Congresso de Métodos Numéricos em Engenharia 2015
Lisboa, 29 de Junho a 2 de Julho, 2015

THE CORRECTION OF THE VESTIBULAR SYSTEM INERTIAL BIOSENSORS

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Palabras clave: Mathematical Model, Correction Signals, Inertial Biosensors, Stochastic Resonance, Galvanic Vestibular Stimulation, Vestibulo-Ocular Reflex.

Resumen *We present a mathematical model that can be used to correct the output signals from the vestibular system, this is a modified model of Hodgkin-Huxley type with functional parameters experimentally determined in vestibular neurons isolated. From a mathematical and computational analysis of this model when we add white Gaussian noise and galvanic stimulation we are found that it is possible to use galvanic vestibular low current to correct the signals of the natural vestibular system. With these results we designed an algorithm that can be used in training pilots to simulate the vestibulo-ocular reflex during a passive rotation of the head.*

1. INTRODUCTION

Is under investigation how the vestibular apparatus and oculomotor system sense the movement when are subjected in extreme situations because they are essential for personal navigation. Sensors of the vestibular apparatus including the semicircular canals and otolith organs are inertial biosensors. With extreme conditions of movement (microgravity, overload), when there are disorders of the vestibular apparatus, or due to aging, the functioning of these sensors is limited. This creates the need for its correction. For this purpose various prototypes of vestibular prostheses have been proposed [1, 2, 3], but in the clinical practice they have not yet been implemented. One condition for the successful development of a vestibular function corrector is to design a software and device to detect and analyze human movement and generate the necessary corrective signals. In this work, the mathematical model of primary neuron activity, which is an output signal of vestibular inertial biosensors, is presented. A brief description of the model dynamics is presented in this work. The model can process corrective signal of the vestibular output in varied conditions. It has been found that in microgravity there is a gaze stabilization lag, which can lead to disastrous results for manual control of a spacecraft, or for working in open space [4]. In these circumstances the need for correction of vestibular function of vestibule-ocular reflex is needed. Improving the professionalism of the pilots can be achieved with the help of simulators. We also propose the use of an algorithm developed for flight simulation that can be used in training. For these purposes, the use of surface electrodes to apply vestibular galvanic stimulation is proposed [5]. This raises a question about the adequate parameters for the galvanic stimulation to be used to avoid unwanted side effects. We found that a weaker galvanic current can be applied using stochastic resonance.

2. MATHEMATICAL HODGKIN-HUXLEY MODIFIED MODEL OF VESTIBULAR AFFERENT NEURON

We present a mathematical model to generation of action potentials of vestibular afferent neuron. We shall consider a description of action-potential- generation stochastic process, where the latter represents self induced relaxation oscillations with constant amplitude and time variant frequency (propagation of these auto oscillations in the form of auto-waves is not being considered here).

The mathematical model is based on the Hodgkin-Huxley equations [6], and was developed to simulate the action potential discharge dynamics of the vestibular afferent neurons of the rat [7, 8]. In contrast with other models [9, 10], our model is based in experimentally defined physiological parameters obtained from mammalian vestibule; and it includes a new coordinate related to the inactivation parameter of the potassium current, whose dynamics is described by the Kolmogorov equation for the Markov processes with a discrete number of states.

The novelties of the modified system that we are proposing are the following:

In the description of the potassium current (I_k), we introduced an inactivation parameter h_k of the I_k and as a consequence we use one more equation of Kolmogorov for the description on the average dynamics of this parameter [8]. The reduction of an order of the mathematical model in the presence of a small parameter τ_m at a derivative of the subsystem describing the average dynamics of the activation parameter m of I_k has been justified. The integral $n+h=c=$ *constant*, where n is the activation parameter of the I_k and h is the inactivation parameter of the sodium current (I_{Na}), were used as a simplification of the Hodgkin-Huxley equations in various models. In our work it is modified according to experimental data as $n+h=C(V)$ where V is the membrane voltage. Thus, the modified Hodgkin-Huxley model is introduced in Couchy’s third order form with small parameter on the right side of the equation, with the perturbation describing the probabilistic parameter dynamics h_k [8]. In this work we do not consider the time dependence of this parameter. Here the modified Hodgkin-Huxley model is introduced as a second order system:

$$C_m \frac{dV}{dt} = I_{com} - I_{Na} - I_K - I_L \tag{1}$$

$$^{2}{}_{n}(V) \frac{dn}{dt} = (n_\infty(V) - n)Q \tag{2}$$

With

$$I_{Na} = g_{Na} m_{\infty}^{3}(V)(C(V) - n)(V - V_{Na}),\ I_K = g_K n^4 h_K (V - V_K),\ I_L = g_L (V - V_L),$$

$$C(V) = n_{\infty}(V) + h_{Na\infty}(V),\ \mathrm{m}_{\infty} = \frac{1}{1 + \mathrm{e}^{-\frac{(V+33.8)}{5.2}}},\ \mathrm{h}_{\mathrm{Na}} = \frac{1}{1 + \mathrm{e}^{\frac{(V+60.5)}{9.9}}},\ \mathrm{n}_{\infty} = \frac{1}{1 + \mathrm{e}^{-\frac{(V+35)}{5}}},$$

$$\tau_{\mathrm{n}} = \frac{68}{\mathrm{e}^{-\frac{(25+V)}{15}} + \mathrm{e}^{\frac{(V+30)}{20}}}.$$

Where

- $I_{com} = I_{com}(I_{syn}, I_{cor})$ is the input current, I_{syn} - synaptic current, I_{cor} - output signal of corrector (galvanic current).
- V – variable “membrane potential” of afferent neuron.
- n – variable, which describes the process of potassium current activation. This parameter is a probability of the presence of potassium current activation particle in the potassium channels,
- h_k - a parameter, which describes the process of potassium current inactivation. This parameter represents the probability of absence of potassium current inactivation particles.
- h_{Na} – a parameter, which describes the process of sodium current inactivation,
- τ_n – time constant of potassium current activation process,
- n_∞, m_∞ - stationary values of potassium and sodium current activation processes,
- $h_{Na\infty}$, h_K- stationary values of potassium an sodium current inactivation processes,
- *Q –parameter “temperature factor”.*

  Numerical parameters are shown in table 1.

Numerical Parameters	Value	Units	Numerical Parameters	Value	Units
C_m	1	µF/cm^2	Q	6.47	
V_{Na}	52	mV	I_{syn*}	1.1477	µA/cm^2
V_K	-84	mV	g_{Na}	2.3	mS/cm^2
V_L	-63	mV	g_K	2.4	mS/cm^2
h_K	0.73		g_L	0.03	mS/cm^2

Table 1. Model parameters.

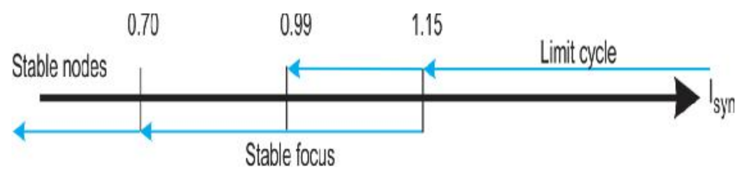


Figure 1. Localization critical points to model (1-2) in the interval [0.1, 70] (μA/cm^2).

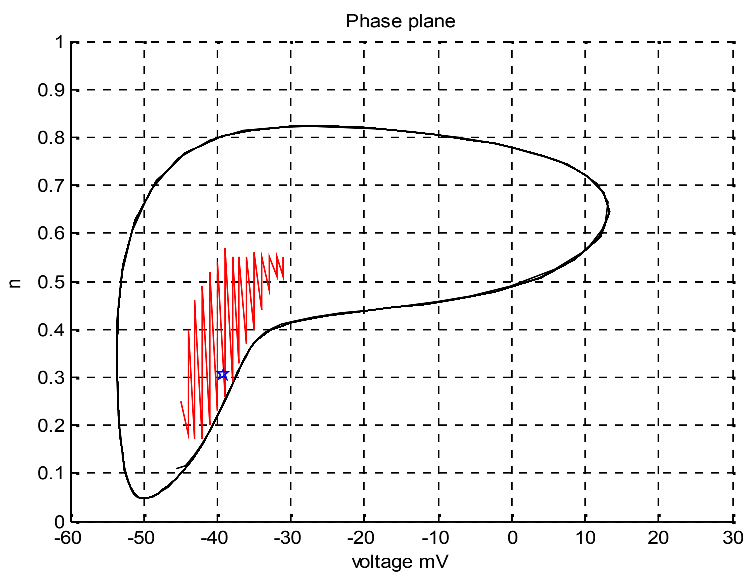


Figure 2. Limit cycle. Phase space diagram of the model (1-2) with a bifurcation point I_{syn*} = 1.1477 (μA/cm^2). The star is a critical point, an unstable focus with coordinates (-38.1131mV, 0.3052) and her attraction region in red. A path is shown with I_{com} =1 (μA/cm^2).

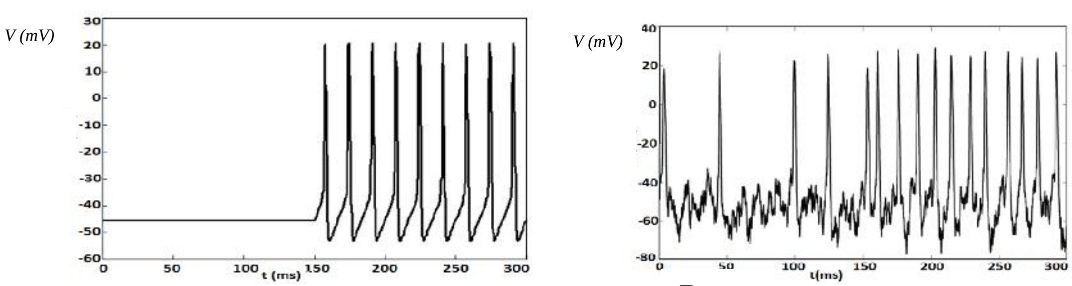
Computer analysis of average stochastic activity in primary afferent neuron (1-2), which form the output of vestibular apparatus lead to the following results:

With the constant synaptic current I_{com} = I_{syn}, that has a value in the interval [0.1, 70] (μA/cm^2) there is only a point Hopf bifurcation I_{syn*} = 1.1477 μA/cm^2 which is the "center". To the left of this point there is a single critical point that is an asymptotically stable focus. To the right, there is a single critical point that is an unstable focus (Figure 1). For some values of I_{syn} in the left side of I_{syn*} (Figure 1) there is a stable focus and for I_{syn} in the right side of I_{syn*} (unstable focus) there is a limit cycle. Thus, the bifurcation point is the threshold sensitivity to inertial vestibular biosensors. If synaptic current is less than 1.1447 μA/cm^2, for initial conditions in attraction region of a stable focus there are not action potentials generation, but

for initial conditions in attraction region of the limit cycle there are action potentials generation, if the synaptic current is more than I_{syn*} a burst of action potentials is generated (Figure 2). The presence of an unstable focus is accompanied by the existence of an attractor that is an asymptotically orbital stable limit cycle. Frequency of action potential discharge, corresponding to the limit cycle is proportional to synaptic current value; action potentials amplitude is constant (Figure 2). Thus, bifurcation point is a sensitivity threshold of inertial vestibular biosensors. If synaptic current is less than 1.1447 μA/cm^2, there may be only a single action potential. If the synaptic current is more than I_{syn*}, a burst action potentials is generated (Figure 2).
For our modified simplified model of the second order were found: The Andronov-Hopf bifurcation point; two attractors: asymptotic stable focus and orbital asymptotic stable limit cycle; bifurcation interval when there are two attractor with correspondent areas of attraction. In this way, our Hodgkin-Huxley modified mathematical model with synaptic input current belonging to the bifurcation interval is a bistable (on the classification of Pontryagin-Andronov) dynamical system.

3. STOCHASTIC ANALYSIS OF DE HODGKIN-HUXLEY MODIFIED MODEL

Article [9] provides a review of works about presence of a stochastic component in deterministic models of the Hodgkin-Huxley type. Of three options, the presence of stochastic components has been chosen the most simple variant of the three listed options of the presence of the stochastic components where the synaptic current propagation has been chosen as a sum of two terms (Equation 3), the no stationary-average $I_{syn}(t)$ that presents in traditional Hodgkin-Huxley type models and Gaussian white noise G(t).
Experiments have shown [13, 14] that when white noise of a certain intensity was added to the program signal. $I_{com}=I_{syn}+I_{cor}=I_{syn}+\varepsilon(\mathrm{P}(t)+rG(t))$ where $rG(t)$ is Gaussian white noise with intensity "*r*" it is possible to get stochastic resonance. This makes the galvanic stimulation more effective and allows the use of a weaker current. As a criterion, consider the finding of a maximum of the average number of action potentials ($\overline{NSP}$) on a given interval with variable intensity of Gaussian white noise "r". NSP - number of spikes (Figure 3B). For modeling let us assume $I_{syn}=\varepsilon(I_{syn}(t)+rG(t))$. To model the stochastic component $rG(t)$, based on [13], we



A. B.

Figure 3. A. The model output without noise. B. The model output with noise.

apply the Ornstein-Ulenbeck process $U(t)$ with the correlational function $R_u(s)=(1/2c)Exp(-|s|/c)$, dispersion $1/2c$ and one sided spectral density $\Psi_u^{o.s.}(\omega)=2/(1+c^2\omega^2)$(which is connected with the spectral density as $\Psi_u^{o.s.}(\omega)= \Psi_{u^{\cdot}}(\omega)+ \Psi_{u^{\cdot}}(-\omega)$. Then the process $G(t)= (2c)^{1/2}U(t)$ is characterized by one side spectral density $\Psi_G^{o.s.}(\omega)=4c/(1+c^2\omega^2)$.
Results correspond with the value $c=0.01$, at which we can examine $rG(t)$ as a process with spectral density close to constant value $\gamma^2=2cr^2$ (where γ is the intensity of the white noise $\gamma G_0(t)$). We shall note that the dimension of coefficient r equals μA/cm^2, whereas that of $G(t)$ process is dimensionless.
For $G(t)$ we can apply an approximation with Katz-Shinozaki series $G_N(t)=(2/N)^{1/2}\Sigma^N_{i=1}Cos(\omega_i t+\varphi_{oi})$, where phases are uniformly distributed in the interval $[0,2\pi]$, and frequency distribution is characterized by the following density of probability $f_\omega(\omega)=(1/2\pi)\Psi_G^{o.s.}(\omega)=(1/\pi)(2c/(1+c^2\omega^2))$ (figure 3). Calculations were done under Matlab environment with N=100.The second order equation system was integrated applying Matlab function ode23 at constant value $\varepsilon P(t)$=0.98 μA/cm^2 t ϵ $[t_1, t_2]$=[1.5; 3] (seconds) and different realizations $rG(t)$, which correspond to different values r and at the same starting condition (V, n)=(-39 (mV); 0,3).
Figure 4 shows the dependence of this statistical evaluation at different intensity values of "r". The presence of a maximum allows to ascertain that it is possible to select an optimal intensity of white noise in the second block of the corrector (Figure 5). In each of the five evaluations with length 1000 ms for ten intensity values r, the number of action potentials has been calculated (thus, at every value r we have a selection with scope 10 for random variable NSP). In Figure 4 shows the dependence of mean $\overline{NSP}$ from intensity $\gamma^2=2cr^2$.
Thus, when t ϵ $[t_1; t_2]$, $\varepsilon P(t)$ are fixed we have a maximum of the average number $\overline{NSP}$. Applying Shapiro consent criterion, it can be shown that the necessary condition of the hypothesis of normality of the NSP probability distribution are fulfilled. Confidence intervals of statistical evaluation to $\overline{NSP}$, corresponding to the normal distribution were shown in [15]. Therefore, it can be assumed that the stochastic component:

$$P(t) = 1+Sign(Sin(\omega_o t)) \quad (3)$$

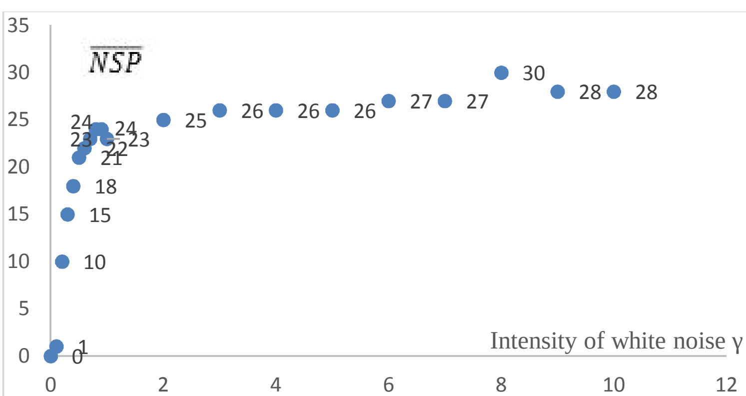


Figure 4. Average number (0 to 30) of action potentials $\overline{NSP}$ (with I_{com} = 0.98 μA/cm^{2}and n=10 realizations.

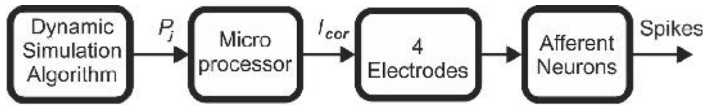


Figure. 5. Block diagram for vestibular inertial biosensors corrector.

Then the Equation 1 can be written in next form:

$$C_m \frac{dV}{dt} = [I_{syn*} + \gamma G(t)] + \gamma_1 P(t) - I_{Na} - I_K - I_L \qquad (1')$$

G - Gaussian white noise.
γ- Optimal intensity of Gaussian white noise for stochastic resonance.
γ_1- Galvanic current intensity.

4. AUTOMATIC CORRECTION WITH GALVANIC STIMULATION

Let us consider experiments in movement simulation [11, 12]. Due to geometric constraints on the kinematics of the dynamic simulator platform, galvanic stimulation of the vestibular apparatus is used in order to simulate the effects of inertial forces encountered in flight and to act on the gravito-inertial mechanoreceptors and other inertial biosensors. Absence or presence of inertial forces can be described by the piecewise continuous function *P(t)* that corresponds to the small galvanic current $I_{cor}=P(t)$ *(Fig. 5).* $P_0\equiv 0$ on [t_0, t_1] and $P_1\equiv$ *constant* is not zero on the [t_1, t_2]. Here *P(t)* is the program signal generated in accordance with the dynamics of controlled flight. Let us suppose that the synaptic current I_{syn} is less than I_{syn*} because the simulator platform is motionless. Then the presence of $I_{com}=I_{syn}$ on the interval [t_0, t_1], that corresponds to the absence of inertial forces, does not lead to the relaxation auto oscillation (Figure 3A, $t_0 \le t \le t_1$). If there is an inertial force presence, the program signal *P(t)* is not zero on the interval [t_1, t_2] and produce a burst of action potentials with high frequency. Here the model (1'-2) is introduced as second order system with small galvanic current P(t) (Equation 3).

Recently, the number of publications based on results of experimental researches of the galvanic vestibular stimulation efficiency is increasing rapidly [14]. The most secure placement of electrodes have been suggested on the mastoideus (Figure 6). Within the framework of the discussion among physiologists about galvanic stimulation effects on different parts of vestibular mechanoreceptor, let us consider the simplest variant of influence to galvanic current on the primary vestibular neuron.

Let us consider the stimulation scheme of vestibular-ocular reflex for passive rotation of the head to the left (Figure 7). Suppose that it started turning. In order to reproduce the desired response of lateral semicircular canals that corresponds to real reaction, you should increase the frequency of impulses (spikes) from the left canal primary neuron and, if possible reduce the frequency of impulses from the right canal primary neuron.

Thus, if at the beginning of the motility the synaptic current value is located at the bifurcation interval and initial conditions of the model in the presence of galvanic correction belong to the attraction domain of stable focus, then for the search of algorithm parameters, you can use the

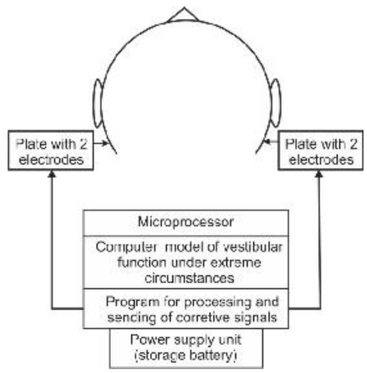


Figure 6. Scheme of automatic vestibular corrector.

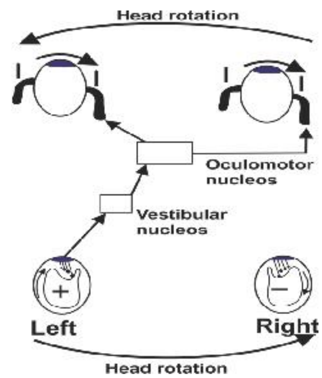
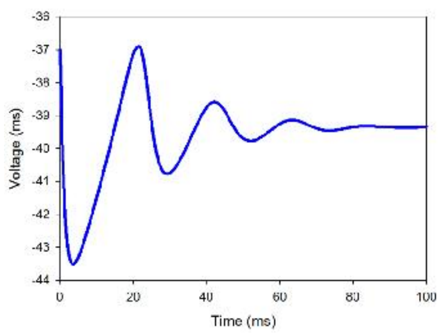
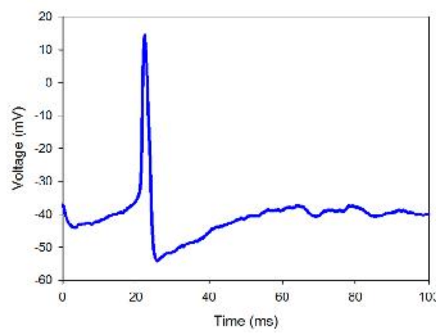


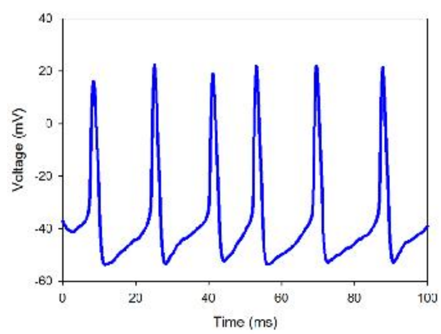
Figure 7. Scheme of vestibular-ocular reflex when the head have a passive rotation to the left.



A.



B.



C.

Figure 8. Realizations of model (1'- 3). A. For $\gamma = \gamma_1 = 0$. B. When $\gamma = 0.2$, $\gamma_1 = 0$. C. For $\gamma = 0.2$, $\gamma_1 = 1$. Here $I_{st} = 1$ µA/cm^2 with initial conditions $(V_0, n_0) = (-37, 0.5)$ and an unstable critical point $(V_c, n_c) = (-39.1131mV, 0.3052)$.

bilinear equations in deviations from a point attractor. Then we have a constant action galvanic signal *P(t)*, which is the galvanic current that presents in bilinear model as an additive correction and parametric correction that modifies the conductivity of sodium and potassium current.

Coefficients by *P(t)* are adjusted experimentally, the function *P(t)* can choose as picewise constant function with double-frequency compared to its own frequency in the absence of additive component. Following the work on stochastic models of Hodgkin-Huxley type the Gaussian white noise to the permanent synaptic current can be added. Figure 8 show the effectiveness of the proposed galvanic correction algorithm compared with the situation when this correction is not available.

When galvanic correction is not available, spikes are absent (Figure 8A), which leads to the vestibulo-ocular conflict (VOR imitation is missing). Given the presence of white noise, then there are spikes bursting (16 spikes per second, Figure 8B). At galvanic correction spikes number increases up to 26 per second (Figure (8C).

5. CONCLUSIONS

- A simplified mathematical model of the primary neuron activity of vestibular apparatus has been developed. The model describes in average the signal formation that is a stochastic Markov process. It gives the output information from gravito-inercial mechanoreceptors of the otolith and inertial biosensors of semicircular canals as a variable frequency of spikes. This model can be used to process correction signals of the vestibular apparatus output.
- The mathematical model and computer simulation show that applying Gaussian white noise of optimal intensity in addition to the program signal increases the number of action potentials at a fixed time interval due to the presence of stochastic resonance. Thus, a weaker galvanic stimulation can be used.
- Our results open the possibility of generating a pattern of the corrective output signal (I_{cor}) as in (3), and using it in the simulator to train pilots. The software component of a corrective signal is formed by an algorithm of the dynamic simulation of controlled flight in real time. It is accompanied by Gaussian white noise of optimal intensity and vestibular galvanic current, which are from a table determined by the function of two parameters (γ and γ_1). The table is created prior to training with the use of models (1’), (2) and (3).
- To analyze the possibility of correction of the vestibular output signal it has been developed a functional scheme, whose output is used as an input to model system to generate the correction signals.

6. ACKNOWLEDGEMENTS

This work is partially supported by VIEP 2015 Projects.

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