumentation, I gave the correct stimulation current for a maximum electrode impedance of 1K.

The patient was unable to define what electrode impedance value he is using, since he uses commercial disposable electrodes, which would not be indicated for stimulation.

On 9/11, the patient was at the IFIBIO and we did the following rehearsals:

- We verified that R3 was 250E instead of 10E; We put the right one. A current of 7.5mA (measured in R3) was sufficient to stimulate.
- We added a preset to regulate the current intensity. We agreed to place it on a DAC pin of the Arduino and control the current by software, or something similar.
- It's likely that the reason why it didn't work with the BC548 is because the value of R3 was wrong and I also recalculated R1 and it should be less than 2K2 instead of 10K as it was originally.

[1] Barbara Morera Maiquez, Hilmar P. Sigurdsson, Katherine, Eleri Clarke, Polly McGrath, Matthew Pasche, Anupriya Rajendran, Georgina M. Jackson, Stephen R. Jackson, "Entraining Movement-Related Brain Oscillations to Suppress Tics in Tourette Syndrome," Current Biology, Volume 30, Issue 12, 2020, Pages 2334-2342.

Redesign of the stimulation circuit

I am currently making changes to the design, in order to maximize the use of the power bank and be able to replace it with alkaline batteries. The block diagram and final circuit would be those in Figures 4-a and 4-b

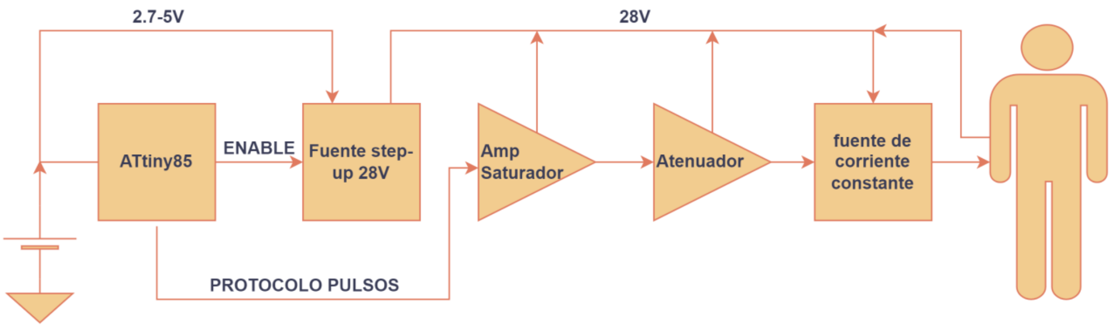

Fig. 4-a. Block diagram of the stimulator

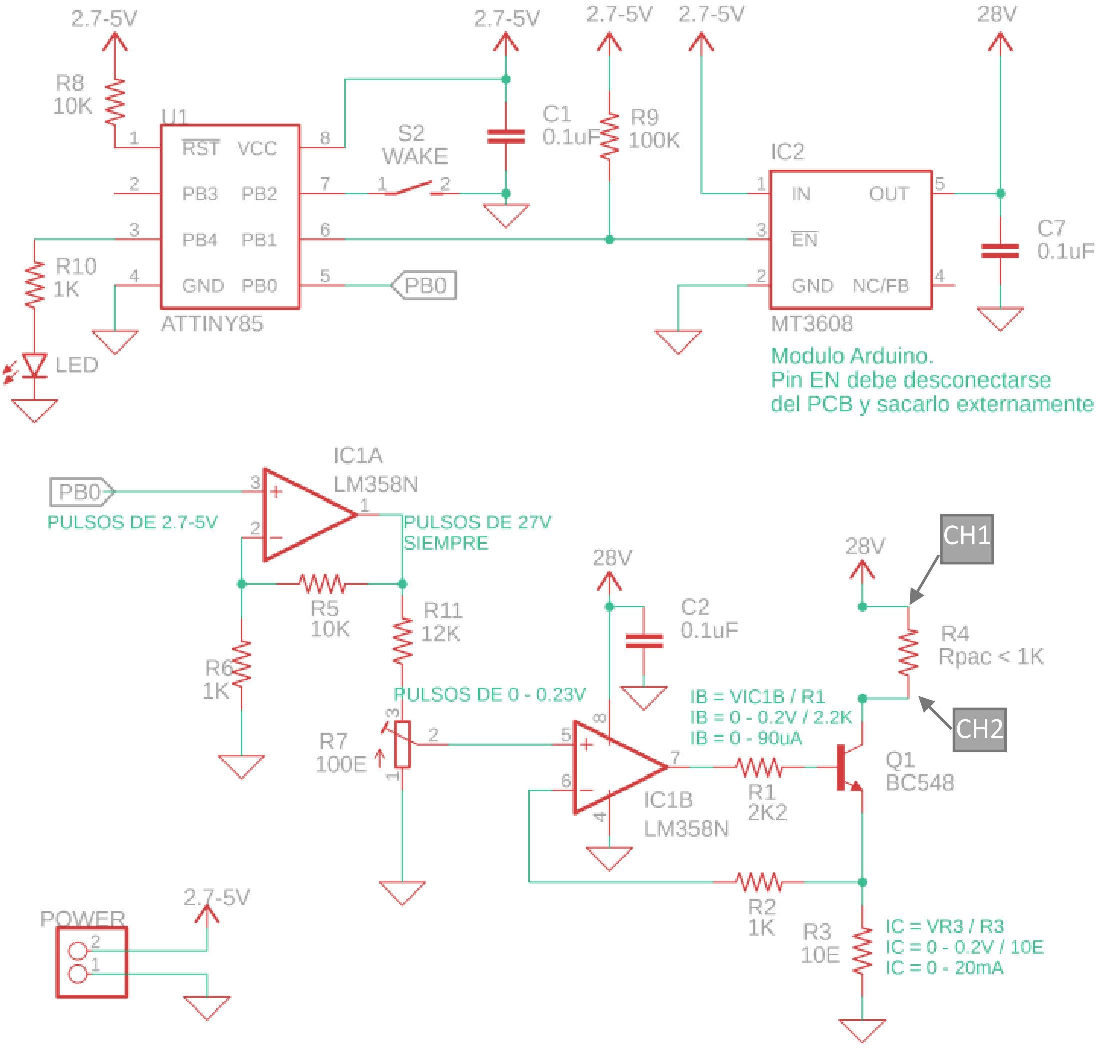

Fig. 4-b. Complete Stimulator Circuit

The circuit in Figure 4-b has the following characteristics:

- The pulses are controlled by an ATtiny85 microphone. This mic will be programmed in Sleep mode, and will only wake up by using an Interrupt (INT0) to deliver the current pulse protocol. It will then enter Sleep mode again. This will be repeated according to the total dose indicated in the work of Bárbara Maiquez et. al. [1], and will fall asleep until the patient initiates a new stimulation protocol, using the S2 button (WAKE).

- A potentiometer is added to choose the current level. The most basic line of Atmel mics do not have a DAC converter, but instead use PWM to "simulate" a DAC conversion. They are also low frequency. It wouldn't be good for such short-lived pulses. As a first measure, a preset is used that the patient will adjust to their liking, but later it can be changed for a MCP4725, 12-bit resolution DAC and adjust the current level digitally.

- The entire high-voltage circuit (28V) is powered from the MT3608 step-up source. From this source you get control of the Enable (EN) pin, which connects to a mic output pin. When the EN pin is brought to a logical zero, the MT3608 source shuts down and disconnects power to the power circuit. This leads to significant battery savings, since this circuit will not be consuming current when the stimulation protocol (microphone sleep) is not present. Remember that the protocol stimulates for approximately 1 second and then goes 4 seconds without stimulating. Depending on the dose (e.g. 15 minutes of stimulation), after this time the device falls asleep (Sleep) until the user turns it back on, using the S2 button (WAKE).

- In this condition, the total consumption would be approximately the preset stimulation current for one second and then on the order of uA during the 4 seconds of waiting and practically zero during the sleep period.

In case of using the Arduino MT3608 module, it is necessary to disconnect the EN pin from the circuit to control it externally, as shown in Figure 5.

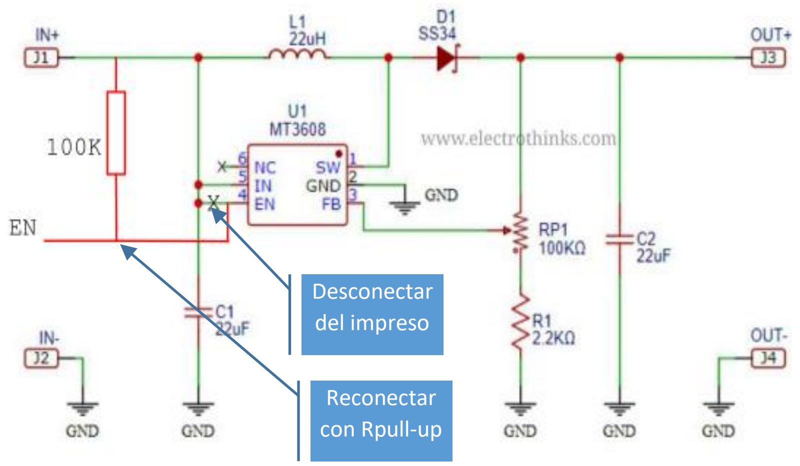

Fig. 5. MT3608 Step-Up Source Circuit and Its Modification to Control the EN Pin

The waveforms obtained, for a supply voltage of 4.5V (equivalent to 3 x 1.5V alkaline batteries), are shown in Figure 6. Channel 1 (CH1) of the oscilloscope is in Magenta and channel 2 (CH2) is yellow. Both voltages are approximately at 4.5V. This happens because during the shutdown of the high-voltage source (MT3608), with the pin EN = 0V, the step-up source stops regulating and the output voltage is directly connected to the input voltage through the L1 inductor and the D1 diode (see Figure 5). When the power supply is turned on, EN = 4.5V, the output voltage of the source is approx. 28V.

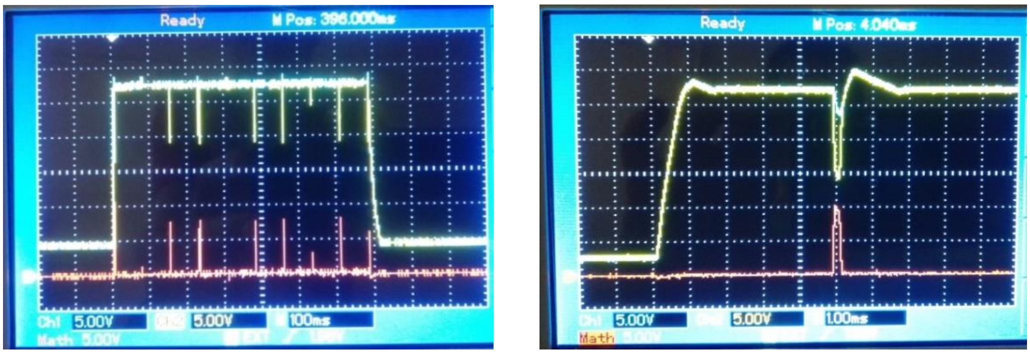

Fig. 6. Left) Feed waveforms and stimulation current, in red. Right.) Detail of the first current pulse. It is observed that the ignition of the high voltage supply, for a 2.7V supply, is 1msec. At 5V power, the ignition lasts less than 0.5msec.

During the power supply, which lasts one second, the 10-pulse train is sent at a frequency of 12Hz. In the same figure, the difference between CH1 and CH2 can be seen in red. It corresponds to the voltage drop in RPAC (patient) in Figure 4. In this case, a 500 W patient resistor was used. Due to definitional issues on the oscilloscope screen it is not observed, but opening the time scale it can be seen that the amplitude of the pulses is approximately 12V, which divided by 500Ω gives a stimulation current of 20mA.

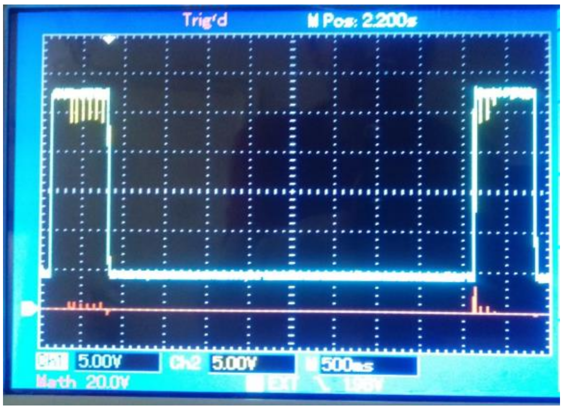

Fig. 7. Stimulation protocol

Figure 7 shows the wait time (4 seconds) between one pulse train and the next. During the period when the fountain is on, a consumption of 11mA was observed. As the protocol indicates 1 second of stimulation and 4 seconds of rest, we can calculate that the average consumption during the protocol is 11/4 = 2.75mA. This average consumption is maintained during the 15 minutes that the protocol lasts. Then everything shuts down until the patient presses S2 and starts a new protocol.

It can be seen in the same figure that the time between stimuli is greater than 4 seconds. This is due to the mic's clock settings. This one is set to "internal RC clock" as there is no external crystal or clock source. According to the ATtiny85 datasheets, the internal RC clock is accurate to 10%, i.e. between 3.6 and 4.4 seconds for a 4-second delay, which is a design limitation.

While the ATtiny85 data sheets indicate that it operates from 2.7V, and that the MT3608 boots from 2V, it is observed in the actual circuit that the entire set stops working below 2.7V power. In this case, the current during stimulation is 15mA. It would be desirable to actually measure how long a set of 3 alkaline batteries last to power this circuit and check if the system works only with 2 alkaline batteries.

It can be seen in Figure 4 that IC1 receives the pulses from the mic and amplifies them 10 times before attenuating to the desired stimulation current (saturator amplifier). For a pulse amplitude range of 2.7-5V, depending on the battery load, after amplifying 10 times ensures that the output pulses of the IC1, before entering the attenuator, always have an amplitude of 27V (when the power supply is 2.7V the gain gives just 27V and when it is greater than 2.7V IC1 is saturated and the output pulses are at 27V). In this way, with this simple saturator and attenuator amplifier, it is ensured that the amplitude of the stimulation pulses are independent of the supply voltage of the ATtiny85 and are regulated between 0-200mV to feed the constant current source.

Software Development

The flow chart of the software is as shown in Figure 8. The program's main loop counts the number of pulses in the protocol, so that a train of 10 pulses is sent every 4 seconds for 15 minutes. A 10-pulse train lasts 760msec: 5msec standby for 28V source start-up + 10 pulses of 200useg + 83.133msec standby between pulses, to reach 12Hz before 28V source shutdown. If the protocol lasts 15 minutes, the loop should be repeated 15min/4,760sec ≈ 190 times. Consequently, the constant MAXTRIALS = 190.

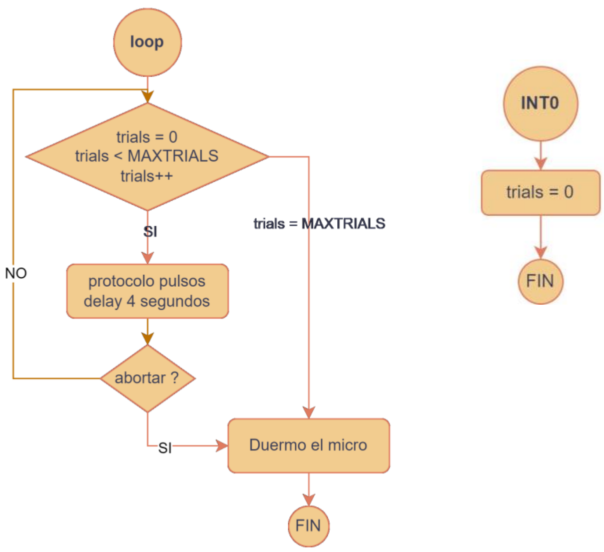

Fig. 8. Main loop that sends the pulse trains.

Then, when the microphone is awakened, using the button associated with pin 4 of the microphone (INT0), the trials variable is brought to zero and increased until. In each cycle, the pulse train is delivered by the PB0 pin and 4 seconds are waited. In addition, the same INT0 pin is reconfigured as a digital input pin and the level of this pin is monitored during the 4-second standby. When you go to LOW, it is understood that the patient is aborting the protocol. Consequently, the protocol is cancelled and the microphone is sent to sleep mode. Figure 9 shows the protocol itself.

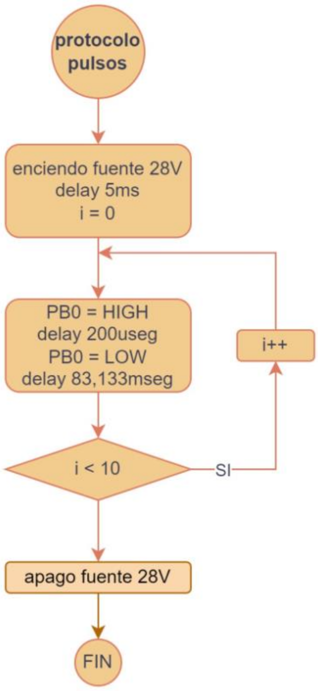

Fig. 9. 10-Pulse Train Algorithm

It first turns on the 28V high voltage source, then waits 5 msec for this voltage to set and sends 10 pulses of 200useg, separated by 83,133msec. This gives a total of 83.333msec which corresponds to 12Hz of stimulation frequency. Finally, 5 msec is expected to turn off the 28V source.

Figure 10 shows the initialization of the program and the algorithm used to put the mic to sleep and leave the INT0 hardware interrupt active. The latter was taken from internet forums and has a sequence of instructions that must be respected in the same order for a correct sleep mode of the microphone.

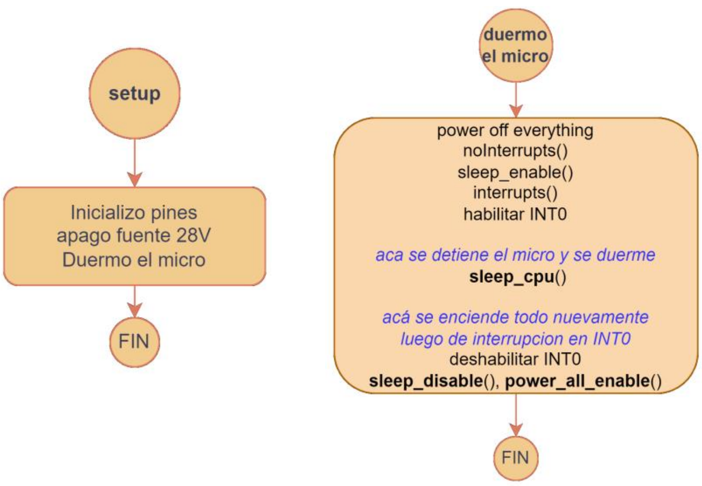

Fig. 10. Initialization of the program and algorithm to put the mic to sleep and leave INT0 and WDT active.

It can be seen in Figure 10, left. That the INT0 is initialized once. It is a set of the following instructions

```
GIFR &= ~bit(INTF0); // clear any outstanding interrupts
GIMSK |= bit(INT0); // enable pin change interrupts
```

Finally, INT0 is disabled by the following set of instructions, and in turn the same pin is enabled as digital input for the "abort" routine.

```
GIFR &= ~bit(INTF0); // clear any outstanding interrupts
GIMSK &= ~bit(INT0); // unable pin change interrupts
pinMode(PININT0, INPUT););); // I set the PIN as Digital Input
digitalWrite(PININT0, HIGH); // internal pull-up
```

The full program, with a few more instructions, is attached to this file.