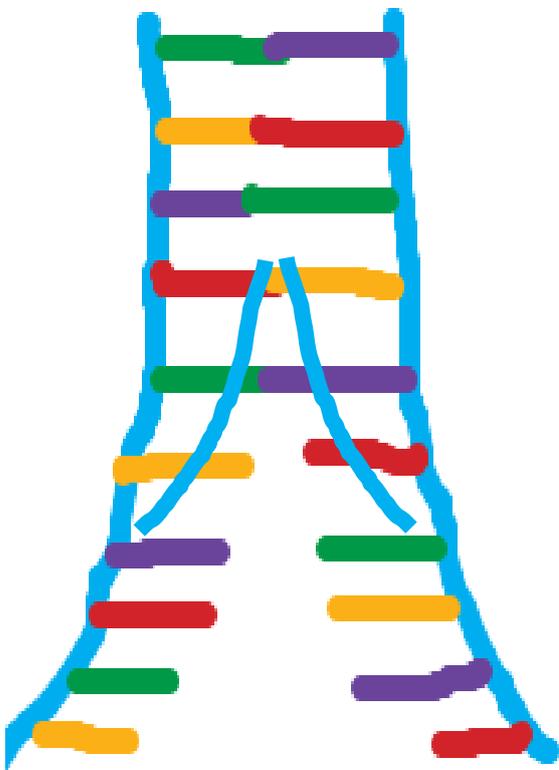


Splitting may give high amplitude brief MUP spikes

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High amplitude brief components in a MUP in myopathy

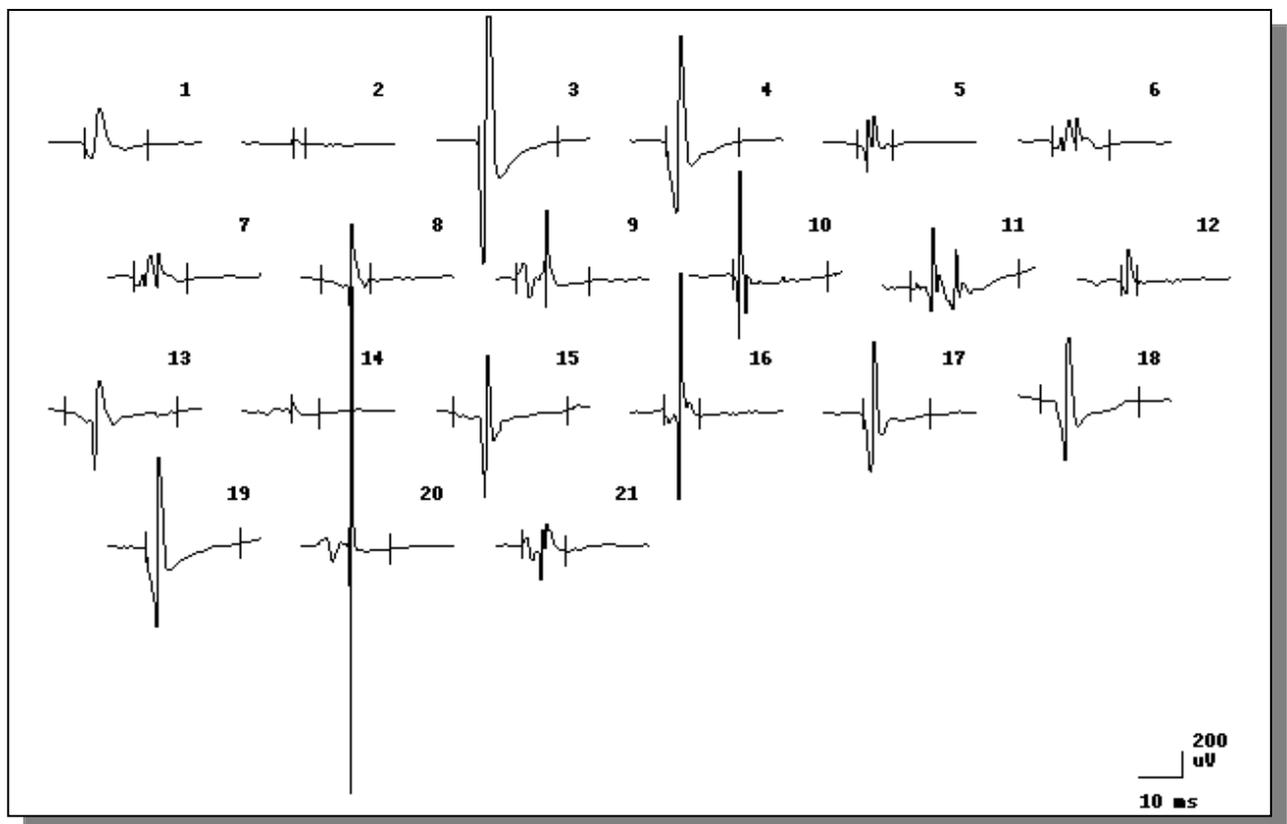
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1. Background

Occasionally the MUPs in a myopathic muscle show brief components of **high amplitude**. Their amplitude has sometimes been misinterpreted as a sign of neuropathy.

I have put forward the idea⁵ that these signals are generated by **hypertrophic muscle fibers** not uncommonly seen in myopathy. This idea has then been accepted and appears in many publications by others.

Note a few (rec 10,16,20) high amplitude brief spikes in a patient with myopathy



Some characteristic do not always fit to that hypothesis and additional explanations may be possible, as discussed here. The signals may come from the area of longitudinal **splitting of a muscle fiber**, another common sign of pathology⁷.

Just after the branching, TWO or MANY time locked signals may give rise to these signals. Note, that if the signal is generated as a sum of many sfaps, their amplitude does not represent large fast conduction muscle fibers, thus an exception that amplitude and velocity have a strong correlation

2. Why do we need additional explanations compared to the existing?

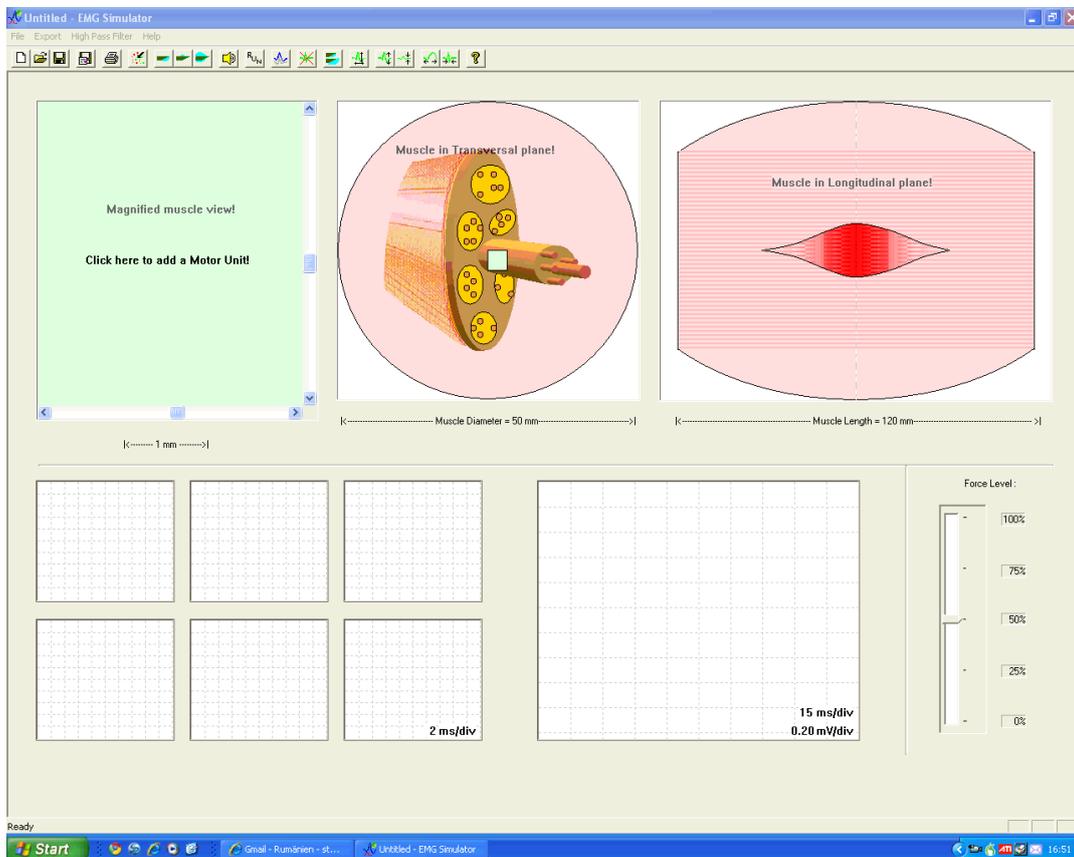
Intuitively, signals from generally large muscle fibers should occur early in the MUP. This can be confirmed in simulation studies and thereafter will be tested in analysis of such signals in myopathy.

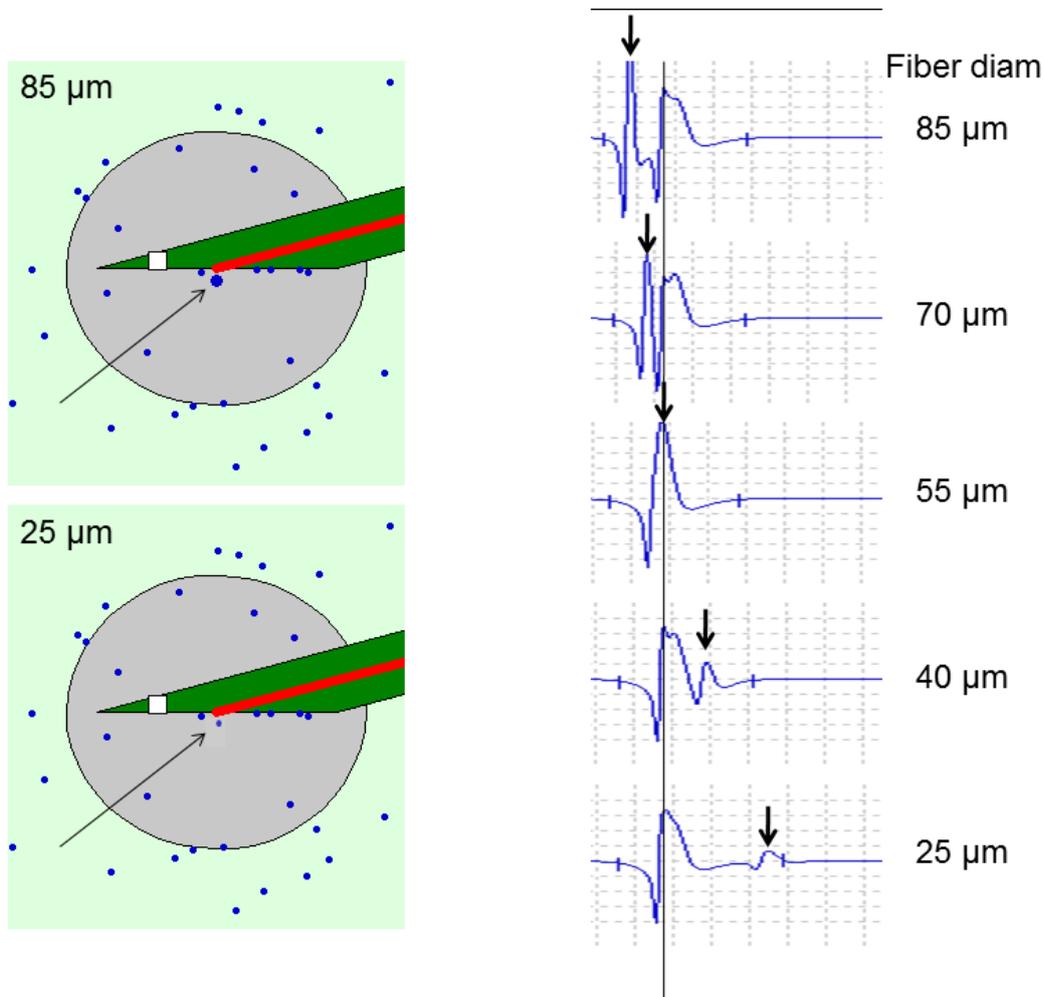
2.1. Effect of spike position in a MUP in relation to fiber size, simulation studies

Propagation velocity along a muscle fiber is closely positively related to fiber diameter. Large fibers conduct faster. In this first simulation, the fiber size is varied from 85 μm to 25 μm . (normal fiber diameter about 50 μm). If a fiber diameter exceeds 90 μm , there is a clear tendency to longitudinal splitting (Swash⁷).

As seen from the simulations, the spike part, indicated with an arrow, changes position depending on fiber diameter as well as the amplitude (measured from the center of the fiber). Large fibers give early spike component of high amplitude, and vice versa.

By means of simulation (Stålberg, Karlsson, 2003²) the relationship between signal generator (the muscle fiber) and the recorded signal can be studied.



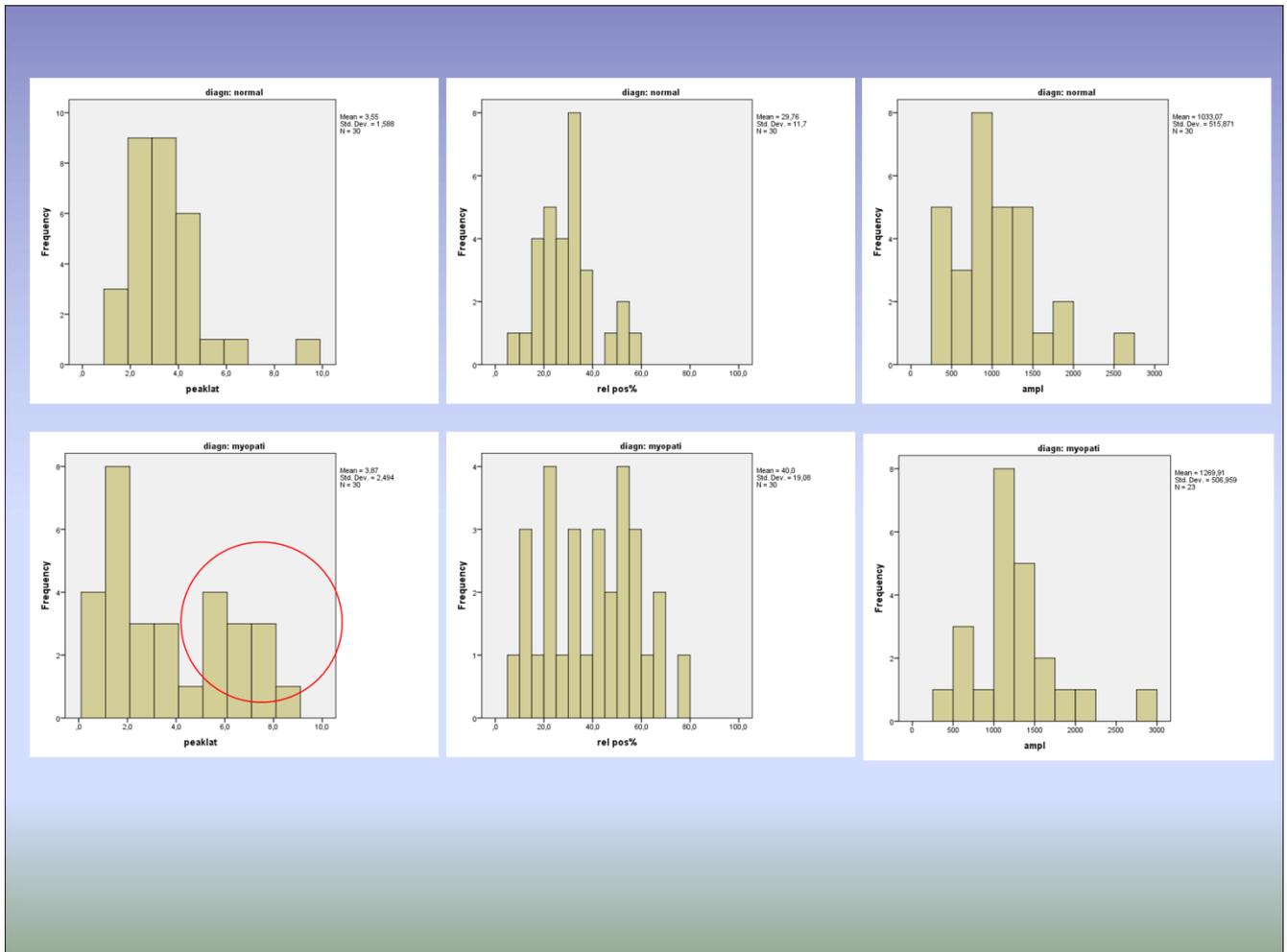


As seen, it is quite clear that large fibers give rise to higher amplitude signals (depending on distance), but most important, occur early in the MUP.

Is this generally seen in MUP recordings in myopathy?

2.2. Measurements on actual recordings

Thirty MUPs from patients representing different types of myopathy, mainly myositis were analyzed. Recordings were usually from tib ant muscle but some were from biceps brachii or vastus lateralis. The control material was taken from tibialis anterior recordings. Spikes that were visually scored as being of high amplitude (more than double amplitude compared to the spikes in that MUPS) and short duration, were analyzed regarding time position with the MUP total duration. **In this small material, the time position in the MUP was similar to that what is found in normal muscle.** There were some spikes in myopathy, that seemed to have somewhat longer latency and also some appearing at the very beginning of the MUP. Plots showing the relative position in the MUP (middle column) may not be very useful information, since MUPS in myopathy are usually shorter than in normal muscle.



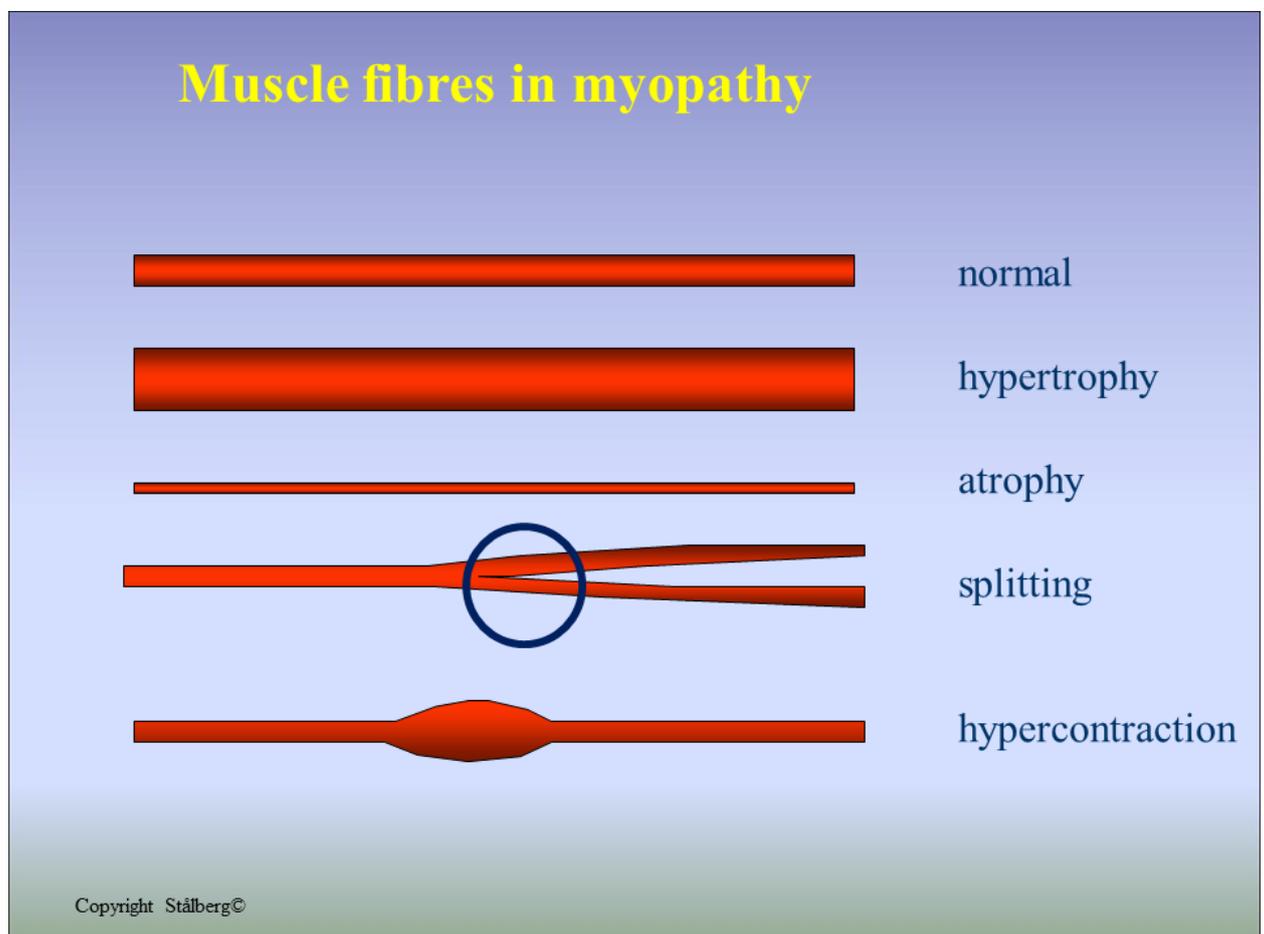
High amplitude short spikes in myopathy compared t the max peak of a MUP in normal. In myopathy, the spike may occur very early, but occasionally also in the middle of the MUP (rel lat). No statistical conclusion can be drawn from this small material of 30 MUPs representing recordings from about 90 patients. The 30 MUP in normal is obtained form 6 subjects. (Copyright Stålberg, unpublished)

2.3. Possible explanation to the spikes

It is not striking finding that all high amplitude short spikes in myopathy appear very early in the MUPS, on the contrary, there are also some that are seen late in the MUP, perhaps more than in normal muscle. Thus additional explanations that high short spikes generally represent large fibers may be looked for such as;

- One possibility is that the muscle fiber is locally hypertrophic. This has been called hypercontraction, and is by many pathologists considered as an artifact. This should not necessarily give early components since delay depends on the conduction all the way from the end-plate.
- Splitting of muscle fibers is a common histological finding in muscular dystrophies (but is exceptionally also seen in normal). Obviously, fiber splitting is not easy to quantitate histologically, since this would require a large number of serial sections. In SFEMG, the multiple APs derived from split fibers¹ have a mutual jitter less than 5 μ s, and in one of the studies as many as 27% of recordings in dystrophic muscles had jitter within this range (Hilton-Brown, Stålberg 1983).

When a splitting occurs, two single fiber action potentials should be generated a few hundred μ m from the splitting site without jitter between the components. Depending on the relation in fiber size in the split muscle fibers, their signals may be more or less synchronized. Usually they are separated in time (see fig).



Schematic presentation of suggested changes in myopathic muscle fibers.

In case the velocity is different between the branches one of the signals will be lagging behind (depending on distance from the split) and be seen either as a non-jittering irregularity of the signal

(see fig) or as time separate spikes of normal amplitude but not jitter or as separate spikes. With perfect synchronization, the amplitude should interact additively giving rise to a large signal.

More detailed analyses of the single fiber action potentials shape in myopathy, may prove or disprove the proposed hypothesis.

One complicating factor that makes it difficult to test the hypothesis of splitting as a cause for high amplitudes based in latency, is that splitting, also in pathology, occurs preferentially in large fibers. Thus the signals are early in the MUP, whether general hypertrophy or splitting of large fibers. If spitting could occur in small fibers, they may have high ampl signals and appear late in the MUP. This important question needs an answer.

Some of these ideas have been tested and are described below

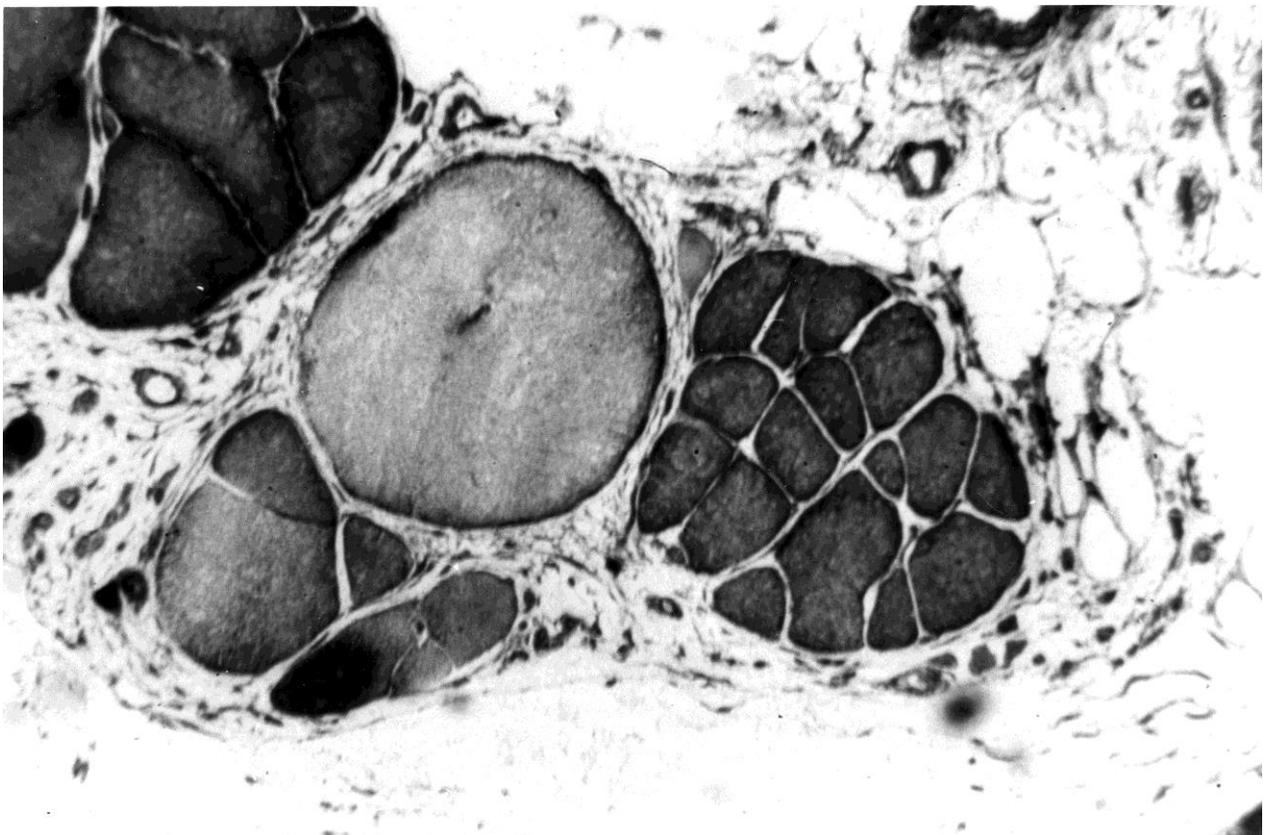
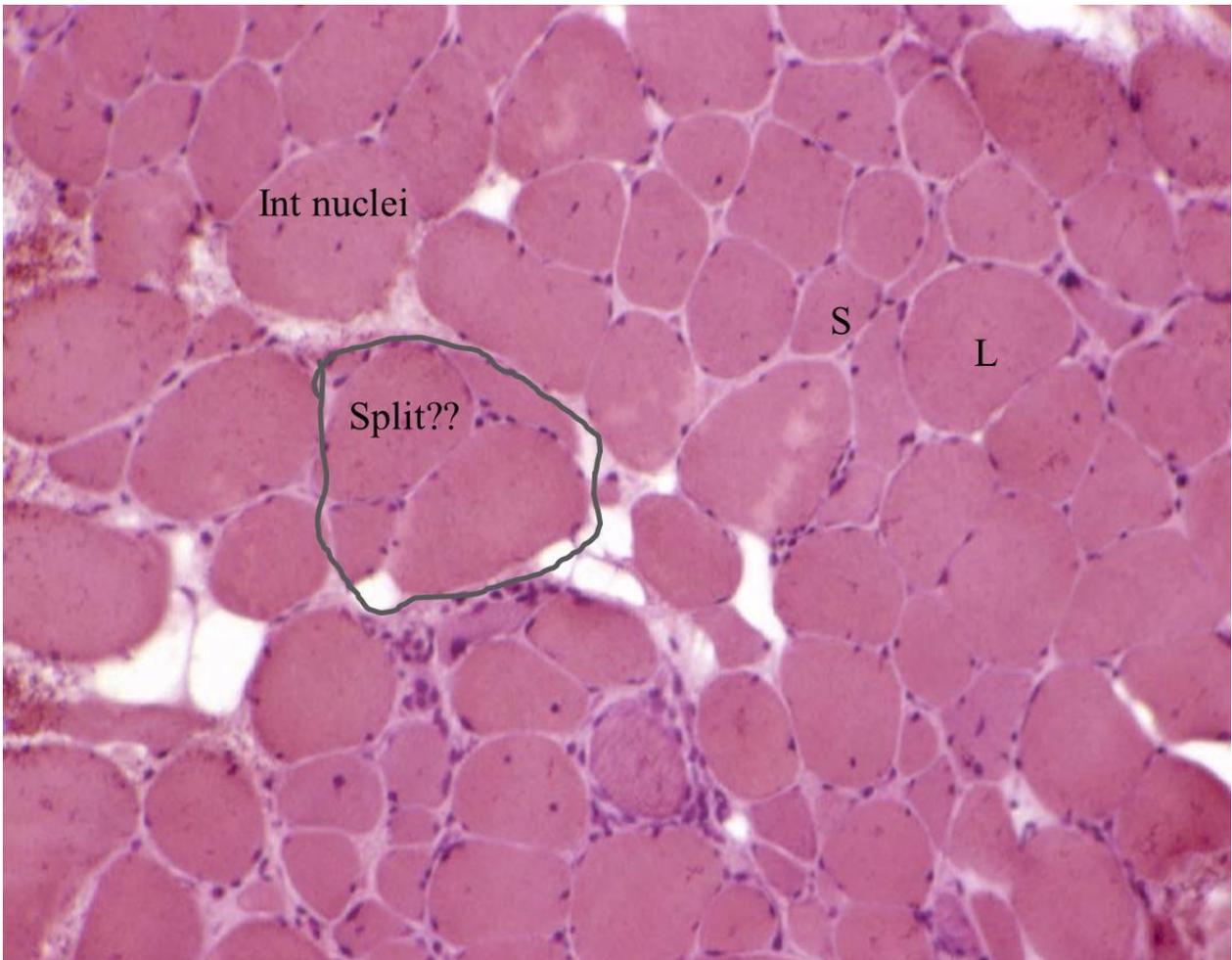
What about splitting in myopathies?

3. Muscle biopsy

(in a patient with Emery-Dreifuss muscular dystrophy, X-linked type 1; (EDMD; emerinopathy).

The pathologist (Kalimo) noted ;Mild to moderate dystrophic changes: Fiber size variation, a few necrotic fibers, central nuclei, increase of fibrous con-nective tissue and fat between myofibers.

Note fiber size variation (L= large, S= small), internal nuclei, often the site close to longitudinal splitting may be seen (Swash^{6,7}), and a possible grouping of muscle fibers as effect of splitting (other examples are seen in this picture. In normal muscle, hypotrophic muscle fibers (training) will show splitting close to a site with central nuclei. Central nuclei are also typical in myopathy, but not only in large fibers (see fig).) Whether they announce splitting after a short distance is not known.



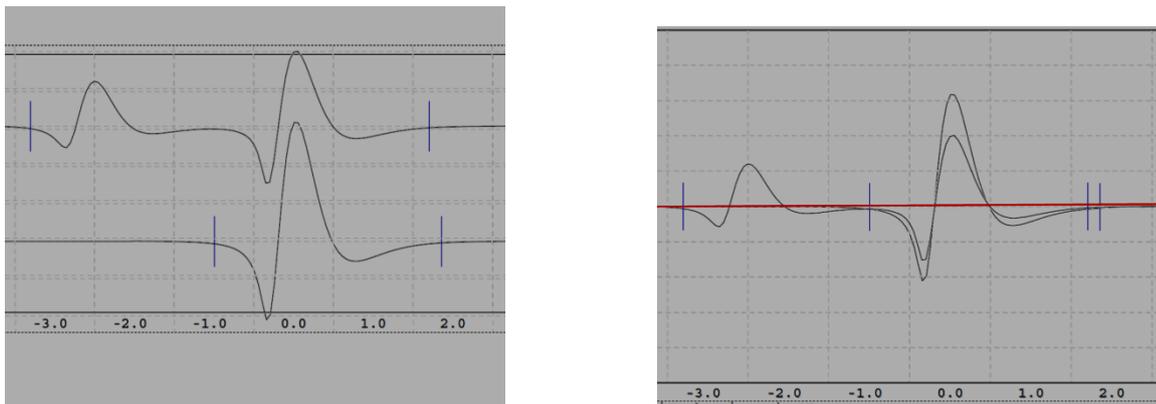
Excessive splitting of a muscle fiber (Stålberg 1976)

4. So, what happens if a recording is made from a split muscle fiber?

That depends on their temporal relationship. The main characteristic is that there is no jitter between the spikes. If they appear with nearly no time difference, they will summate to a spike with constant shape on consecutive discharges (see below). If they are separated, a double spike without jitter will be seen in SFEMG, a confirmed finding.

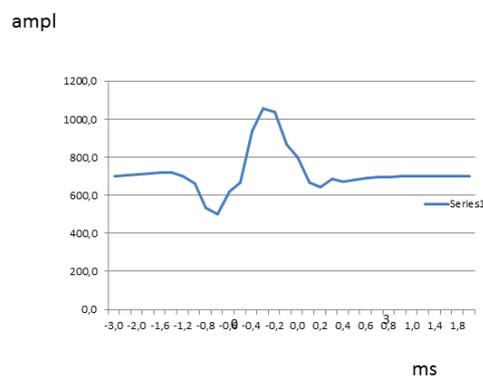
4.1. Simulation of spike summation

Two spike components are moved in relation to each other. The first smaller spike is moved from -3 to 3 ms in relation to the triggering larger spike. The result is seen in the following 3 figs. As seen the summation will decrease of the largest spike, or at absolute time coincidences increase to the algebraic sum of the signals.



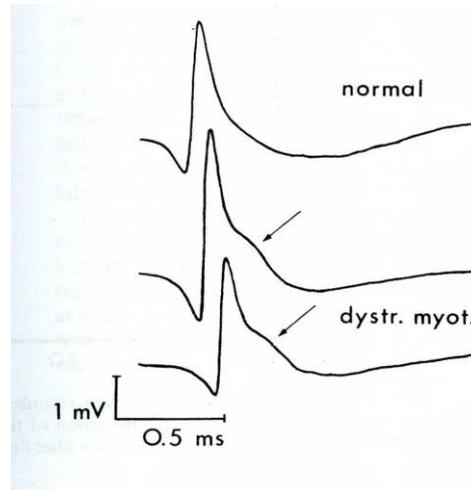
Simulation study. Two spikes of different amplitudes (356 and 704 μV) are moved over each other. Their sum occurring at time difference of 0 μs , gives a perfect spike with an amplitude of 1056 μV . These are two examples, and the entire simulation is summarized in next fig.

Sum of 2 sfaps, 356 and 704 μV resp. Summation will give both reduced and increased p-p ampl.



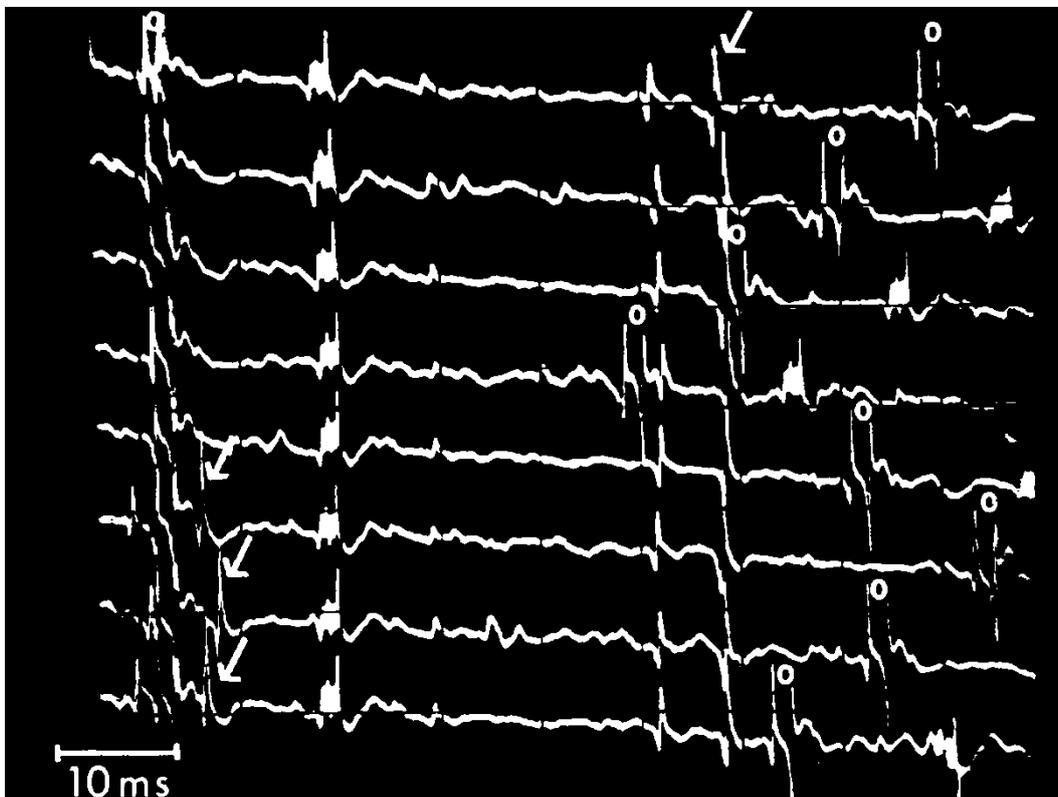
4.2. Close spikes in splitting

Fiber pairs with a jitter less than 5 usec is supposed to be generated from split muscle fibers (Ekstedt, Stålberg¹) as exemplified in fig above. Occasionally the time between the spikes is so short that their sum only gives a shape change of the recorded signal. This is noticed in some patients with myopathy (Fig below) (Stålberg³). The extra late component had no jitter, and change in amplitude in parallel with the main spike when the electrode was moved.



SFEMG signals from a patient with myotonic dystrophy. Note the stable late component, not seen in normal muscle.

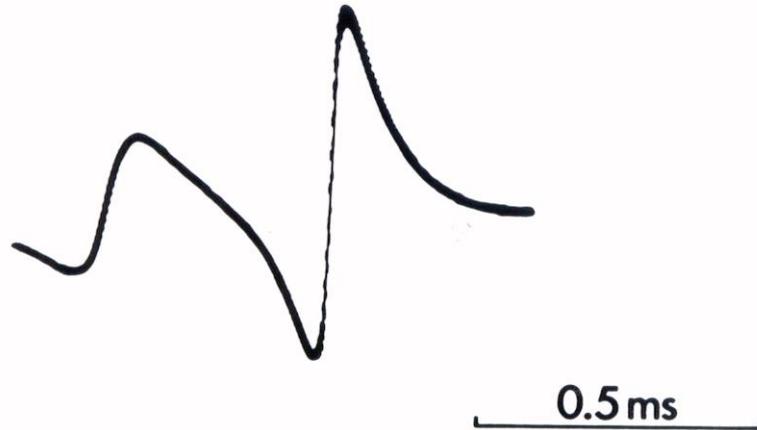
Sometimes concentric needle EMG in myopathy may show signals that should be tested for splitting (fig below)



A MUP in myopathy (Duchenne). Note that long total duration (from o to arrow). Sometimes the new discharge starts before the previous MUP has ended. In this recording the complex group of spikes

seen 20 ms from the beginning, can well be generated by one split muscle fiber with many branches. This was not tested.³

4.3. Separate spikes



Spontaneous activity in a denervated muscle, which can be interpreted as fibrillation in one muscle split muscle fiber (ephaptic transmission would be another possibility).⁴

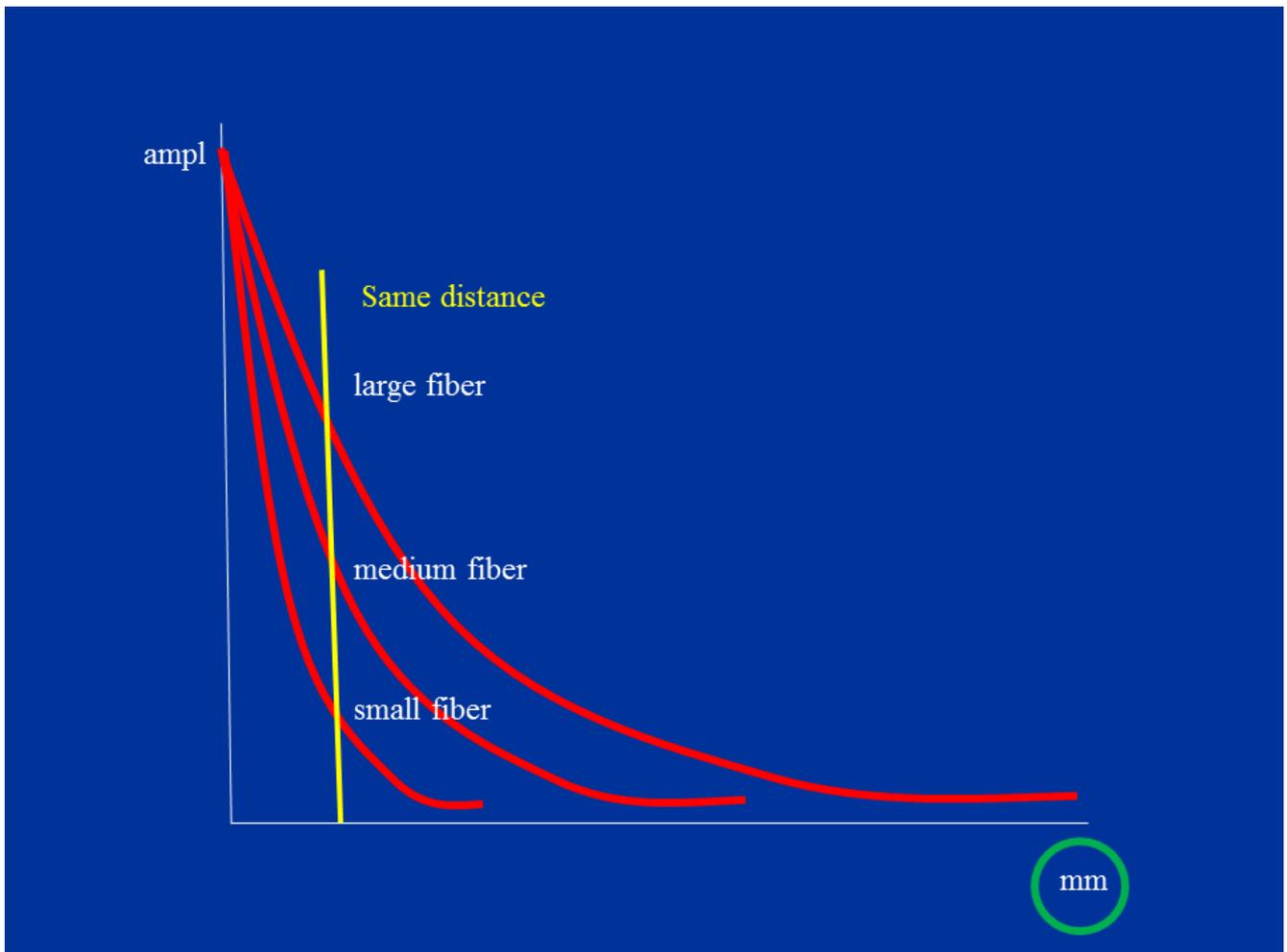
Comments separate from the high short spikes

Amplitude decay in large and small muscle fibers, simulation

Action potential amplitude decay with distance is related to muscle fiber diameter. If distance is measured in “radius” the different fibers have similar distance decay, but if the distance is measured in μm , the amplitude from small fibers decays much faster than from large fibers.(Figs)

This should lead to a bias in recorded spike amplitudes. Small fibers, e.g. branches of a split (there may be many branches form one fiber), or atrophic muscle fibers may not be detected.

In general this will also cause a bias in the EMG recording from a muscle with large fiber diameter variation and also time dispersion (polyphasic), so typical of myopathy.



Note the steeper amplitude drop with distance for small fibers when distance is measure in mm

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